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Blood Loss in Surgery of Brain Tumors in Infants

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1N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow; 2Russian Medical Academy of Postgraduate Education, Moscow, Russia

Brain tumors in infants were believed to be uncommon and made only 3% of the overall number of brain tumors diagnosed in children under 15. Since the early 1980s, literature has been demonstrating higher numbers, 8–15%, which have been corrected due to the new techniques of visualization [7, 8, 24, 25, 27, 28]. Wide application of computed tomography (CT) and magnetic resonance imaging (MRI) of the brain along with neurosonography (NSG) made it possible to diagnose brain tumors in infants during the first twelve months of life.

Early diagnosis of brain tumors in infants has stimulated the enhancement of surgical activity. However, functional immaturity of all organs and systems and high risk of complications in surgery of brain tumors in infants. One of the most serious complications is the massive blood loss and severe disorders of hemostasis. In a recent series of observations, perioperative mortality in these children varies from 13 to 33%. The purpose of this study was to determine risk groups of blood loss in surgery of brain tumors in infants on the basis of the analysis of topography, morphology and features of the operations and to suggest the best surgical strategies. When intraoperative blood loss exceeds 100% of the calculated blood volume, persistent violations of coagulation homeostasis developed, which could cause uncontrolled bleeding and death on the operating table or postoperative bleeding. Intraoperative blood loss could be reduced by improvement of surgical techniques, as well as by improving anesthesia. The first type includes preoperative embolization of the afferent vessels, careful planning of surgical approach (including using neuronavigation); deep stromal tumor coagulation during debulking, primary coagulation of the main feeding blood vessels, two-stage surgery, and optimization of the speed of tumor removal. All these methods have reduced the overall intra- and post-operative mortality rate from 13 to 5%.

**Keywords:** brain tumor in infants, surgery, massive blood loss, large choriocarcinoma in infants.

The study was retrospective-prospective in design: retrospective analysis reviewed the seven-year data, from 2000 through 2007, (n=39); prospective — three-year data, from 2008 through 2010 (n=41).

The same team of neurosurgeons and anesthesiologists performed neurosurgeries in all infants using the facilities of the Burdenko Neurosurgical Institute.

The infants were distributed into three groups according to the volume of intraoperative blood loss: less than 100% of the calculated total blood volume (CBV) – 55 (69%) of infants; 100 – 200% of CBV – 11 (14%); more than 200% of CBV – 14 (17%).

**Material and Methods**

Eighty surgeries for tumors in 1–12 months old infants were performed in the N.N. Burdenko Neurosurgical Institute during 2000–2010. Seventy eight of them were radical or partial removal of tumors; 2 surgeries were biopsies.

The study was distributed into three groups according to the volume of intraoperative blood loss: less than 100% of the calculated total blood volume (CBV) – 55 (69%) of infants; 100 – 200% of CBV – 11 (14%); more than 200% of CBV – 14 (17%).

**Diagnostics.** All patients were diagnosed using CT and/or MRI of the brain with or without contrast enhancement. Neoplasms with cross-over diameter more than 4 cm, according to the CT or MRI results, were referred as large tumors – 47 (59%). The degree of tumor vascularization was determined by the results of preoperative contrast-enhanced MRI of the brain, HCT angiography, and total cerebral angiography. The conclusive analysis of the intensity of tumor blood supply was performed after a surgery with allowance for the intraoperative blood loss.

**Surgical techniques.** Total cerebral angiography was performed in seven observations according to the standard technique. Selective catheterization and embolization of afferents feeding a tumor was successfully performed in three observations only.

Rigid fixation of the infant’s head with a Mayfield headrest was used in 17 observations, 13 of them – in a sitting infant. Circular fitting of the head with a frame...
made of adhesive tape was used to prevent calvarial bones from being punched with pins. In other observations, the infant’s head was fixed on a soft head support with pressure-reducing support surface.

The transfontanellar-transcallosal approach was used in 17 observations, while various transcortical approaches were used in 36 other cases. The following basal approaches were used: subfrontal — in 6 cases; pterional — in 2 cases; combined transcallosal-pterional — in 3 cases, and subttemporal or transtemporal — in 2 cases. In 12 observations, we used the suboccipital approach to posterior fossa.

Tumor was removed under microscope control. The removal technique was chosen according to tumor histology and topography. The endoscopic assistance was used to control radicality of removal when a tumor was spread beyond the microscopic view region, and to visualize a vascular pedicle feeding the tumor (n=9). The angled optics with 0°, 30° and 45° view angle was used.

The radicality of a surgery was subjectively assessed by the surgeons performing the surgery and after the operation according to the results of postoperative CT and MRI of the brain. The patients were distributed into three groups according to the radicality of surgery: radical (resection of over 85% of a tumor, according to the CT or MRI results), partial (<85%), and biopsy.

Anesthesia techniques. One of the peripheral veins was catheterized immediately after taking a patient into the operation room; two or more central veins (subclavian, femoral or jugular veins) were catheterized as well. Body temperature was maintained with heated blankets and heat guns from the beginning of the surgery through its end.

Over the recent years, we have visually estimated the volume of blood loss: the volume of liquid used for on-table lavage was subtracted from the content of disposable plastic graduated reservoirs; this technique was considered to be reasonably accurate.

The lungs were ventilated artificially with the oxygen-air mixture through a semi-closed circuit at the stages of massive operative blood loss, FiO₂ was increased up to 1.0 in the regimen of moderate hyperventilation (EtCO₂=34–35 mm Hg).

In all infants, anesthesia was maintained with intravenous Propofol infusions and bolus fentanyl injections in age-related doses corrected by the traumatizing effect of a certain stage. In case of massive operative blood loss and unstable systemic hemodynamics, anesthesia was maintained as follows: both propofol infusions and fentanyl injections were discontinued and displaced with bolus intravenous injection of 25–50 mg ketamine, the only intravenous anesthetic having no depression effect on systemic hemodynamics. Rapid blood replacement could be achieved by supplementing with colloid infuse solutions. All infants whose tumors were removed (n=78) received transfusions of donor blood components. Infusion of fresh frozen plasma (FFP) (n=78) and donor erythrocyte concentrate (n=69) started at the stage of approach or at the beginning of the main surgery stage. Hemoglobin contents, hematocrit volume, and erythrocyte and platelet counts were determined before and during the surgery: immediately after induction, several times (about once an hour) at the peak of blood loss, and during its compensation, at the end of the surgery, and further at the intensive care unit – every 6–12 hours.

Blood-saving techniques. In 8 cases of surgery of large highly-vascularized tumors, hemostasis disorders were corrected and prevented at the stage of approach with the recombinant activated coagulation factor VII (rFVII, Coagil, Russia, 70–90 μg/kg) along with the conventional FFP infusion. Efficiency of the product was monitored mainly by the clinical observation of clots forming in a surgical wound.

In addition to donor blood components, a system blood reinfusion was used to compensate for operative blood loss in five cases. A cell-saver was used mainly in a High quality wash mode. The procedure was applied only when the cardiotomy reservoir contained a sufficient volume of blood, 300 mL or more. The resulting autologous erythrocyte concentrate with 65% hematocrit was diluted and filtered through leukocyte filters to remove potential tumor cell impurities.

Statistical analysis. The data were processed with the Statistica 7.0 software. It included ANOVA dispersion analysis in addition to the standard methods of sample uniformity evaluation (retrospective and prospective data). Significant influence of a number of factors [infant’s age (months), body mass/n Initial CBV, duration of the tumor resection procedure, and volume of intraoperative blood loss] on surgery outcome was evaluated with the Kruskal-Wallis non-parametric test.

Results

Our material contains the data of both prospective and retrospective observations; therefore, the uniformity of the sample parts was urgent for the further analysis. We compared the observations by three parameters: tumor topography, tumor histology, and infant’s age/body mass ratio (for different months); the analysis revealed no significant differences in any parameter. Therefore, we could consider both, the retrospective and prospective, groups to be relatively uniform and combine the data into a single sample. The further analysis of the material depended on tumor size (over or under 4 cm in the maximal transverse section according to CT or MRI data) and volume of intraoperative blood loss (see above).

Group of low risk for intraoperative blood loss

This group includes 55 (69%) patients with intraoperative blood loss less than 100% of the calculated CBV.

1. Almost a half of observations, 24 (44%), included large (over 4 cm in size) brain tumors, optic tract gliomas predominating, 6 (25%). Due to low blood supply of the tumors and in spite of their large size, the intraoperative
blood loss in this group did not exceed 100% CBV. Histological distribution of tumors and their dimensions are presented in Table 1.

2. Papillomas of vascular plexus were the most common ones: they were observed in 11 (45%) cases among the tumors under 4 cm in size (31 (56%)). Three observations included large choroid plexus papillomas of lateral and the III ventricles.

3. In posterior fossa, the tumors were presented by anaplastic ependymomas and ATRT. Blood loss in the posterior fossa tumors did not exceed 100% of the calculated CBV, although the tumors were large and highly malignant.

Some cases were presented by the histological forms uncommon in infants: glioblastoma, craniopharyngioma, and hamartoma.

Thus, the group of low risk for intraoperative blood loss includes mainly tumors of the following topographical and histological forms (regardless of tumor size): chiasm glioma, choroid papilloma, all tumors of posterior fossa. All of them have typical CT and MRI patterns and can be easily diagnosed in the preoperative period.

Group of medium risk for intraoperative blood loss

This group includes 11 (14%) patients with intraoperative blood loss ranging from 100 to 200% of the calculated CBV.

This group includes mainly (90%) large malignant tumors of supratentorial localization, anaplastic astrocytomas and ependymomas, open with cystic components, facilitating surgical removal and reducing blood loss.

Some observations included pineoblastomas, malignant teratomas, and malignant schwannomas.

Distribution of these tumors according to their size, histology, and topography is presented in Table 2.

Group of high risk for intraoperative blood loss

This group includes 14 (17%) patients with intraoperative blood loss higher than 200% of the calculated CBV.

This group includes only large supratentorial tumors; more than a half of them, 8 (60%), are plexus carcinomas. In all cases, tumors had large size and high vascularization, and localized in the lateral and/or III ventricles.

The following tumors were mentioned in some observations: anaplastic astrocytoma, glioblastoma, malignant teratoma, and ATRT.

Histological distribution of tumors with blood loss over 200% of the calculated CBV with respect to their size and topography is presented in Table 3.

Thus, the group of high risk for intraoperative blood loss includes mainly plexus carcinomas, reaching large size (over 4 cm) and intensively supplied with blood.

Surgical treatment

Techniques and volume of tumor resection depended on the degree of tumor malignancy, localization and size.

Table 1. Tumors with blood loss less than 100% of calculated CBV, n=55 (69%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Less than 4 cm (n=31)</th>
<th>More than 4 cm (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supratentorial localization</td>
<td>supratentorial localization</td>
</tr>
<tr>
<td>Grade I—II (n=38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillomas of plexus — 11</td>
<td>Astrocytoma — 1</td>
<td>Papillomas of plexus — 3</td>
</tr>
<tr>
<td>Astrocytoma — 4</td>
<td>Gliomas of CSR — 6</td>
<td>Astrocytoma — 1</td>
</tr>
<tr>
<td>Glioma of CSR — 3</td>
<td>Craniopharyngioma — 1</td>
<td>Gliangioma of CSR (biopsy) — 1</td>
</tr>
<tr>
<td>Hamartoma — 1</td>
<td>Glioma of CSR (biopsy) — 1</td>
<td>Anaplastic ependymoma — 1</td>
</tr>
<tr>
<td>Myofibroma — 1</td>
<td>Anaplastic astrocytoma — 1</td>
<td>Histiocytoma — 1</td>
</tr>
<tr>
<td>Gliangioma — 1</td>
<td>PNET — 1</td>
<td>Teratoma of CSR (biopsy) — 1</td>
</tr>
<tr>
<td>Grade III—IV (n=17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaplastic ependymoma — 2</td>
<td>Medulloblastoma — 4</td>
<td>Anaplastic astrocytoma — 1</td>
</tr>
<tr>
<td>Pineoblastoma — 1</td>
<td>ATRT — 1</td>
<td>Anaplastic astrocytoma — 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaplastic ependymoma — 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant schwannoma — 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pineoblastoma — 1</td>
</tr>
</tbody>
</table>

Note. CSR — the chiasm-sellar region; ATRT — atypical teratoid rhabdoid tumor; PNET — primitive neuroectodermal tumor.

Table 2. Tumors with blood loss 100–200% of the calculated CBV, n=11 (14%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Less than 4 cm (n=1)</th>
<th>More than 4 cm (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supratentorial localization</td>
<td>supratentorial localization</td>
</tr>
<tr>
<td>Grade I—II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade III—IV</td>
<td>Malignant teratoma — 1</td>
<td>Anaplastic astrocytoma — 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaplastic ependymoma — 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant schwannoma — 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pineoblastoma — 1</td>
</tr>
</tbody>
</table>
Low risk group

**Plexus papillomas (PP)** \((n=11, \text{Fig. 1})\). The approach was planned on the basis of preoperative CT and MRI of the brain, where a vessel pedicle feeding the tumor was verified. The best strategy minimizing the risk of intraoperative blood loss in PP surgery was coagulation of the vascular pedicle, which prevented severe bleeding during tumor removal.

Indications for surgical treatment of chiasm glioma in infants include progressing growth of a tumor with occlusion of cerebrospinal fluid pathways, diencephalic syndrome, and/or inefficient chemotherapy (Fig. 2).

The purpose of chiasm glioma surgery is to remove the exophytic part of a tumor, since the removal of its diffuse part is dangerous and unreasonable. The tumor localization (optic tracts, diencephalic region), required the attenuated techniques of its removal, that is, slow stage-wise removal with the use of ultrasound suction system, and with resection of the exophytic part of a tumor in small fragments. This surgical technique reduced the risk of damaging safe optic nerves and traumatizing of hypothalamic structures.

Vascularization of chiasm-sellar gliomas was poor in most infants (90%). According to preoperative MRI or HCT angiography, tumor vasculature could not be contrasted; this fact was confirmed by the minimal intraoperative blood loss.

Surgery of the posterior fossa tumors was performed in sitting infants; nevertheless, air embolism occurred in few cases. The tumor was removed mainly through the foramen of Magendie or (for large tumors) via transection of the medium parts of the cerebella vermis. Thin layer of the tumor was left in this region in case of floor infiltrations in patients with medulloblastoma. The aim of surgery in ependymoma patients was maximal radical removal of a tumor. Important issue is that tumors of cerebellum and the fourth ventricle are supplied blood from branches of the posterior inferior cerebellum artery; therefore, their due coagulation can prevent excess blood loss.

Disturbance of coagulation hemostasis in the low risk group was registered only in one case. It was caused by thrombocytopenia following the preceding chemotherapy. The early postoperative period was complicated by development of hemorrhage and formation of hematomas in the tumor bed and in brain ventricles. Although the surgical wound was revised and hematoma was evacuated, the infant’s condition worsened and the infant died 15 days after the surgery.

Medium risk group

Large malignant supratentorial tumors were the most common ones in this group — 6 (67%); anaplastic epen-
dymomas and astrocytomas, often with the cystic com-
ponent. Although the cystic component was large, the solid parts were less than 4 cm. Puncturing and drainage of the tumor cyst were the first stages in three observations. This procedure not only improved the clinical condition of the infant but also allowed for better visualization of the solid part of the tumor in the course of its unfolding, thus facilitating the further more radical surgery. The second stage was the main surgery for resecting the solid component and macroscopically visible cyst walls.

The resection was performed according to the general surgical principles: debulking of the central part, then mobilization and removal of the peripheral portions up to the infiltration zone of healthy brain tissues.

No complications related to coagulation hemostasis disorder and no lethal outcomes were registered.

High risk group

Large plexus carcinomas along with other malignant tumors with the solid part over 4 cm in size provoked the highest risk of fatal blood loss. The carcinomas of the lateral ventricle plexus are blood supplied from the anterior choroid artery, and medial and lateral branches of the posterior choroid artery. Far not all feeding arteries could be coagulated at the beginning of the surgery due to the large size of the tumor. In all retrospective observations in this group, inner decompression of a tumor caused high acute blood loss, and a minimal tumor injury was followed by excessive bleeding.

The retrospective analysis of this group showed that rapid aggressive resection caused rapid massive blood loss and a critical decrease in arterial blood pressure. Slower resection with intermediate stops for hemostasis increased the surgery duration but allowed the anesthesiologist to replenish the blood loss and prevent acute disorders in hemodynamics. Meanwhile, an undue delaying of tumor resection in small fragments caused exceeding of the 300% threshold of the calculated CBV and stable disorders of coagulation hemostasis: CBV was replenished but coagulation factors never restored. This was manifested by uncontrolled bleeding in the surgical wound, and the lethal outcome could happen on an operating table, independently from the rate of tumor removal. Lethality in the retrospective group was as high as 57%.

The best compromise had to be achieved between the tumor resection technique and new blood saving methods, including angiography with embolization of tumor feeding afferents and the use of the recombinant activated factor (rFVIIa).

Angiography with an attempt to embolize the tumor feeding afferents had its disadvantages: problems of selective catheterization of an infant’s anterior or posterior artery (these arteries usually being a site where a tumor feeding pedicle originated) and the high risk of embolization of terminating branches of the choroid artery [6, 14, 15]. We managed to apply the selective catheterization and embolization of tumor feeding afferents in three infants with plexus carcinomas (Fig. 3).

Partial excluding of a tumor from the blood circulation allowed a surgeon to remove the embolized part of the tu-

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Fig. 3. Large choroid carcinoma of the right lateral ventricle.

a — contrast-enhanced MRI; b — angiography before embolization; c — angiography after embolization of choroid carcinoma feeding afferents (medial and lateral posterior choroid arteries).
Injection of rFVIIa \((n=8)\) was most efficient when started at the approach stage \((n=3)\), and repeated every 15–20 minutes. When tumor resection was accompanied with rFVIIa injection, clinical (decrease in wound bleeding) and thromboelastographic normalization of coagulation was registered.

Two-stage tumor resections in the presence of rFVIIa injection and absence of visually available tumor afferents were performed in two cases until the critical threshold of intraoperative blood loss \((300\% \text{ of the calculated CBV})\) was reached (Fig. 4).

Under conditions of rapid intraoperative blood loss, blood replenishment and blood saving were performed mainly without control blood analyses, first of all, because the anesthesia care team was busy with life support. Therefore, the laboratory parameters were estimated at the stage of stabilizing infant’s condition. Table 4 presents the summarized data on blood loss and its replenishment in the groups of low, medium and high risk.

Perfecting the surgery technique along with efficient implementation of transfusion techniques improved surgical outcomes in the prospective group and decreased mortality rate from 57 to 28%.

No relation between the outcome and the degree of blood loss was revealed when analyzing the duration of tumor resection in the high risk group (Fig. 5).

**Radicality**

The highest radicality was achieved in the groups of tumors in: lateral and the third ventricles \((85\%)\), cerebral hemispheres \((81\%)\) and posterior fossa \((83\%)\). The lowest radicality \((15\%)\) corresponded to the tumors in the chiasm-sellar region, mainly large gliomas in the optic tract (Table 5).
Table 4. Characteristics of blood loss and its replenishment in infants with brain tumors in groups of low (A), moderate (B) and high (C) risk

<table>
<thead>
<tr>
<th>Group (blood loss in % of the calculated CBV)</th>
<th>Duration of tumor resection, min</th>
<th>Maximal decrease in hematocrit level, % (normal level 33—45%)</th>
<th>Maximal decrease in platelet level, % (normal level 150—400·10^9/mL)</th>
<th>Transfusion support, % of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A, n=55  (5 — 91%)</td>
<td>30—240</td>
<td>28</td>
<td>200</td>
<td>FFP, er. concentrate — 80%</td>
</tr>
<tr>
<td>Group B, n=11  (105 — 160%)</td>
<td>80—280</td>
<td>15</td>
<td>176</td>
<td>FFP — 100%, er. concentrate — 100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Coagil (rFVIIa) — 9%</td>
</tr>
<tr>
<td>Group C, n=14  (200 — 650%)</td>
<td>35—300</td>
<td>14</td>
<td>77</td>
<td>FFP — 100%, er. concentrate — 100%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IOMR — 36%, Coagil (rFVIIa) — 50%</td>
</tr>
</tbody>
</table>

Note. er. concentrate — erythrocyte concentrate; IOMR — intraoperative mechanical reinfusion of auto-erythrocyte concentrate.


<table>
<thead>
<tr>
<th>Topographic group</th>
<th>Tumor resection, abs. (%)</th>
<th>Intraoperative lethality</th>
<th>Postoperative lethality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>radical resection (&gt;85%)</td>
<td>partial resection (&lt;85%)</td>
<td>biopsy</td>
</tr>
<tr>
<td>Tumors of lateral and III ventricles (n=34)</td>
<td>29 (85)</td>
<td>5 (15)</td>
<td>0</td>
</tr>
<tr>
<td>Tumors of hemispheres (n=21)</td>
<td>17 (81)</td>
<td>4 (19)</td>
<td>0</td>
</tr>
<tr>
<td>Tumors of the chiasm-sellar region (n=13)</td>
<td>2 (15)</td>
<td>9 (70)</td>
<td>2 (15)</td>
</tr>
<tr>
<td>Tumors of posterior fossa (n=12)</td>
<td>10 (83)</td>
<td>2 (17)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>58 (72)</td>
<td>20 (25)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>
Lethality

In all observations, the lethal outcomes, 7 (9%), were caused by the factors listed in Table 6.

In three cases, death occurred during the surgery as a result of rapid blood loss, lack of time for replenishment of CBV, which caused a decrease in arterial blood pressure and failure of cardiac activity.

In four cases, lethal outcomes were registered on day 2, 3, 14, and 16 after the surgery, due to the following reasons: blood stroke into the tumor remnants (n=1), hematomata formation in the tumor bed (n=2), and developed syndrome of disseminated intravascular coagulation (n=1).

In these observations, the CBV was replenished but massive blood loss exceeding 300% of the calculated CBV disrupted coagulation hemostasis. In one of these observations, the situation was complicated by the initial thrombocytopenia that followed the preceding chemotherapy.

Surgery duration (speed of tumor resection) in the prospective group was the same as earlier; therefore, improvement of the surgery outcomes was related, in particular, to perfecting the blood saving methods, which decreased the rate of blood loss at the stage of tumor debulking and hence the total blood loss became not higher than 300% of CBV.

The use of up-to-date blood saving techniques combined with details of the surgery strategy (preoperative embolization of afferent vessels; meticulous planning of the approach; deep coagulation of the tumor stroma during debulking; time-urgent coagulation of the vessels feeding the tumor; two-stage surgery, and optimization of the speed of tumor resection) when removing large grade III–IV tumors in the high risk group (17%): mainly plexus carcinomas and anaplastic ependymomas, and less common ATRTs, PNETs, anaplastic astrocytomas, glioblastoma, and pineoblastoma.

The tumors included into the group of high risk of intraoperative bleeding topographically localized in the lateral and third ventricles, and in the cerebral hemispheres. The hemostatic disorders occurred concomitantly with the massive blood loss and corresponding infusion therapy. Several problems should be taken into account: small CBV in infants, high percentage of head-directed cardiac output, and immaturity of some coagulation factors, which are formed by the sixth months of life in healthy infants [4]. The large size of the tumors, their good vascularization, and high malignancy complicated surgery to a significant extent.

In a similar series of studies by foreign researchers, many surgeries of such tumors were also followed by massive blood loss, which in some cases several-fold exceeded the initial CBV causing the intraoperative lethal outcome [6, 19]. Thus, according to B. Due-Tonnesen et al. [10], intraoperative blood loss varied from 5 to 524% of the calculated CBV, and in two observations lethal outcomes were caused by uncontrolled intraoperative bleeding. In our series, the range of intraoperative blood loss was 30 – 650% of the due CBV. The intraoperative lethal outcomes caused by uncontrolled bleeding were registered in three observations. Lethality in the early postoperative period was registered in four observations.

In modern series of studies focused on surgery of brain tumors in infants, operative lethality varies from 13 to 26% and is related mostly to the intensive blood loss during surgery of highly malignant tumors, whose share is as high as 50% [14, 16, 23].

C. Rickert et al. [26] and R. Rivera-Luna et al. [23] recommended the multistage surgery, preoperative chemotherapy or selective embolization as preventive massive blood loss measures. And this is the case: in our series the large tumors (histological diagnosis: choroid carcinoma and anaplastic ependymoma) were removed in two patients using the two-stage surgery due to intensive uncontrolled bleeding and acute hypocoagulation (in one patient with choroid carcinoma and preliminary embolization).

H. Do et al. [9] reported successful catheterization and embolization of afferents of choroid papilloma in the third ventricle; however, publications of such sort are few, and their authors mention technical difficulties associated with selective catheterization in infants [10, 18, 19]. In seven observations of our work, angiography of cerebral vessels was performed in infants with tumors in hemispheres, and in lateral and third ventricles. Successful embolization was performed in three observations.

Table 6. Lethality in various groups of risk, abs. (%)/total

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total</th>
<th>Retrospective</th>
<th>Prospective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall number of patients</td>
<td>7 (9)/80</td>
<td>5 (13)/39</td>
<td>2 (5)/41</td>
</tr>
<tr>
<td>Low risk group</td>
<td>1 (2)/55</td>
<td>1 (4)/26</td>
<td>0 (0)/29</td>
</tr>
<tr>
<td>Moderate risk group</td>
<td>0 (0)/11</td>
<td>0 (0)/6</td>
<td>0 (0)/5</td>
</tr>
<tr>
<td>High risk group</td>
<td>6 (43)/14</td>
<td>4 (57)/7</td>
<td>2 (28)/7</td>
</tr>
</tbody>
</table>

Discussion

In our series comprising 80 infant patients with brain tumors who had been operated on, large tumors were diagnosed in more than a half of observations (59%), and large grade III–IV tumors – in 41%.

The main surgical problems in our series of observations were caused by massive intraoperative blood loss during the resection of grade III–IV tumors in the high risk group (17%): mainly plexus carcinomas and anaplastic ependymomas, and less common ATRTs, PNETs, anaplastic astrocytomas, glioblastoma, and pineoblastoma.

In four cases, lethal outcomes were registered on day 2, 3, 14, and 16 after the surgery, due to the following reasons: blood stroke into the tumor remnants (n=1), hematomata formation in the tumor bed (n=2), and developed syndrome of disseminated intravascular coagulation (n=1). In these observations, the CBV was replenished but massive blood loss exceeding 300% of the calculated CBV disrupted coagulation hemostasis. In one of these observations, the situation was complicated by the initial thrombocytopenia that followed the preceding chemotherapy.

Surgery duration (speed of tumor resection) in the prospective group was the same as earlier; therefore, improvement of the surgery outcomes was related, in particular, to perfecting the blood saving methods, which decreased the rate of blood loss at the stage of tumor debulking and hence the total blood loss became not higher than 300% of CBV.

The use of up-to-date blood saving techniques combined with details of the surgery strategy (preoperative embolization of afferent vessels; meticulous planning of the approach; deep coagulation of the tumor stroma during debulking; time-urgent coagulation of the vessels feeding the tumor; two-stage surgery, and optimization of the speed of tumor resection) when removing large grade III–IV tumors – in 41%.

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while in four observations it failed due to the lack of factors accessible for embolization and diffuse blood supply of tumors.

Degree and type of coagulopathy are mainly assessed by intraoperative changes in the platelet level, hematocrit value, and volume of intraoperative blood loss. According to N.V. Lemeneva et al. [2], when blood loss is equal to one CBV, only a slight increase in prothrombin index (PI) and activated partial thromboplastin time (APTT) occurs. In our observations, the minimal blood loss had already occurred at the stages of vein puncture and catheterization, and blood sampling for the cross-match test and other analyses, thus reducing the hemoglobin content, hematocrit value, and platelet count on the background of the infusion therapy. Unfortunately, in practice, laboratory analyses take much longer than an anesthesiologist taking a decision on transfusion under conditions of intramassive operative blood loss. No method allowing for rapid and maximally accurate assessment of a patient’s blood loss volume is available up to now. Some authors [21] use the calculation methods, including serial determination of both the hemoglobin and hematocrit levels in blood samples followed by the calculation. However, these methods cannot provide even approximately accurate figures, the more so, for an infant receiving the infusion therapy at the moment. Our method of determining the intraoperative blood loss based on the evaluation of aspiration reservoir content is simple and, as we can see, rather correct.

According to the Guidelines issued by the British Committee for Standards in Hematology in 2004 [5], introduction of FFP for replenishment of coagulation factors under conditions of intraoperative bleeding must be justified with the results of coagulation test and performed only when both PI and APTT are at least 1.5-fold higher than the standard values. On opinion of M. Piastra et al. [20–22], when we deal with the infants with large highly vascularized tumors and rapid intraoperative blood loss, erythrocyte mass and FFP should be injected earlier than the results of coagulation test are available. In our series, injection of the blood products in infants with highly malignant tumors was started at the approach stage and continued at the tumor removal stage before laboratory confirmation of the progressing coagulopathy.

Intraoperative system reinfusion of erythrocytes was applied in five patients from our series of observations (the initially low CBV level in infants was a limitation factor for extensive use of the method). According to E.S. Gorobets et al. [1], the use of this method in neurooncology allows one to significantly reduce the volume of transfused donor erythrocytes and, being combined with leukocyte filters when the infusate is returned into the circulation, is a safe procedure.

At the N.N. Burdenko Neurosurgical Institute, since 2003, the recombinant activated factor VII (rFVIIa) is used in infants to activate the hemostasis system immediately at the injury site by forming the complex between the tissue factor (TF) and factor VIIa. According to N.V. Lemeneva et al. [2], injection of rFVIIa was efficient in six out of nine patients included in the series of 6 month — 15 year-old children operated on for brain tumors [1]. M. Heisel et al. [11] reported successful use of rFVIIa in eight children with brain tumors, two of which were 3 month-old infants.

In our series, rFVIIa was used in eight observations. In four cases, the product was injected when blood loss volume had already reached 2 CBV, and standard neurosurgical methods of hemostasis and infusion-transfusion therapy failed; in three cases, rFVIIa injection preceded the surgery due to high vascularization and large size of a tumor. In all cases but two (a 7 month-old infant with giant choroid carcinoma and a 7 month-old infant with anaplastic ependymoma), injection of rFVIIa promoted bleeding arrest and surgery success. In five cases, repeated injection of rFVIIa was necessary: with 15–20-min intervals (at the absence of the effect) or 1.5 hours later. Identically to the literature [2, 11], the early use of the product in our series (before the laboratory confirmed hypocoagulation had developed) at the early stage of tumor resection was maximally efficient. It is most likely conditioned by the mechanism of action of rFVIIa, that is, activation of the hemostasis system immediately at the injury site by forming the TF–rFVIIa complex. When high doses of the product are injected, this process does not depend on the availability of coagulation factors VIII and IX [15]. When exposed to the TF – rFVIIa complex, thrombocytes are activated, and thrombin formed on their surface compensates for its deficiency in patients with thrombocytopenia and thrombocytopenia [15]. Early introduction of rFVIIa is absolutely reasonable, since coagulation factors are formed not earlier than by the 6th month of life [4].

No unequivocal recommendations on the techniques of resecting highly malignant tumors are available in the foreign literature. For example, A. Albright et al. [3] mentioned that the use of blood saving methods does not ensure the absence of a potentially adverse outcome. The authors recommend the following measures to reduce blood loss volume: coagulation of the tumor surface before its debulking and planning of such an approach that would ensure control of the tumor feeding vessels. However, when dealing with large highly vascularized grade III—IV tumors (plexus carcinomas, anaplastic ependymomas, ATRT), such a surgery may be unavailable due to the large size of a tumor and its topography. In our study, resection of an infant’s tumor before the level of intraoperative blood loss reaches its critical threshold exceeding 300% of the calculated CBV resulted in favorable outcomes. A. Albright et al. [3] mentioned that the recognition of the small CBV (80 mL/kg) in infants is an indication for early, as soon as blood loss reaches 100% of a calculated CBV, injection of plasma and platelet concentrate. We started to inject plasma at the approach stage; in addition, recognition of immaturity of coagulation fac-
tors in infants was an indication for the early injection of rFVIIa. Tumor debulking was performed intensively and was controlled by the blood loss volume. When the volume of removed tumor comprised \( \frac{1}{2} \) of the initial and intraoperative blood loss approached 300\% of the calculated CBV, the surgery was stopped, and the tumor remnants were removed at the second stage, 10–14 days later. When the volume of the removed tumor approached 100\%, before the blood loss reached 300\% of the calculated CBV, the tumor was removed completely, and the external drainage was left in the tumor bed, since slight postoperative bleeding was inevitable in 100\% of observations. The blood saving methods (early injection of plasma and blood products, and use of rFVIIa) were applied alongside with the tumor removal.

The comparison of surgery outcomes is complicated by the ratio between malignant and benign tumors in different series of observations and by the lack of differentiation according to tumor topography and degree of its malignancy. The data available from the literature are generalized. The outcomes of infant surgery from various series of observations compared with our own data are presented in Table 7.

In our series, lethal outcomes in the surgery of large highly malignant tumors of hemispheres (including lateral and III ventricles) were recorded in all observations with the volume of intraoperative blood loss over 300\% of the calculated CBV. Under the conditions of rapid intraoperative blood loss, clinical signs of disturbance of coagulation hemostasis in form of diffuse bleeding from a tumor stroma started as soon as the volume of blood loss reached 200—250\% of the calculated CBV. In all series with the volume of blood loss under 300\% of the calculated CBV, the surgeries were completed and disturbance of coagulation hemostasis was corrected without lethal outcomes.

**Conclusion**

When performing surgeries of brain tumors in infants, allowance must be made for the immaturity of all organs and systems of the first year of life. The following parameters should be considered when determining the risk criteria: 1) initial blood parameters (CBV, presence of thrombocytopenia, etc.); 2) tumor size (tumor over 4 cm is a high risk); 3) tumor localization (hemispheres, lateral and third ventricles are high risk); 4) grade of tumor malignancy (grade III—IV are high risk).

The following topographical and histological criteria could be formulated for generalization.

The group of **low risk** of intraoperative blood loss includes tumors of the following topographical and histological forms regardless of a tumor size: chiasm gliomas, choroid papillomas, all tumors of cerebellum and the fourth ventricle.

The group of **moderate risk** of intraoperative blood loss includes large (>4 cm) malignant tumors of supratentorial localization (mainly anaplastic astrocytomas and ependymomas) with a cyst component.

The group of **high risk** of intraoperative blood loss includes large (>4 cm) solid malignant tumors (mainly choroid carcinomas, less commonly ependymoblastomas, pineoblastomas, ATRT).

All the aforementioned topographical and histological forms have typical signs that are shown by MRI and CT data and can be with high probability suspected before a surgery. Description of the X-ray pattern is beyond this publication.

When the intraoperative blood loss exceeds 300\% of the calculated CBV, chronic disturbance of coagulation hemostasis occurs, leading either to uncontrolled bleeding and death on the operating table or to postoperative bleeding. The intraoperative blood loss volume can be decreased by mastering both the surgical technique and anesthetic support. The former includes preoperative embolization of the afferent vessels; meticulous planning the approach, including the use of neuronavigation; deep coagulation of a tumor stroma during its debulking; primary debulking of the tumor feeding vessels; two-stage surgery, and optimization of the speed of tumor removal.

Our analysis demonstrated that rapid resection in an aggressive manner causes rapid massive blood loss and critical decrease in arterial blood pressure. A slower resection with the intermediate hemostasis-related stops increases the surgery time but allows an anesthetist to replenish the blood loss and prevent the acute hemodynamic disorders. Meanwhile, an unreasonable

**Table 7: Outcomes of surgical treatment of brain tumors in infants (comparison with literature)**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Number of observations</th>
<th>Radical removal, %</th>
<th>Perioperative lethality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. Sakamoto et al., 1986 [27]</td>
<td>17</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>C. Lapras et al., 1988 [16]</td>
<td>76</td>
<td>58</td>
<td>13</td>
</tr>
<tr>
<td>R. Rivera-Luna et al., 2003 [23]</td>
<td>61</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>N. Mehriza et al., 2009 [17]</td>
<td>18</td>
<td>44</td>
<td>17</td>
</tr>
<tr>
<td>T. Jaing et al., 2011 [12]</td>
<td>22</td>
<td>50</td>
<td>13</td>
</tr>
<tr>
<td>Own data</td>
<td>80</td>
<td>72</td>
<td>9</td>
</tr>
</tbody>
</table>

*Note.* Data on radicality are not entirely consistent due to different criteria of radicality assessment used by different authors.
delaying of tumor removal in small fragments causes exceeding of the 300% threshold of the calculated CBV and chronic disturbance of coagulation hemostasis: CBV can be replenished but coagulation factors are not restored, thus resulting in uncontrolled bleeding in the surgical wound.

Preventive measures against disorders of coagulation hemostasis should be started as early as possible in addition to the conventional blood saving methods. It is reasonable to use early injection of plasma and platelet concentrates, early injection of rFVIIa, and intraoperative system reinfusion of autologous blood.

REFERENCES


The study focuses on the relevant problem of pediatric neurosurgery: neurosurgical assistance in the first-year life in infants with brain tumors. The authors’ team includes both neurosurgeons and anaesthesists; which is quite reasonable, since the main problems of surgery in these patients are intraoperative blood losses requiring correction by both groups of specialists. Bleeding during the resection of brain tumors in infants is primarily related to the giant size of the tumors in this age group, their high blood supply, and malignant nature of the most tumors. On the other hand, the circulating blood volume in infants is so small (80 ml/kg) that a blood loss that is insignificant and often needs no correction in adults and in older children becomes critical in infants.

The authors distinguish three groups of patients according to the blood loss risk: low (less than 100% of the calculated CBV), moderate (from 100 to 200% of CBV), and high (more than 200% of CBV). These criteria are the basis for further review of the findings on tumor localization, its size, and histological structure. It allowed the authors to predict the degree of blood loss before a surgery and to start the preventive measures.
from the very beginning of surgical intervention. These measures included the changes in surgical strategy and technique of blood loss replenishment along with injection of plasma, and erythrocyte and platelet concentrates before a hemorrhage began; the use of the recombinant activated factor VII, and autohemotransfusion. All these measures reduced the perioperative lethality from 57 to 28%. The proposed anesthetic techniques of blood loss replenishment and maintenance of blood coagulation properties can be approved unequivocally.

Evaluation of the surgical technologies is not so simple. Preoperative embolization of tumor feeding vessels should undoubtedly be welcomed, although it is successful fairly rare in children of the analyzed age, even with plexus papillomas.

The wide use of electrocoagulation techniques for hemostasis is sound. Optimization of the speed of tumor resection remains a very controversial issue. On the one hand, the authors argue against rapid (aggressive) regimen of tumor removal and propose slower resection with intermediate stops; on the other hand, resection of small fragments of the tumor causes exceeding of the 300% of calculated CBV threshold and chronic disruption of coagulation hemostasis: CBV can be replenished but coagulation factors do not restore, leading to uncontrolled bleeding in a surgical wound. There is no comprehensive answer yet.

Our material has much in common with the authors’ data concerning the histological structure and localization of tumors, and approaches to managing of bleeding and blood loss in this age group. It includes 82 observations with 36.7% lethality for the period of 1980—2004 [Yu.A. Orlov, A.V. Shaversky. Intracranial tumors in infants (review of our own and literature material). Ukr Neurokhirurg Zh 2005; 1]. The only parameter not confirmed in our material was the effect of the malignancy degree on blood loss intensity and postoperative lethality. This could be related to the high percentage of plexus carcinomas in the authors’ material (60% in patients of high risk).

In general, the work is very relevant and will be interesting both for neurosurgeons and anaesthesists.

Yu.A. Orlov (Kyiv)
Deep-seated tumors, such as tumors of the midbrain and thalamus, have a different growth direction and can deform the adjacent deep structures, including spreading into the ambient cisterns. Surgical approach depends on the tumors’ preferential localization. The goal of a surgeon is to use the least traumatic approach to deep-seated tumors with the possibility of complete resection of the tumor and minimizing the risk of development of neurological symptoms.

The main surgical approaches for the removal of midbrain and thalamus tumors that extend to the ambient and interpeduncular cisterns include the pterional, infratemporal, occipital interhemispheric, and infratentorial supracerebellar approaches.

Some tumors of the midbrain and basal parts of the thalamus spread to the ambient cistern and can deform the medial regions of the temporal lobe. In these cases, infratemporal and pterional surgical approaches are usually performed. The advantage of these approaches is the possibility to access the tumor without brain dissection. The main drawback of these approaches is the narrowness of the surgical field, possible risk of damaging the vein of Labbé and veins of the basal surface of the temporal lobe during the brain traction, and the presence of branches of perforating vessels in the field of view of a surgeon during the pterional approach [8, 11].

The temporal transchoroidal approach can be used as an alternative approach for deep-seated brain tumors that spread to the ambient cistern [2, 3, 5, 8, 9, 13].

This article describes the use of temporal transchoroidal access for resection of the midbrain and thalamus tumors and assesses its advantages and disadvantages.

Materials and Methods

During the past 4 years, 12 surgeries for resection of deep-seated tumors were performed using the temporal transchoroidal approach at the N.N. Burdenko Neurosurgical Institute. Four illustrative examples (three female patients and one male patient; 3, 4, 7 and 18 years old) on removal of piloid astrocytomas of the midbrain and thalamus using this approach are described in this article. In two cases, the tumor localized within the cerebral peduncle, in the other two cases it localized in the cerebral peduncle and basal parts of the thalamus.

In all cases, the tumor was accessed through the temporal transchoroidal approach. Two cases resulted in total tumor resection, and the other two resulted in subtotal resection. In all cases, a decrease in the neurological symptoms severity was observed during the postoperative period. No speech disorders after the tumor removal from the dominant hemisphere were observed.

Approach description and the clinical cases

In 1988, S. Nagata et al. [9] published a description of the microsurgical anatomy of the choroidal fissure and approaches to the medial temporal lobe and ambient cistern through the temporal horn of the lateral ventricle. The temporal transchoroidal approach described in the literature [1, 3, 4, 7, 10, 11, 14, 18] as a low-traumatic approach to access the vascular aneurysms of the P2 segment of the posterior cerebral artery (PCA), to arteriovenous malformations in the field of vascular slits and ambient cistern, to the bulk tumors of supracellar retrochiasmal localization, to diencephalic area and the midbrain.

The patient was positioned on the operating table lying on his back with head turned sideways at 90° angle. Arcuate malacotomy within the frontotemporal region of the scalp was conducted. The temporal muscle was displaced as a single flap with skin and subcutaneous tissue. The supraorbital region and temporal bone scales were skeletonized. Osteoplastic pterional craniotomy was performed, inclu-
Ding temporal bone scales up to its foundation. The dura mater was dissected by arch-like path, with its base facing the greater wing of the sphenoid bone. The lateral brain slit and the pole of the temporal lobe are exposed.

Corticotomy was performed in the lower regions of medial temporal gyrus; it was 1.5—2.5 cm long and located 3—4 cm posterior to the anterior edge of the temporal lobe pole. Its projection was aligned with the lower section of the lateral ventricle temporal horn and lower choroidal point (inferior choroidal point) — the terminal part of the choroidal fissure (Fig. 1). The approach direction was perpendicular to the temporal lobe plane. The entrance into the temporal horn localized at a depth of 2—3 cm. The depth of entry into the temporal horn depended on the expansion of the ventricular system in the cases of occlusive hydrocephalus. For slit ventricles, ultrasound examination or neuronavigation was performed to determine the lumen of the temporal horn. Fig. 1 schematically shows the approach to reach the choroidal fissure of the lateral ventricle temporal horn and the ambient cistern.

After temporal horn had been opened, it was important to identify anatomical structures in its lumen for easier navigation in the wound. The main anatomical landmarks on the medial surface are the choroid plexus and the hippocampus (Fig. 2). The choroid plexus is a mark for the choroidal fissure. In the temporal horn, the choroid plexus is attached to the walls of the choroidal fissure between the thalamus in the upper medial sections and fimbria of the hippocampus in the lower-lateral sections (Fig. 2).

During the displacement of the choroid plexus medially and upward, the choroidal fissure became exposed. During the choroidal fissure dissection, the tenia fimbria hippocampi was dissected starting from the bottom of the choroidal point. The hippocampus was moved downward and laterally. During widening of the choroidal fissure, the upper sections of the ambient cistern became exposed. In the medial part of the cistern, the lateral surface of the midbrain was visualized. The optic tract with the oculomotor nerve were located in the anterior direction; the lateral geniculate bodies and the thalamus localized in the posterior direction. Vascular structures localized in the lumen of the ambient cistern are P2 segment of the PCA, the posterior communicating artery (PIA), and the anterior ciliary artery (ACA).

Depending on their size, tumors of the midbrain, the thalamus and the optic tract, may expand to the ambient cistern area and deform the hippocampus, the choroidal fissure, and the lower horn of the lateral ventricle. Therefore, a thorough study of the MRI data may contribute to the selection of not the standard subtemporal pterional approach, but the temporal transchoroidal approach instead, which in these cases is less traumatic and allows for greater surgery radicality.

The examples of resection of deep-seated tumors (pilocytic astrocytomas) through the temporal transchoroidal approach are presented below.

**Case 1.**
Patient O., 3 years old. The delay in motor skill development was observed since early childhood. Over the last 3 months, a left-sided hemiparesis most distinct in...
the hand developed and began to propagate. The brain MRI revealed a tumor in the right side of the midbrain and the thalamus (Fig. 3a). A slight hydrocephalic expansion of the ventricular system was noted.

The clinical picture during the examination in the N.N. Burdenko Neurosurgical Institute revealed the left-sided pyramidal syndrome in form of hemiparesis that was most distinct in the hand (score of 3), along with the central type paresis of facial muscles and the failure of third nerve on the right.

Taking into account the preferential tumor location within the right cerebral peduncle and basal parts of the thalamus, the spread of the tumor into the lumen of the ambient cistern, choroidal fissure and medial temporal lobe deformation, it was decided to remove the tumor through the temporal transchoroidal approach.

Description of the surgery: the patient’s head was turned 90° to the left. Arcuate malacotomy in the right frontotemporal region within the scalp was performed. The pterional osteoplastic craniotomy was carried out. The dura mater was opened in an arcuate manner, with the base facing the wing of the sphenoid bone. Corticotomy of the anterior parts of middle temporal gyrus was performed (Fig. 3b). At a depth of 2.5 cm, the right inferior horn of lateral ventricle was revealed. The choroid plexus and choroidal fissure with extended original parts were revealed. In the lumen, the tumor of gray-yellow color was exposed (Fig. 3b). A tumor tissue sample was taken for histological examination. Tumor removal was performed using bipolar coagulation of the conventional and ultrasonic suction devices. The tumor was large, localized within the cerebral peduncle of the thalamus basal parts, and occupied the ambient cistern. Upon removal of the upper part of the tumor, the tumor cyst was revealed. The tumor had clear boundaries with the brain, except the areas of infiltration in the medial part. Gradually, the entire tumor volume was resected till the border with visually unaffected brain. During the tumor removal, the optic tract in the anterior part of surgical field was detected and PIA and PCA were visualized above. After the tumor removal, a large cavity was formed. Hemostasis using bipolar coagulation and hemostatic cotton was carried out. The dura mater was sewn up tight. The bone was laid in place and fixed. Soft tissues were sutured up. Urgent biopsy revealed astrocytoma with mitosis tumor type.

By the time of discharge from the hospital, in the neurological score there was an increase in the strength and range of motion in the left hand. Field of view was not examined due to the low age of the child.

Morphological diagnosis (after immunohistochemistry) revealed piloid astrocytoma; the treatment index of the Ki-67 proliferative marker was less than 5%.

The contrast-enhanced control MR images of the brain 2 months after the surgery revealed a small tumor remnant within the right cerebral peduncle. Narrow wound path was observed in the right temporal lobe (Fig. 3c).

The stereotactic surgical tumor irradiation was planned.

**Case 2.**

Patient D., 7 years old. Ten months prior to admission to the N.N. Burdenko Neurosurgical Institute, inconstant strabismus in the left eyeball was developed. The headache appeared simultaneously. The periodic nausea and vomiting gradually developed. In the dynamics, the gait disturbance was observed, along with tremor in the right hand. Brain MRI revealed a lesion of the left cerebral peduncle with a formed cyst.

During the examination at the N.N. Burdenko Neurosurgical Institute, the neurologic score detected the hypertension syndrome (headache, nausea, vomiting, initial stagnation in the fundus), right-sided pyramidal syndrome (central type of the right facial nerve paresis, right hemiparesis, most pronounced in the hand, score of 3–4), extrapyramidal syndrome (intention tremor in her right hand amplified in purposeful movements); mesencephalic symptoms (mild anisocoria d> s, convergence disorder, nystagmus). Field of view was found to be without blind spots.

According to the brain MRI data, a cystic tumor of the left cerebral peduncle was found. The solid portion of the tumor had a clear border with the adjacent brain and was homogeneously and rapidly accumulating the contrast agent. The ventricular system was hydrocephalically expanded (Fig. 4a).

Tumor resection was performed through the temporal transchoroidal approach. The choice of the approach was based on the tumor presence in the dominant hemisphere cerebral peduncle, hydrocephalic enlargement of lateral ventricles, and deformation of the medial temporal lobe and choroidal fissure.

After the osteoplastic pterional craniotomy and dura mater opening, the enlarged inferior horn of the left lateral ventricle was visualized using an ultrasonic scanner at a depth of 2.5 cm. The top layer of the inferior temporal gyrus was coagulated and resected at the length of 1–1.5 cm in middle sections. The lower horn of the lateral ventricle was accessed; the wound began to produce clear cerebrospinal fluid decreasing the brain tension. During the examination of the lower horn, the choroid plexus was found. The choroidal fissure was opened and the cistern of the cerebral peduncle side surface was exposed; ACA at its entry into the choroidal fissure and ICA were visualized. Below, the protrusion of the medullary substance was noted; it was perforated using the microsurgical forceps. A tumor cyst was revealed, and the cyst contents of yellow color were extracted. In the anteromedial parts of the cyst, the tumor tissue of gray-pink color was detected. The tumor was removed using bipolar coagulation and using the conventional and ultrasonic suction devices.

A tumor tissue sample was taken for histological examination. The tumor was located within the cerebral peduncle, had clear boundaries, which allowed its com-
Fig. 3. Contrast-enhanced MR images of the brain in the axial and frontal projections (a, c) and the intraoperative photograph (b). Case 1. Patient O., 3 years old.
a — prior to surgery: revealed delimited tumor of the right cerebral peduncle and basal parts of the thalamus with a cystic component. Tumor node intensively and homogeneously accumulates the contrast agent. Tumor extends to the interpeduncular and ambient cisterns, deforms the hippocampus and choroidal fissure. Lateral ventricles are widened; b — intraoperative photos. An extended vascular fissure and the tumor tissue in the area of ambient cistern and the cerebral peduncle are visualized in the depth of the wound. Defect of the brain in the region of the middle temporal gyrus after tumor resection is observed; c — 2 months after surgery. Small residual tumor fragment in the cerebral peduncle is observed. Deformations of the midbrain and thalamus regressed.

Complete resection. Hemostasis was done by bipolar coagulation and using the hemostatic gauze. The dura mater is sewn up tight. The bone was laid in place and fixed. Soft tissue was sutured up layerwise. Urgent biopsy revealed piloid astrocytoma tumor.

The clinical condition after the surgery displayed almost complete regression of the right hemiparesis and extrapyramidal tremor in the hand. Field of view in the postoperative period was without blind spots.

Brain MR images 6 months after the surgery (Fig. 4b) revealed no evidence of a residual tumor or its continued growth. Postoperative defect in the left cerebral peduncle and the left temporal lobe was observed.

Case 3.

Patient B., 18 years old. Six months prior to admission to the N.N. Burdenko Neurosurgical Institute, the patient developed a headache with increasing frequency and intensity, nausea, vomiting. Diplopia and weakness in the right extremities developed over time. At the time of headache, an episode of convulsive paroxysm was observed. MRI of the brain revealed a tumor of the midbrain and thalamus on the left side with noticeable occlusive hydrocephalus. Torkildsen’s ventriculostomy was performed at the patient’s home residence. Postoperative period was complicated by liquorrhea development. The liquorrhea regressed during the treatment.
At the time of examination in the N.N. Burdenko Neurosurgical Institute the following symptoms were revealed in the clinical picture: 1) rough mesencephalic symptoms, such as the lack of pupillary response to light, the lack of spontaneous upward gaze, upward gaze palsy; 2) right-sided pyramidal syndrome in the form of central type facial nerve paresis, right-sided hemiparesis with a decrease in muscle strength up to 4 points. Field of view was without distinct blind spots.

MR images of the brain revealed the cyst tumor of the left half of the midbrain and basal parts of the thalamus. Tumor had deformed the adjacent brain structures, including the choroidal fissure in the temporal horn of the lateral ventricle. The ventricular system was expanded and hydrocephalic (Fig. 5a).

Taking into account the localization of the tumor in the dominant hemisphere and the existing risk of speech disorders during the temporal lobe traction through the infratemporal approach, spreading of the tumor into the ambient cistern, the deformation of choroidal fissure and medial temporal lobe, and hydrocephalic expansion of the ventricular system, it was decided to access the tumor through the temporal transchoroidal approach.

Pterional osteoplastic craniotomy was carried out. The dura mater was very tense. In this regard, the inferior horn of the left lateral ventricle was punctured. After the excessive cerebrospinal fluid had been removed, the tension of the brain regressed. The dura mater was opened using a semi-oval incision, with its base facing the wing of the sphenoid bone. Corticotomy in the anterior middle temporal gyrus for about 1.5 cm in length was performed; the access to the lower horn of the lateral ventricle was carried out. The choroid plexus, deformed hippocampus and parahippocampal gyrus were visualized. Choroid plexus was allocated upwards. Arachnoid adhesions were separated and primary parts of the choroidal fissure were stretched. A tumor of gray-yellow color was discovered. A tumor tissue sample was taken for histological examination. The tumor had a heterogeneous structure, sometimes it was soft and removed by suction device; in some places it was denser, where it was resected using the ultrasonic suction device. The tumor localized within the cerebral peduncle and the basal parts of the thalamus. During the removal of the tumor, a large cyst was revealed. The tumor had compact structure; however, it had infiltrated the brain in the peripheral regions. The entire volume of the tumor to the borders with externally unaltered brain was resected. The cerebellum tentorium edge, ICA, PCA, and the basal vein were visualized. Hemostasis was done using bipolar coagulation and hemostatic cotton pads. Urgent biopsy revealed astrocytic glioma tumor.
Postoperatively, the mesencephalic syndrome regressed, the strength in right extremities increased. No speech disorders were observed.

The control contrast-enhanced CT scan of the brain (Fig. 5b) revealed postoperative changes in the bed of the removed tumor. No evidence of residual tumor was revealed. The wound path in the left temporal lobe was observed.

The histological diagnosis data revealed the piloid astrocytoma with noticeable polymorphism of the nuclei and cells and a large number of eosinophilic granule cells. Immunohistochemical study revealed positive expression of glial fibrillary acidic protein (GFAP), synaptophysin expression in some single cells, and CD34 expression in the vascular wall. The labeling index of proliferative marker Ki-67 was less than 5%.

Case 4.

Patient V., 4 years old. Five months prior to the examination and treatment, weaknesses developed in the left hand (the patient stopped using hand while playing, in the self-care), and in the leg: the patient often stumbled when walking, was running awkwardly. Weakness in the left extremities was slowly increasing. In the overall dynamics periodic vomiting in the morning, headache, weakness, and fatigue appeared. Contrast-enhanced MRI of the brain revealed a large tumor of the right half of the midbrain uniformly accumulating the contrast agent; the cystic component was detected. The tumor considerably deformed the adjacent deep structures of the brain, medial temporal lobe, temporal horn, and the choroidal fissure (Fig. 6a).

The tumor was resected through the temporal tranchoroidal approach.

Osteoplastic pterional craniotomy. The dura mater was opened in an arcuate manner, with base facing the wing of the sphenoid bone. Corticotomy in the anterior middle temporal gyrus was performed; the access to the lower horn of the right lateral ventricle at a depth of 3 cm was performed. Deformed choroidal fissure was visualized. It was extended and a gray-pink color tumor was discovered (Fig. 6b). A tumor tissue sample was taken for histological examination. Tumor mainly consisted of a soft texture tissue. It was removed using gripping forceps, a suction device, bipolar coagulation, and a dissector. Tumor stroma contained a large number of small vessels and some larger branches of perforating vessels. First, the central part of the tumor was resected. Afterwards its peripheral divisions were resected. During the tumor removal few cysts were discovered. ICA, PCA, PLA, ACA, and the oculomotor nerve were visualized (Fig. 6b). In the medial area, the tumor was removed up to the borders with visually unaltered brain, the floor of the third ventri-
The removal of the tumor formed a large cavity. Hemostasis using bipolar coagulation and hemostatic gauze was carried out. The brain sharply sunk down. The dura was sutured tightly. The bone was laid in its place and fixed. Soft tissues were sutured up. Urgent biopsy revealed astrocytoma tumor.

Postoperatively, the hypertension syndrome regressed, left-sided hemiparesis significantly regressed, and fine motor skills appeared in the palm. At the time of discharge, the motor skills deficit was minimal and central facial nerve paresis has regressed. Field of view examination revealed no major defects.

Histological diagnosis revealed piloid astrocytoma tumor. The labeling index of proliferative marker Ki-67 was less than 5%.

Contrast-enhanced control brain MRI revealed a small residual tumor within the right cerebral peduncle (Fig. 6c). Deformation of the adjacent structures has regressed.

Due to the small volume of the residual deep-seated tumor, stereotactic radiosurgery was planned after patient had been examined by a radiologist.

Discussion

Tumors of the midbrain and thalamus are the most challenging ones for surgical removal. Choice of surgical approach to these tumors depends on the preferential localization and direction of tumor growth. Main surgical approaches to tumors spreading into the ambient cistern...
are pterional, infratemporal and occipital interhemispheric transtentorial approaches. The advantage of the above approaches is the ability to reach the tumor without brain dissection. The disadvantage of these approaches is the narrowness of the surgical field, the risk of damaging the temporal lobe, the vein of Labbé, and veins of the temporal lobe basal surface with the excessive brain traction, which can result in venous infarction in the temporal lobe and can also lead to speech disorders upon the dominant hemisphere damage.

The temporal transchoroidal approach is an alternative access for tumors of the midbrain and thalamus, extending into the ambient cistern [3, 6, 9, 10, 13, 15–17].

This approach was described in literature [1, 3, 4, 7, 10, 11, 14, 18] during the access to vascular malformations in the area of ambient cistern and basal-medial temporal lobes, aneurysms of P2 segment of PCA, tumors of the midbrain, tumors of retrochiasmal and diencephalic localization during amygdala–hippocampal ectomy.

During this approach, the corticotomy has to be performed in the lower regions of the medial temporal gyrus, on the border with the inferior temporal gyrus 3 cm posterior from the temporal lobe pole. This allows the access into the temporal horn of the lateral ventricle without damaging the optic radiation that passes in the top part of the temporal horn. Some authors [5] prefer approach in the temporal horn through the inferior temporal gyrus, fusiform gyrus, and collateral gyrus in order to preserve the optic tract. Corticotomy in this field allows one to preserve the sensory speech center located in the upper and middle temporal gyrus of the dominant hemisphere 5–6 cm posterior from the edge of the temporal lobe pole.

The difficulty of the access to the temporal horn could be its lumen narrowness in the absence of hydrocephalus. In these cases, the use of neuronavigation and an ultrasound scanner can be helpful.

During the approach to a deep-seated tumor through the temporal transchoroidal approach, it is important to know the anatomical landmarks in the temporal horn lumen and the anatomical structures and vessels in the ambient cistern. The choroid plexus, choroidal fissure, and lower choroidal point are the main landmarks in the temporal horn. It is important to identify them in the ventricular lumen, especially in cases of deformation of the midbrain and the thalamus medial temporal lobes by the tumor.

A. Hamlat et al. [3] proposed partial resection of the hippocampus and amygdala to widen the access during the resection of retrochiasmal craniopharyngiomas and tumors with diencephalic localization, including hypothalamic hamartomas.

During the resection of the midbrain and thalamus tumor in the ambient cistern area, depending on the length of the cistern, it is necessary to identify PIA, PCA, AVA, oculomotor nerve, and the optic tract.

Advantages of the temporal transchoroidal approach include the greater angle of attack during the deep-seated tumor resection with less brain traction compared to the subtemporal approach and the lack of risk of damaging the vein of Labbé and veins of the temporal lobe basal surface (Fig. 7). This approach, unlike the subtemporal one, allows inspection of both the lower and the upper parts of the ambient cistern (Fig. 7). The disadvantage is the need for dissection of the medullary substance, the risk of damaging the optic radiation in the top part of the lateral ventricle temporal horn. However, with a good anatomy knowledge, the proper choice of corticotomy in the lower middle temporal gyrus, and the selection of correct path to access the temporal horn, the risk of damaging the visual pathway is minimal.

**Conclusions**

Temporal transchoroidal approach is less traumatic during access and removal of delineated tumors of cerebral peduncle, basal parts of the thalamus, or the optic tract. This approach, in contrast to the infratemporal and pterional, allows one to visualize the lower and upper sections of ambient cistern with less traction of the brain. This is important during the resection of deep-seated tumors in the dominant hemisphere, where there is a risk of speech disorders with excessive traction of the temporal lobe. With a good knowledge of anatomy of the ventricu-
The approach described above seems to be optimal and low-invasive for resection of deep-seated tumors that extend into the ambient cistern and deform the choroidal fissure.

REFERENCES


Commentary

Hard-to-reach deep-seated brain tumors still represent a complex microsurgical problem. Attempts are being made to optimize the minimally traumatic surgical approach options when using the optimal angle of the surgery for the maximum possible resection of these tumors and therefore to obtain favorable postoperative results. These issues are addressed in the present work: to improve microsurgical opportunities for resection of tumors localized in the midbrain, thalamus, extending into the ambient cistern, and superior and interpeduncular cistern, which ultimately will have a positive impact on the results of treatment of this serious category of cancer patients.

The article analyzes the data obtained in the N.N. Burdenko Neurosurgical Institute, RAMS, over the past 4 years. A total of 12 patients with cystic tumors of the midbrain and thalamus were operated on through the temporal transchoroidal approach; its advantages and disadvantages were assessed.

A total of 4 detailed clinical cases are described in the article to clearly demonstrate the benefits of the microneurosurgical approach used to remove two piloid astrocytomas localized in the cerebral peduncle, and two other tumors localized in the cerebral peduncle and the basal parts of the thalamus. In all cases, the positive dynamics in neurological score was observed after the surgical procedure, and more importantly no voice disorders developed after the removal of the tumors in the dominant hemisphere.

A very brief historical experience of using this method is provided: the method was developed mostly for removing anaplastic astrocytomas of the posterior cerebral artery and arteriovenous malformations in the area of ambient cistern, tumors of retrochiasmatic localization, and some tumors of the diencephalic area. Nuances of the present approach are described in detail, starting from the position of the patient on the operating table, planning of the skin incision and bone flap formation, incision of the dura mater, and corticotomy performance in the lower middle temporal gyrus. The importance of internal landmarks identification (the choroid plexus, choroidal fissure and lower choroidal point) during the surgical access is emphasized. Options for accessing to the hydrocephalic temporal horn are discussed. All these steps are vividly illustrated with diagrams, intraoperative photographs, and correlative comparison of preoperative and postoperative MRI studies.

The conducted studies allowed the authors to clarify the benefits of the approach: a greater angle of attack during resec-
tion of deep-seated tumors; less brain traction compared to the
subtemporal approach; virtually no risk of damaging the vein
of Labbé and basal surface veins; the possibility of visual eva-
luation of the top parts of the ambient cistern.

The drawbacks of the approach include necessity of brain
tissue dissection, with some risk of damaging the optic radia-
tions in the roof of the temporal horn of the lateral ventricle.

There is no doubt that the accumulation of clinical cases
can be even more convincing for evaluation of the role of this
interesting and important approach in the arsenal of possible
microneurosurgical interventions.

The article is rather interesting, informative, especially
for the practicing neurosurgeons, and reflects the latest trends
in the determination of the best ways to improve the microsur-
gical procedure and to develop various versions of approaches
for the treatment of deep-seated brain tumors.

V.L. Puchkov (Moscow)
Surgical Aspects of Endoscopic Treatment of Sagittal Craniosynostosis (Scaphocephaly) in Children

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The article focuses on surgical treatment of sagittal craniosynostosis in children. Sagittal craniosynostosis (scaphocephaly) is the most common nonsyndromic monosynostosis. Treatment of children with craniosynostosis should be started as early as possible. Endoscopic method is a low-invasive technique in surgical correction of craniosynostosis. This article describes the features of surgical treatment at all stages of the endoscopic cranioplasty. The data presented are based on the experience of treating 20 children with primary sagittal craniosynostosis. Treatment was performed using endoscopic techniques and special tools designed for endoscopic cranioplasty.

Keywords: nonsyndromic craniosynostosis, scaphocephaly, endoscopic cranioplasty.

Sagittal craniosynostosis is the most common nonsyndromic monosynostosis. Its incidence rate ranges from 0.2 to 1 per 1000 liveborn infants, being 40–60% of all nonsyndromic forms [6, 7]. Relationship to gender is observed: 70–90% of all cases are found in boys [6]. Treatment of children with craniosynostosis should be started at young age [2, 4]. Therefore, it is strongly desirable to use low-invasive techniques. The endoscopic method is a low-invasive technique used for surgical correction of craniosynostosis, which should be preferred for treating this pathology in children [3, 4]. Description of surgical aspects of endoscopic treatment in children is of high practical relevance due to the availability of this method and high incidence of scaphocephaly among nonsyndromic monosynostoses.

This work was aimed at studying surgical features at all stages of endoscopic treatment of sagittal craniosynostosis.

Material and Methods

Endoscopic cranioplasty was performed in 20 children with primarily detected sagittal craniosynostosis. All children were routinely examined following the standard procedures approved for craniosynostosis in our clinic, comorbidities were analyzed, and the neurological status was estimated in accordance to child’s age. CT followed by 3D skull reconstruction was performed in all patients; its results were used to detect abnormalities typical of scaphocephaly; craniometric measurements were made. Treatment was performed using endoscopic technique; special tools designed for endoscopic cranioplasty were used: endoscopic retractor (Dura-Scalp Retractor acc. to JIMENEZ, Karl Storz) with a rigid 4 mm endoscope (Forward–Oblique Telescope Hopkins II, Karl Storz) 0° and 30° and two 5 and 10 mm wide exchangeable extendable plates (Fig. 1). The endoscopic retractor was fixed in

Fig. 1. Endoscopic retractor (Dura-Scalp Retractor acc. to JIMENEZ, Karl Storz).

a – 4 mm endoscope (Forward–Oblique Telescope Hopkins II, Karl Storz) 30°; b – assembled retractor (ready to be used).
the chosen position with a special rigid mounting system equipped with an adapter (KS-Lock, Karl Storz) (Fig. 2a). A kit of curved raspatories of different curvature and shape of the operating unit and a bone cutting kit were used to dissect soft tissues and resect bones (Fig. 2b). A multifunctional endoscopic unit (Karl Storz) equipped with a H3-Z Full HD camera (Karl Storz) to transmit the image was used for imaging (Fig. 3a). Gel head supports of different shapes were used for convenient positioning of child’s head (Fig. 3b). Comprehensive photo- and video-recording of the key moments of intervention was performed at all stages of surgery in accordance with ethic principles.

Results and Discussion

Cranial deformities have always attracted scientists’ attention. Hippocrates has mentioned the tower-like shape of the head in his manuscripts; he regarded to it as a constitutive abnormality and presumed that there was an association between this abnormality and the cranial sutures [6]. In 1791, S. Soemmering, a German physiologist, anatomist, and anthropologist, admitted that premature fusion of the cranial suture played a significant role in pathogenesis of craniosynostosis. It was Rudolf Virchow who further advanced the fundamentals of modern knowledge of craniosynostosis development in 1851. He postulated that stricture formation of the cranial suture causes restriction of cranial growth in the direction perpendicular to the axis of the damaged suture (the Virchow’s rule) [6]. Notably, craniosynostosis was earlier considered to be an incurable disease and was not of no interest for surgeons. Currently, taking into account the modern methods for diagnostics and treatment, the tactics for this pathology have been significantly changed. There is a clear trend for early diagnosis; earliest possible correction of craniosynostosis is considered to be crucial. Over than a century of surgical treatment of this pathology, multiple surgical techniques have been proposed for different types of craniosynostosis; some of them have been proposed by Russian surgeons. Several of these methods are still used in clinics. Surgery of sagittal craniosynostosis has a long history. The first surgeries of this type (linear craniotomies) were performed by Lanne-
facilitation of the formation of skull shape by rapidly growing brain: residual bone defects are healed easier in younger children. In our opinion, craniosynostosis should also be corrected as early as possible. Endoscopic cranioplasty is the method for removing open surgery artifacts. It was proposed in 1998 by D. Jimenez and C. Barone [5]. It is noteworthy that the first treatment of craniosynostosis was performed in a patient with sagittal craniosynostosis in a same manner as over 100 years ago. Other advantages are reduction of the blood loss caused by conventional reconstruction, reduction of the incision size, surgery duration, and hospital length of stay.

In the present study, scaphocephaly was detected in 20 children (18 boys and 2 girls) out of 40 children with craniosynostoses. The mean age of patients was 10.05 months. There were 16 (80%) of patients under 1 year of age (mean age was 5.81±3.02 months); this age was considered to be optimal for endoscopic treatment. CT followed by 3D reconstruction of the skull was used to perform craniometric measurements and to analyze the cephalic index, which was 67.84±7.45 on average. This value is a criterion of dolichocephaly, one of the manifestations of sagittal craniosynostosis. Endotracheal anesthesia was used to fix a child on the operating table. In all cases, the supine position with the head flexed forward to a maximum possible angle. It is most convenient to use the main endoscopic instrumentation for a patient lying in this position. The artificial lung ventilation data were used to monitor the adequacy of head position. Moreover, child’s body position was adjusted using surgical table handles. No special tools were used for head fixation; C-shaped silica gel head supports were used to ensure convenient head positioning. This provided a sufficient level of head fixation in the proper position. An important issue is prevention of bed sores and injuries from surgical electrodes. For this purpose, disposable sticky electrodes that ensure the maximal contact surface area with child’s skin and isolation were used. Another important thing is to control of child’s body temperature. Various body warming systems (WarmTouch WT-5900, Covidien AG, USA; Thermomatress Bioterm 5-U, Russia) were used to maintain the normal body temperature.

An important step in preparing for the surgery is to mark the surgical site. A median cranial line (a projection of the sagittal sinus), the coronal suture, anterior fontanel (if it is present), and external occipital protuberance were used as the main landmarks. In all cases, the surgical site was treated with iodopyrone and alcohol. Proper fixation of the surgical clothing is needed to prevent overlying and traction of the soft tissues in the projection of intervention, to prevent restriction of freedom of surgeon’s actions. We fixed the surgical clothing along the border between the facial and cerebral head sections, leaving the cranial vault uncovered.

The next step of the surgery was the installation of a special mounting system with adapters (KS-Lock, Karl Storz) for an endoscopic retractor. This system allows
protrusions (lacunas 2–4 cm and 1.5–2.5 cm wide). The most typical lacuna localizes in the parietal area near the medial edge of the central gyrus [1]. Additional difficulties when the dura mater is dissected emerge when anterior to fix the retractor in the selected position and easily adjust it, thus changing the view angle in the wound. Skin incision is made 1.5–2 cm posterior from the coronal suture or anterior fontanel (if it is not closed). The possible damage to the large terminal branches of the superficial temporal artery should be avoided to prevent intense bleeding. In our study, the anterior fontanel was opened in 6 children with verified scaphocephaly. The median line of the incision coincided with the sagittal suture. An additional incision was made in the projection of the point at the intersection of the lambdoid suture and median (sagittal) line. S-shaped incisions were made instead of linear incisions due to fact that they are more cosmetic and can be better hidden under hair; incisions were no longer than 4–5 cm. Bone resection was performed by the subperiosteal method. The peristium was stripped with a common raspatory in the incision projection by 1.5–2 cm in the anterior direction to visualize the coronal suture, which is a jagged line in front of the pathological sagittal suture. It can also be projected as a diagonal of the rhombus of the anterior fontanel perpendicular to the sagittal line and can be used as an additional landmark. It is extremely important to avoid damaging skin when using raspatories. The peristium was detached in the projection of the sagittal suture and at 3–4 cm to the sides, as well as in the projections of the coronal and lambdoid sutures on both sides (3–4 cm wide). No large-scale detachment of the peristium is needed (it may cause additional hemorrhage). The stenosed sagittal suture is defined as an area with bone hyperostosis; its relief can be palpated; there is no broken line typical of the serrate suture at the conjunction of two bones (Fig. 4). A trephination aperture 0.5 cm in diameter was made by 1.5–2 cm in the posterior direction from the coronal suture and 1.5–2 cm in the lateral direction from the sagittal line using a high-speed drill (Midas Rex Legend EHS Surgical Drill, Medtronic) equipped with a special burr (Match Head Fluted, Medtronic). The cutting edge of the burr in proper position prevents damage to the scleromeninx.

After making the trephination aperture, the bone was punched using bone forceps in the incision projection. If the anterior fontanel is present, there is no need in perforating the trephination aperture. In this case the scleromeninx can be dissected from the bone in the projection of the anterior fontanel. An important action during the surgery is detachment of the dura mater from inner surface of bones in the craniotomy area. The dura mater is often rigidly attached near the cranial suture; quite large emissary veins are sometimes present. There is a risk of damaging the sagittal sinus when detaching the dura mater from the bone. Under endoscopic visualization, the sagittal sinus always has a medial position and appears as a long dome-like formation. Sometimes a low blood flotation can be observed due to pulsation of brain vessels. Under inner-side visualization, the surfaces of parietal bones in its projection protrude into the skull cavity. One should also bear in mind that in 76% cases the sinus has lateral protrusions (lacunas 2–4 cm and 1.5–2.5 cm wide). The most typical lacuna localizes in the parietal area near the medial edge of the central gyrus [1]. Additional difficulties when the dura mater is dissected emerge when ante-

Fig. 4. Schematic and endoscopic views of periosteal dissection.

а — scheme for detaching the periosteum, top view: 1 — coronal suture, 2 — area of stenosed sagittal suture; b — scheme for detaching the periosteum, lateral view: 3 — coronal suture, 4 — lambdoid suture; c — endoscopic view after periosteum dissection, endoscope axis is indicated: 5 — scalp, 6 — periosteum, 7 — area of the stenosed sagittal suture, 8 — dura mater.
rior fontanel is present. In this case, fontanel tissues participate in fixation of the dura mater to bone edges. A Polenov guidewire and a Penfield dissector were used to detach the dura mater from bone. These tools were used in all cases to perform dissection at the area required for resection without damaging the dura mater. The dura mater was detached along all the sagittal, coronal and lambdoid sutures. Detachment of the dura mater near the skull base was performed using a raspatory with wide cutting edge under endoscopic control, since the dura mater here is rigidly attached to the bones.

The subsequent manipulations were performed under endoscopic control (Fig. 5). Scalp structures in the projection of the resected suture were moved upward. It is important to control the child’s head position. The most convenient is the endoscope position in a plane parallel to the bone suture and moving the operating unit along the suture during bone resection. Osteotomy was performed along the sagittal suture from its intersection with the coronal suture to the lambdoid suture; the average resection width was 3.57±1.38 cm. In order to obtain additional mobilization, paracoronal osteotomy was performed in several cases in a posterior direction from the coronal suture until the skull base with resection of a part of the greater wing of sphenoid bone and paralambdoid osteotomy anterior to the lambdoid suture until its intersection with the parietotemporal suture at both sides.

The resection volume was 1.45±0.12 and 1.69±0.63 cm, respectively.

Notably, there are no known landmarks today to define osteotomy borders. The sagittal sinus is used as a landmark to dissect the sagittal suture, but there are no clear landmarks for additional osteotomies. A special landmark to define the borders of additional bone resection was the greater wing of sphenoid bone. It was partially removed using a high-speed drill and a diamond burr. The osteotomy area here was limited by posterolateral (temporal) surface of the greater wing of sphenoid bone. It is slightly concaved and is involved in the formation of a wall of the temporal fossa. The lower part of this surface is limited by the infratemporal crest. One needs to keep in mind that in 51% of cases, arteries localize in the osteal canal in the anteroinferior part of the sphenoid bone [1]. The hemorrhage is stopped by bipolar coagulation and applying bone wax. At this stage, an important advantage of rigid fixation and endoscopic control can be seen: the possibility to perform manipulations with both hands (bimanually). A point before the intersection with the parietotemporal suture was used as a landmark of the border when conducting paralambdoid osteotomy (Fig. 6).

Hemostasis is another important problem. Hemostasis should be performed at each stage during the surgery. Bones of the cranial base and vault are characterized by a sponge structure and intense blood supply. Large

**Fig. 5.** Dissection of the dura mater and resection of a bone portion.

- a — resection of bone in the trephination projection: 1 — bone forceps; 2 — start of dissection of the dura mater from the bone; 3 — dura mater, 4 — Penfield dissector; c — detachment of the dura mater from the inner surface of parietal bone in the projection of sagittal sinus: 5 — dissector, 6 — the site of dura mater fixation; d — endoscopic anatomy of the sagittal sinus: 7 — periosteum, 8 — parietal bone, 9 — sagittal sinus.
emissary veins often lead to the dura mater; coagulation is needed if they are revealed. Another important feature of venous component of the cranial vault is the presence of intraosteal venous system localized in the spongy bone layer together with the external (intracutaneous) venous system. These systems are tightly interconnected and interact with the deep venous system localized between the dura mater layers [1]. Bone wax and treatment of the bone edge using a high-speed drill with a diamond tip can be used to stop bone bleeding. Another well-known technique is the use of an aspirator with bipolar coagulation. The use of this tool allows one to stop bone bleeding. However, when using it in hemostasis it is extremely important not to damage and not to coagulate the dura mater; a brain spatula is used to protect it. This method is of best choice in the youngest children, when bones are thin. It is also possible to use such hemostatic agents as SURGIFLO Hemostatic Matrix (Ethicon LLC). Hemostasis is performed under the endoscopic control. An endoscopic retractor is removed after the hemostasis was thoroughly performed. Only resorbable material is used for sealing due to the small size of incision, low tissue mobility in this area, and good healing. The wound is sealed with intracutaneous sutures; the surface is treated with sterile medical glue Dermabond Pro Pen (Ethicon LLC, USA) (Fig. 7). Wound condition is monitored during the hospitalization period.

The mean duration of surgery for sagittal craniosynostosis was 163.3±43.25 min. Blood loss was 103.46±58.43 ml and increased with child’s age. Patients stayed in the Resuscitation Department for less than 1 day. Control CT followed by 3D reconstruction of skull was performed 1–2 day after surgery. In all cases, no damage to the dura mater, sagittal sinus, air embolism were detected. Neither inflam-
Fig. 7. Types and methods of hemostasis in endoscopic cranioplasty.

a – the use of SURGIFLO Hemostatic Matrix (Ethicon LLC): 1 – view after applying the matrix; b – hemostasis with bone wax: 2 – spatula; c – the use of an aspirator with bipolar coagulation: 3 – aspirator coagulator; d – view of the postoperative wound treated with sterile medical glue Dermabond Pro Pen (Ethicon LLC, USA): 4 – incision area.

mation, nor infection complications, nor postoperative wound inconsistency were observed. There was no need for puncture in the intervention area. The length of a hospital stay after endoscopic cranioplasty was 3.1±0.5 days.

Therefore, endoscopic surgical treatment of scaphocephaly was performed in 20 children. Treatment results were estimated after 1, 3 and 6 months in dynamic follow up according to the CT scanning followed by 3D reconstruction of the skull and anthropometric measurements. An orthotic helmet (“helmet therapy”) was used after regression of postoperative swelling of soft tissues in order to ensure additional correction of the head shape and for protection. The CT and 3D reconstruction data were used to calculate the cranial (cephalic) index for unbiased estimation of treatment results. In the dynamic follow-up after 6 months, the cephalic index was 77.29±4.17 (being 67.84±7.45 at hospitalization), which was considered to be an efficient outcome of intervention. These values, as well as the CT and 3D reconstruction data were used to determine the duration of wearing a helmet. The com-
Comparison of the preoperative cephalic index with the data from control examination revealed significant differences (U-test, *p*<0.01) (Fig. 8).

**Conclusion**

The possibilities of modern endoscopic tools and instrumentation allow one to perform successful surgical treatment for scaphocephaly.

Endoscopic cranioplasty for correction of scaphocephaly is a low-invasion method to treat patients with this pathology.

In contrast to the conventional approaches, this method lowers the risks of complications connected with the volume of surgical interventions due to its low-invasiveness.

Since the method is low-invasive, there is no need for long hospital stay.

**Fig. 8.** Change in the cephalic index (CI) before and after the endoscopic surgery in children with scaphocephaly after 6 months (U-test, *p*<0.01).

**REFERENCES**


**Commentary**

The article is devoted to the relevant problem of surgical treatment for sagittal craniosynostosis in children. The purpose of the study was to analyze the features of endoscopic surgical treatment in children with scaphocephaly.

A total of 20 patients with sagittal craniosynostosis were analyzed. The equipment for these surgeries was thoroughly described. The stages and technical features of the surgery, as well as the anatomical landmarks, were precisely described.

The method proposed by D. Jimenez and C. Barone and described in the study has been widely used over the past 16 years. The method consists in performing craniotomy with endoscopic assistance through small incisions of soft tissues. During the surgery, the cranial vault is resected in projection of the synostosed suture with formation of a linear bone defect. Similar surgeries were performed without endoscopic tools in the early XX century and were considered to be low-efficient. Hence, there was a demand for developing reconstructive surgical techniques to be used in patients with craniosynostoses. Development of the methods for orthopedic correction of skull deformities using cranial orthoses (helmets) allowed one to return to using the cranioectomy methods.

Therefore, treatment of patients with craniosynostoses yields good results neither when using the conventional cranioectomy nor when using the endoscopic assistance modification. This was also proved by an analysis of the unsuccessful results by D. Jimenez and C. Barone who had developed this technique. The main reason for bad results was the lack of orthopedic treatment. Thus, it is more correct to talk about complex surgical and orthopedic treatment of patients with craniosynostoses.

The radiography protocol (in particular, CT) was used in the study; 3D anthropometric measurements were performed. The evidential basis of the study relies on measurements performed using 3D CT reconstruction images. The use of X-ray computed tomography causes significant radiation exposure of young child’s brain and should not be used as a routine control technique; it is used only in the presence of indications.

Craniomeric parameter (the cranial index) was used to evaluate the intervention efficiency. The results were statistically analyzed. Statistically significant differences were found in patient groups before and after the treatment, which led to a conclusion about sufficient efficiency of the surgeries. The
cranial index should be used beyond any doubt to assess the treatment results in patients with scaphocephaly, which was also proved by the literature data.

The features of surgical technique that differs from the previously described one are of especial interest: the use of the rigid fixation system for an endoscope with a retractor, which would enable bimanual performing of the surgery; subperiosteal bone resection in the area of the synostosed suture with forceps. Hemostasis methods that are of high importance when performing such surgeries have been described.

Future research should address long-term results of craniectomy with endoscopic assistance. This will allow one to specify indications for treatment and efficiency of the method for treating patients with craniosynostoses.

L.A. Satanin (Moscow)
Carotid Endarterectomy in Patients with High Surgical Risk

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N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow, Russia

The aim of the work was to examine risk factors for carotid endarterectomy (CEA) and their impact on the results of surgical treatment of patients with chronic cerebral ischemia. The study included 340 patients operated on at the Institute from 2007 to 2011. All patients underwent CEA in various modifications. The patients were divided into four groups, based on the classification of surgical risks of CEA proposed by T. Sundt. In the course of the subsequent analysis, perioperative outcomes of surgical treatment in the 3rd and 4th groups were evaluated; the rate of intraoperative placement of temporary intraluminal shunt (TIS) was compared, depending on the severity of angiographic risk factors and neurological anamnesis. The rate of perioperative ischemic complications in the 3rd group was 4.2%; in the 4th group – 6.4%. In both groups, TIS placement was required in 15% of operations. In patients operated on under regional anesthesia, shunts were used 2 times less often than in patients under general anesthesia (8.8% vs. 19.8%). A correlation between the severity of angiographic risk factors and tolerance of the brain to hypoperfusion, caused by temporary clamping of the internal carotid artery (ICA), was observed. In patients with contralateral ICA occlusions, shunts were required in 40% of cases; in patients with contralateral stenoses – in 15%, and in patients without angiographic risk factors – in 8% of cases. These findings coincide with the results of similar studies published in the literature.

Taking into account our and foreign data, it should be noted that CEA in patients with high surgical risk by Sundt is accompanied by the increased rate of perioperative ischemic complications and requires a more differentiated approach to the tactics of surgical treatment and to the choice of a method for neurophysiological monitoring during surgery.

Keywords: carotid endarterectomy, surgical treatment, surgical risk, perioperative ischemia, temporary intraluminal shunt.

In the developed countries, stroke is the third leading cause of mortality, giving place only to cardiac and cancer diseases, as well as is the number one cause of disability in the working age population. In Russia, about 500,000 cases of acute cerebrovascular accident are reported each year; in the United States, 700,000 (of which 200,000 cases are recurrent), and in Europe, about 1.3 million [2, 4]. Up to 45% of patients who had stroke die in the acute phase, and the mortality rate is 50% during the first year. Among patients who survived the acute phase of stroke, about 60% have remained severely disabled and only 20% of them are able to return to work [3, 5].

To prevent the development of ischemic cerebral diseases caused by atherosclerotic carotid artery stenoses, carotid endarterectomy (CEA) has been applied since the 1950s. Since the 1990s, after the results of several large studies had been published, CEA has been recognized as an effective method of surgical treatment for hemodynamically significant carotid artery stenosis [1, 4, 6, 7]. According to the NASCET, ECST, and ACST data, CEA allows one to reduce the risk of stroke development in patients with subcritical and critical stenosis of the internal carotid artery (ICA) within the subsequent 2 years in 3 times. The permissible mean perioperative ischemic complication rate for symptomatic patients should not exceed 6%, and for asymptomatic patients – 3% [10, 12].

To predict surgical risks when performing CEA, a surgical risk scale developed by T. Sundt in 1975 [9] has been widely used (Table 1).

Patients with acute cerebrovascular disorders (ACD) of the ischemic type or with past medical history of transient ischemic attacks (TIAs) of not more than 1 month before hospitalization belong to neurologically unstable patients (the 4th group of surgical risks).

According to T. Sundt as well as several other authors [8, 11, 13], the real complication rate after CEA varies from 1 to 15%. The highest probability for the development of perioperative ischemic complications is observed in patients with past medical history of stroke (duration < 6 months) and with TIA immediately before surgery [8, 11, 12]. According to T. Sundt, the risk of perioperative ischemic complications in the 1st group is 1%, in the 2nd – 2%, in the 3rd – 7%, in the 4th – 10%. NYCASS (New York Carotid Atherosclerosis Surgery Study) is one of the recent major studies on CEA, which has reported the results of perioperative ischemic complications [8]. In this paper, the large dispersion in the complication rate, depending on the severity of chronic cerebral ischemia, has been marked: perioperative strokes occurred in 3% of asymptomatic patients, in 6.5% of patients with TIA in anamnesis, and in 14.5% of patients with previous stroke. Despite a high risk for stroke development during the perioperative period, it is these patients who are mostly in need of endarterectomy, because the risk of recurrent...
strokes in the natural course of the disease reaches 10% in the first year and 45–50% over the next 5 years [9, 11].

The modern methods for preoperative examination and intraoperative monitoring of the basic brain functions, a differentiated approach to the choice of an endarterectomy method, the choice of an anesthesia method, as well as dynamic monitoring in the immediate postoperative period, allow the safer use of surgical techniques for correction of stenotic carotid artery lesions in patients with a high surgical risk.

The aim of this work is to evaluate the possibility of improving the results of perioperative surgical treatment in patients from the 3rd and 4th groups of the Sundt surgical risk scale by means of a differentiated approach to the choice of a method for intraoperative neuromonitoring, anesthesia during surgery, and methods for intraoperative cerebral protection from ischemia caused by temporary clamping of the ICA, depending on risk factors identified prior to operation.

**Material and Methods**

A total of 340 patients (240 males) with atherosclerotic carotid artery stenosis had been operated on at the N.N. Burdenko Neurosurgical Institute between 2007 and 2011. The mean age of the patients was 63.6 years (43–88 years). The mean number of perioperative ischemic complications was 4.07%, mortality – 1.17%. More detailed information about complications that occurred in our patients from different surgical risk groups are presented in Table 2.

All patients, depending on the degree of manifestation of perioperative risks for the stroke/myocardial infarction/mortality development, were divided into four groups according to the Sundt surgical risk classification. The 3rd group consisted of 156 patients (178 surgeries), the 4th consisted of 91 (92). The mean age of patients was 66.5 (49–88) and 65.8 years (49–86 years) in the 3rd and 4th groups, respectively. Detailed information on the patients is presented in Table 3.

Making a diagnosis was performed on the basis of ultrasound (US) duplex scanning of the brachiocephalic arteries. Depending on the patient’s condition, spiral computed angiography, magnetic resonance angiography of the brachiocephalic and intracranial arteries, as well as direct angiography, were performed. Additional examinations, if required, were conducted on the individual basis. In the absence of contraindications, antiplatelet agents were canceled a week before surgery.

Transcranial Doppler ultrasound (TCD US) was performed in all patients before surgery to determine the fea-

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**Table 1. Classification of surgical risks for CEA according to Sundt**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st group</td>
<td>Neurologically stable, somatically unburdened patients without angiographic risks</td>
</tr>
<tr>
<td>2nd group</td>
<td>Neurologically stable, somatically unburdened patients with verified angiographic risks</td>
</tr>
<tr>
<td>3rd group</td>
<td>Neurologically stable, somatically burdened patients regardless of the presence of angiographic risks</td>
</tr>
<tr>
<td>4th group</td>
<td>Neurologically unstable patients regardless of the presence of somatic or angiographic risks</td>
</tr>
</tbody>
</table>

**Risk factor**

- **Somatic**: Angina pectoris, myocardial infarction in anamnesis, congestive heart failure, severe obesity, chronic obstructive pulmonary disease, biological age over 70 years
- **Angiographic**: Occlusion of the contralateral ICA, ICA siphon stenosis, the presence of a soft plaque or ulceration on the plaque surface
- **Neurological**: Progressive neurological deficit, multiple transient ischemic attacks, stroke in anamnesis

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**Table 2. The rate of complications (in%) in the different groups of surgical risk**

<table>
<thead>
<tr>
<th>Complication</th>
<th>1st group</th>
<th>2nd group</th>
<th>3rd group</th>
<th>4th group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/mortality</td>
<td>—</td>
<td>2.1</td>
<td>4.8*</td>
<td>6.4*</td>
</tr>
<tr>
<td>Stroke</td>
<td>—</td>
<td>2.1</td>
<td>3.03</td>
<td>4.3</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>—</td>
<td>—</td>
<td>1.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Intracerebral hematoma</td>
<td>—</td>
<td>—</td>
<td>0.6</td>
<td>2.1</td>
</tr>
</tbody>
</table>

**Footnote.** * — *p*<0.05.
sibility of intraoperative US-monitoring of the linear velocity of blood flow (LVBF) in the middle cerebral artery (MCA) on the ipsilateral side. In the absence of “temporal US window” (about 10% of the population) or because of impossibility of TCD US for technical reasons, endarterectomy was performed under regional anesthesia (RA). Direct contact with the patient during surgery allows direct dynamic neuromonitoring (DNM) and thus assessing the degree of compensation of the collateral blood flow during cross-clamping of the ICA, which is a major factor in the choice of intraoperative brain protection methods. RA was also used in patients with burdened somatic pathology, embolic unstable plaque, in patients older than 70 years, as well as in accordance with individual patient’s preferences. RA was not used in patients with gross neurological deficit, apparent encephalopathy (inability to communicate adequately with the patient), aphasic disorders, language barrier with the patient, the anatomical features (distal ICA tortuosity, prolonged stenoses, high bifurcation of the common carotid artery (at the C2 vertebral body level), “short thick neck”).

The temporary intraluminal shunts (TIS) at the time of ICA clamping were placed on the basis of the intraoperative neuromonitoring data. When operating under RA, an indication for shunt placement was the patient’s depressed consciousness or the emergence of focal neurologic deficit: paresis of the limbs, aphasic disorders (the examination was conducted at the moment of clamping, on the 2nd, 3rd, 5th minutes after application of vascular clamps and then every 3 min until the start of blood flow in the ICA). In patients operated on under general anesthesia (GA), intraoperative multimodal neuromonitoring, comprising TCD US and bifrontal cerebral oximetry (CO), was carried out. Relative indication for shunt placement in patients operated on under GA was the reduction of LVBF in the ipsilateral MCA during clamping by more than 50% of the initial values. The reduction of the parameters by more than 10% of their initial values served as a CO threshold, demonstrating subcompensation for the cerebral blood flow. The decision on TIS placement during ICA clamping was made upon the emergence of subcompensation symptoms, based on the outputs of both methods or upon reducing LVBF, according to TCD US, to less than 30–35 cm/s. T-shaped shunts manufactured by Le Maître Vascular company were used in the work.

Treatment outcomes were evaluated by the day of discharge, on the 6th–7th day after surgery. Control US of the brachiocephalic arteries was performed 3 months after surgery.

Results

Patient samples in the 3rd and 4th groups did not differ significantly by gender, age, and the affected side of the artery. Among comorbid somatic diseases, the high incidence rate for diabetes and chronic obstructive pulmonary disease (COPD) has been revealed among the patients of the 3rd surgical risk group (Table 3). In both groups, RA was required in about half of the patients (47% of operations in the 3rd group and 55% of operations in the 4th group). It is noteworthy that the main indications for RA in the 3rd group were the somatic risks: past medical history of angina pectoris, heart attack, heart failure, grade III-IV obesity, COPD, and biological age over 70 years. In the 4th group, RA was mainly conducted in patients with stroke or TIA, which had occurred less than 1 month before surgery, embolic atherosclerotic plaques, and gross atherosclerotic lesions of the contralateral ICA. TIS placement in both groups was required in 15% of cases (the average frequency of placement among all analyzed patients was 14.6%). In patients operated on under RA, shunts were reliably used 2 times less often than in patients under general endotracheal anesthesia (8.8% vs. 19.8%, p<0.05). The analysis of the material showed that up to 40% of patients with contralateral ICA occlusion did not tolerate ICA clamping and needed intraoperative TIS placement. Patients with contralateral stenosis needed shunt placement in 15% of cases, and patients without angiographic risk factors needed TIS placement not more than in 8% of cases. Regarding patients operated on under RA, TIS placement was mostly often required in the 4th group: 17.6% (in the 3rd group – 5.9%, in the 2nd and 1st groups no such cases were detected).

The total rate of perioperative ischemic complications was 4.15%. No sequelae were observed in the 1st group of the surgical risk, and the incidence of ischemic disorders of varying severity during the perioperative period was 2.1% (p<0.05) in the 2nd group. In groups of the increased surgical risk, the greater rate of complications was significantly noted: 4.2% in the 3rd group and 6.4% (p<0.05) in the 4th group. The mortality/stroke parameter was 4.57% overall, it was 0% in the 1st group, 2.1% in the 2nd, 4.8% in the 3rd, and 6.4% in the 4th group.

Discussion

In our work we tried to implement a differentiated approach to the tactics of perioperative treatment for patients with hemodynamically significant atherosclerotic stenoses of the carotid arteries. The main starting points were the clinical picture of the disease, the patient’s neurological status at admission, angiographic risks, accompanying somatic anamnesis, and possibility to perform intraoperative neuromonitoring. The comparative outcome analysis for treatment in patients operated on at the N.N. Burdenko Neurosurgical Institute in 2007–2011 and patients treated in the earlier period (2000–2007) was performed. Implementation of the RA methodology and direct DNM upon CEA (2006) has greatly expanded indications for surgical treatment of patients with severe co-morbidities and high neurological risks. Thus, the proportion of patients with the third and fourth groups of surgical risks in the clinical material of our study was 72%; it did not exceed 50% in the earlier period [7]. Perioper-
tive complications in patients of the 3rd group occurred in 4.8% of cases; in patients of the 4th group – 6.4%, which was less than in studies published by T. Sundt, NASCET, et al. [8, 10].

As mentioned above, in our patients during CEA under GA, TIS placement was required 2 times more often than in surgeries under RA. This difference was due to the difficulties arising from the interpretation of the multimodal neuromonitoring data in some patients operated on under GA. In particular, a reduction of LVBF according to the TCD US data and a decrease in SpO2 according to the CO data are the indicators reflecting the development of subcompensation of cerebral circulation and brain metabolism during ICA clamping, which may either go by without affecting the patient or may turn into irreversible brain ischemia. Direct DNM enables diagnosing the onset for decompensation of the cerebral circulation. Therefore, its diagnostic accuracy is significantly higher

Table 3. Comparative characteristics of patients from the 3rd and 4th groups of surgical risks

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>3rd group</th>
<th>4th group</th>
</tr>
</thead>
<tbody>
<tr>
<td>ab. (%)</td>
<td>abs. (%)</td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>165</td>
<td>92</td>
</tr>
<tr>
<td>Number of performed operations</td>
<td>178</td>
<td>92</td>
</tr>
<tr>
<td>Males/females</td>
<td>120/45 (72/28)</td>
<td>69/23 (75/25)</td>
</tr>
<tr>
<td>Mean age (min–max), years</td>
<td>66.5 (49—88)</td>
<td>65.8 (49—86)</td>
</tr>
</tbody>
</table>

Somatic anamnesis

| Hypertension | 137 (83) | 78 (84,7) |
| Ischemic heart disease | 71 (43) | 36 (39,1) |
| Myocardial infarction in anamnesis | 22 (13.7) | 18 (19.5) |
| Angina pectoris | 49 (30,6) | 26 (28,2) |
| Coronary artery stenting/coronary artery bypass grafting in anamnesis | 14 (8,75) | 11 (11,9) |
| Arrhythmia | 25 (15,6) | 8 (8,6) |
| Diabetes | 35 (21,8) | 15 (16,3) |
| Chronic obstructive pulmonary disease | 23 (13,9) | 9 (9,7) |
| Renal factors | 5 (3) | 3 (3,2) |

Degree of manifestation of chronic cerebral ischemia according to A.V. Pokrovsky

| Asymptomatic | 16 (9,6) | 0 |
| Discirculatory encephalopathy | 45 (27,2) | 0 |
| Stroke in anamnesis | 77 (46,6) | 44 (47,2) |
| TIA | 27 (16,3) | 65 (70,6) |

Angiographic risk factors

| Contralateral ICA stenoses | 33 (20) | 14 (15,2) |
| Including: | | |
| Severe | 10 (6) | 4 (4,3) |
| Subcritical | 22 (13) | 9 (9,7) |
| Critical | 1 (0,6) | 1 (1,08) |
| Contralateral ICA occlusion | 14 (8,4) | 12 (13,04) |

Vertebral artery stenoses:

| contralateral | 2 (1,2) | 0 |
| ipsilateral | 1 (0,6) | 0 |

Vertebral artery occlusion:

| contralateral | 2 (1,2) | 0 |
| ipsilateral | 1 (0,6) | 4 (4,3) |

Extra-, intracranial microvascular anastomosis in anamnesis

| 2 (1,2) | 0 |

Contralateral CEA in anamnesis

| 9 (5,4) | 1 (1,08) |
and, respectively, TIS placement in patients operated on using DNM is required significantly less often.

In the world literature [11, 14], indications for TIS placement upon performing CEA have still been discussed. On one hand, the use of TIS upon performing CEA is accompanied by an increased risk for the development of embolic complications and early ICA thrombosis due to intimal dissection in the distal ICA. On the other hand, some patients are not able in principle to undergo even short-term ICA clamping, which is usually associated with an open circle of Willis and the deficiency of cortical collaterals. We have observed several cases when clamping the ICA for 2 min [the average time required for TIS placement (operation under RA)] caused neurological deficit regressing immediately after the shunt placement. At the same time, in 2 cases focal neurological symptoms appeared on the 10th and 18th minutes of ICA clamping, which evidenced for cerebrovascular reserve exhaustion and transition of the cerebral blood flow from the subcompensation stage to that the compensation stage.

According to our experience, upon a differentiated approach to the choice of neuromonitoring and anesthesia in patients with high surgical risks, CEA is the effective method of surgical treatment if surgical activity of our center is not less than 50 CEAs per year [8]. Application of the neurosurgical methods, as well as opportunities of neuroanesthesiology and neuroresuscitation in these patients allow one to achieve the better results of surgical treatment, as well as to increase the efficiency of the control for possible ischemic complications during the perioperative period. Intraoperative direct DNM, the use of RA, selective TIS placement, and cerebroprotective treatment during the perioperative period allowed us to expand the spectrum of patients undergoing surgery due to the patients who had previously been refused for surgical treatment because of the extremely high risk of neurological and systemic complications. At that, the rate of perioperative complications did not get higher.

Conclusions

1. The combination of biological age (over 70 years) with angiographic and somatic risk is a factor increasing the level of perioperative ischemic complications, which explains the higher stroke/mortality rate in patients: in the 3rd group — 4.8%, in the 4th group — 6.4%.

2. CEA during the early period after stroke (up to 1 month) as well as upon TIA in the ipsilateral hemisphere leads to the increased level of perioperative ischemic complications in patients in the 4th group of surgical risk compared with those in other groups.

3. RA, using direct DNM, is the method of choice in patients with high anesthetic and surgical risk, since it allows diagnosing intraoperative complications at the very early stages and is an indicator for a timely and optimal choice of intraoperative cerebral protection methods. It also expands the range of indications for surgical treatment in somatic burdened patients without significant exceeding the permissible level of perioperative complications.

REFERENCES


Commentary

The work, presented by a team of authors from the leading neurosurgical institution of our country, is extremely topical and timely. Despite significant progress in basic and applied research in the field of cerebrovascular pathology, acute cerebrovascular accidents remain the most important medical and social problem in all developed countries at the turn of the
XXth and XXIst centuries. Moreover, due to the unprecedented increase in the number of senior people in the general population of the Earth, stroke forges ahead among the leading causes of death. In Russia, mortality in the acute phase of stroke is 35%, increasing by almost 15% by the end of the first year of the disease. Post-stroke disability ranks first among all the possible causes of disability. Only about 20% of patients who had stroke return to their previous jobs, while one-third of the patients are people of socially active age. Operative interventions of the revascularization type on the major arteries of the head (MAH) occupy an important and, in some cases, leading position in the complex treatment of ischemic cerebrovascular accidents as well as their residuals, successfully performing the task of restoring the impaired cerebral function and optimizing the parameters of cerebral circulation.

Twenty years ago, MAH surgery was the issue of exclusive competence of vascular surgeons. In this regard, it is encouraging that the presented research and application work is written by a neurosurgical team. Perhaps, of the 16,000 surgeries for MAH annually performed in Russia today, only one thousand is performed by neurosurgeons. It is just 6.25%, but this number has been steadily increasing from year to year. And taking into account the need for such surgeries (up to 60–70 thousands), the question of any competition among professionals is not relevant, but can be seen as mutually beneficial cooperation among different specialists: neurologists, vascular surgeons, neurosurgeons, and X-ray endovascular surgeons.

According to the existing international standards, complications in MAH surgery (which, unfortunately, occur in any surgical practice) are permissible within the following limits: mortality – less than 2%, with general complications less than 5%. In the early 1990s, after the unprecedented international co-operative research (NASCET) had been completed, these figures were as follows: mortality not more than 3%, with 7.5% of common complications. It is possible to speak with confidence that the quality requirements for surgery on MAH were toughened due to the direct participation of neurosurgeons in the development of the diagnostic arsenal and operational tactics. Moreover, this situation allowed improving the immediate results of surgical treatment in patients with pathology of the brachiocephalic arteries.

In this paper, the risk factors for carotid endarterectomy (CEA) directly affecting outcomes of surgical treatment in patients with chronic cerebral ischemia, especially in groups of high surgical risk, have been comprehensively determined. The individual choice of the patient’s cerebral protection in the course of multimodal neuromonitoring proposed by the authors is of practical interest. Of all existing diagnostic methods, the authors selected those that are the most indicative and available for routine practice under conditions of different hospitals in our country. Until now there have been debates about the method of anesthesia (usually, the endotracheal general methodology is preferred), about the use of a temporary intraluminal shunt at the main stage. Personal, solid enough experience of the authors allows one to extremely convincingly make the adequate choice of the cerebral protection during CEA.

I am convinced that this work will be extremely useful and interesting for professionals engaged in the surgical prevention of brain stroke.

G.I. Antonov (Moscow)
Arteriovenous malformations (AVMs) are abnormal vascular lesions arising from impaired angiogenesis during the stage of transformation of primary embryonic arteriovenous anastomoses to capillaries [7, 36]. AVMs most often manifest themselves as spontaneous hemorrhages, less often as epileptic seizures, headache, or focal neurological symptoms. A combination of several symptoms is possible. AVM significantly shortens the longevity. The annual risk of hemorrhage is approximately 2–3% [13, 15]. Each episode of repetitive hemorrhage is associated with an increased risk of death. Most often, the first hemorrhage occurs at the age of 20–40 years. If a malformation localizes in the posterior fossa, the risk of death after the first hemorrhage is up to 67% [25].

Currently, the main techniques for AVM treatment include malformation resection, endovascular occlusion, radiosurgery, and a combination of the above three [22]. Cortical AVMs with the volume less than 10 cm³ can be cured by surgery [26, 27, 41, 49]. Resection of malformations located in the deep and functionally important parts of the brain, even if they are small, carries a high risk of persistent neurological defects and is rarely radical [26, 38, 48]. In these cases, radiosurgery becomes the method of choice [39].

Stereotactic radiosurgery is the method for accurate conformal irradiation of relatively small size targets in one or two fractions. The purpose of AVM irradiation radiosurgery is achieving complete obliteration of its vessels. A disadvantage of the method is the presence of a latent period of 2–3 years, during which obliteration of malformation vessels occurs and a risk of hemorrhage development still remains.

Stereotactic radiosurgery can be performed using a variety of devices and radiations, including narrow photon beams of the Gamma Knife and linear electron accelerators, beams of high energy heavy charged particles, such as protons.

Compared with photon radiation, protons have several beneficial properties regarding the spatial dose distribution, which enables one to significantly increase the total focal dose and simultaneously reduce the integrated dose to the surrounding normal tissues by 2–3 times [3, 4, 11, 12, 45, 46].

In the Soviet Union and later in Russia, proton radiosurgery (PRS) had been developed in the 1970s in the Laboratory of Nuclear Problems of the Joint Institute for Nuclear Research (JINR), Dubna [8], at the Institute of Theoretical and Experimental Physics, Moscow [10], and at the Institute of Nuclear Physics, Gatchina [6].

Sixty-five patients with arteriovenous malformations (AVM) of the brain underwent proton beam radiosurgery at the Joint Institute for Nuclear Research in the period between December 2001 and February 2012. This work analyzes the results of treatment of 56 patients with the follow-up period ranged from 24 to 109 months. The malformation volume varied from 0.92 to 82 cm³. The mean isocenter dose was 24.61±0.12 GyE. The target margin was included in the 70-90% isodose. Most patients were irradiated in two sessions on two consecutive days. Ten patients discontinued participation in the study for various reasons. Complete obliteration of AVM vessels was obtained in 23 (50%) of the remaining 46 patients. In the group of malformations with the volume from 10 to 24.9 cm³, complete obliteration occurred in 46.6% of cases, which was significantly higher than the percentage of complete obliterations for photon radiosurgery of similar size AVMs. Partial obliteration was obtained in 21 patients. Over the entire follow-up period, only 1 female patient developed repetitive hemorrhage from a partially obliterated AVM 60 months after proton radiosurgery. No effect was observed in 2 patients. Late radiation reactions developed in 5 patients 12 months after radiosurgery: in 4 patients they were grade 2 on the RTOG scale of toxicity and resolved within 1 month after the prescription of steroids; and 1 patient had radiation necrosis that resolved 12 months after several courses of steroid and dehydration therapy.

Therefore, proton stereotactic radiosurgery is the effective and safe technique for treatment of inoperable brain AVMs, especially those of medium and large size.

Keywords: arteriovenous malformations more than 10 cm³, proton beam radiosurgery.
However, these techniques had significant limitations: they allowed one to form the dose field of small size and confined shape only (round or oval) as well as to irradiate AVMs located at a short distance from the midsagittal plane of the head. For these reasons, it was not possible to provide optimal irradiation of complex shape and large size AVMs. The emergence of three-dimensional computer systems for irradiation planning in the mid-1980s made it possible to obtain irradiation plans for targets of any shape, size and localization [23, 24].

Cerebral angiography had long remained the primary method for the pre-irradiation diagnostics, as well as for the anatomical and dosimetric planning of "stereotactic radiosurgery" of AVM. The development of computed tomography and magnetic resonance imaging using CT and MRI features in angiography over the past 25 years has allowed conducting pre-irradiation diagnostics by non-invasive methods [9, 30, 53].

In Russia, the new stage in the development of proton therapy came in 1999 when a specialized radiology department was opened at the Laboratory of Nuclear Problems of JINR, where the technique of three-dimensional conformal proton radiotherapy based on CT and MRI diagnosis and three-dimensional conformal irradiation planning has been developed and successfully applied for the first time in Russia [1, 5].

**Material and methods**

Selection of patients had been conducted between December 2001 and February 2012. PRS was performed in 65 patients with brain AVM. Of them, 56 patients, including 26 (45.5%) females and 30 (54.5%) males, aged from 7 to 55 years (mean age 30.7±1.5 years); the follow-up was more than 24 months. Clinical manifestations were as follows: hemorrhage (in 31 patients), epileptic seizures (in 14), headache (in 5), neurological deficit (in 5), incidental finding (in 1). Location was as follows: cerebral hemispheres (in 35), corpus callosum (in 5), basal ganglia (in 7), cerebellum (in 5), and cerebral trunk (in 4). The distribution of malformations according to the Spetzler–Martin grading system [50] was as follows: grade I in 3 (5.3%) patients, grade II in 8 (14.3%), grade III in 29 (51.8%), grade IV in 15 (26.8%), and grade V in 1 (1.8%). The vascular tangle volume varied from 1 to 82 cm³. The mean volume was 14.22±2.14 cm³. To evaluate the effect of the AVM volume on the treatment results, all malformations were arbitrarily divided into four groups: up to 4.9 cm³ in 13 (23%) patients, from 5 to 9.9 cm³ in 18 (32%), from 10 to 24.9 cm³ in 17 (30%), and from 25 to 82 cm³ in 8 (14%). Among 56 patients, 20 received surgical treatment before PRS (decompression trepanation to remove intracerebral hematoma was performed in 3 patients, an attempt to partially remove AVM simultaneously with the evacuation of hematoma was performed in 3 patients; endovascular embolization of AVM vessels with a partial effect of malformation size reduction was conducted in 10 patients; the shunt system for eliminating hydrocephalus was placed in 4 patients); and proton stereotactic radiosurgery was performed in 36 patients as the only treatment.

Upon selection of the irradiation parameters, the dose standardization was performed at the isocenter and was equal to 100%. The isocenter dose for small (volume up to 5 cm³) and medium (volume up to 25 cm³) malformations localized outside of the critical brain structures was 25 GyE (1 GyE is equal to 1 physical Gy multiplied by the relative biological effectiveness of protons, which is 1.1 [2–4]). The isocenter dose for small and medium malformations located in the critical areas of the brain was 24 GyE, and it was 20–23 GyE for large AVMs (volume greater than 25 cm³). The mean dose was 24.61±0.12 GyE. The target margin was included in the 70–90% isodose, 79.46±0.7% on average, and it received 16–22.5 GyE, 19.56±0.22 GyE on average. In most patients irradiation was carried out in two sessions on two consecutive days.

Irradiation was carried out in the treatment box, to which a horizontal proton beam with the energy of 155 MeV was delivered (Fig. 1). The penetration depth for protons of the given beam in water was 160 mm at the 90% isodose. The maximum beam cross-section was 80 mm wide and 77 mm high. A set of comb filters allows one to extend the Bragg peak in depth from 2 to 5 cm. The unmodulated peak was 8 mm. The beam dose rate at the Bragg peak was about 1 Gy per minute.

![Fig. 1. Comparison of dose distributions for single 6 MeV photon (left figure) and 155 MeV proton beams.](image)
A therapeutic chair having four degrees of freedom of movement was placed in the box to accommodate a patient. Opposite to the proton beam and along its axis, the X-ray tube was set at a distance of 1.8 m from the isocenter. The centration laser system determined three mutually perpendicular planes that intersect at the isocenter and the central axis of the beam. Thus, all elements of the stereotactic technology for dose delivery to the pathological focus were implemented in the treatment box.

A mask made of perforated thermoplastic immobilized the patient’s head both during the diagnostic procedures and during irradiation. CT of the head was performed using a GE Hi-Speed CT scanner, to obtain 96 to 200 slices of 1–2 mm thickness, which were used in irradiation planning. A brain MRI with slice orientation same as that in CT scanning was also used for matching images upon the irradiation planning (image fusion).

The three-dimensional conformal computer planning of irradiation was conducted using an OptiRad-3D planning system developed at the world’s first Medical Proton Therapy Center of Loma Linda University Medical Center (Loma Linda, California, USA). The system was adapted at JINR to be used with proton beams. The irradiation plan consisted of 3–8 irradiation fields arranged in the axial plane of the head. The cross-section shape of the proton beam was set by the target projection at a certain angle (beam’s-eye-view), which was formed, upon real irradiation, with an individual collimator made of Wood’s alloy. To provide conformity to the dose distribution in depth, bolus compensators of complex shapes were calculated and were subsequently made of special wax with the density of 0.98. The irradiation plan quality was assessed using the dose–volume histograms for the irradiation target and critical structures.

After completion of irradiation plan preparation, reconstructed digital craniograms for each irradiation field scaled to the real skull images were printed. The digital craniograms provided the following images: the irradiation target, coordinate axis with the isocenter, and reference bone structures and, if available, artificial structures. Craniogram-based stencils were prepared, based on the bone structures of the skull, the centration point with the coordinate axes, and the proton beam contours were transferred.

During PRS a patient is sitting in the therapeutic chair. The patient’s head is initially positioned in the immobilizing mask using laser centralizers, and the final centration of the proton beam on the target is then carried out under the X-ray control. An X-ray skull image from each irradiation field is exposed with a reduced therapeutic proton beam. This image is compared to a digital reconstructed craniogram by overlapping the above described stencil. The accuracy of proton beam pointing at the target is about 1 mm. An irradiation session takes 30 to 50 min on average. In this case, most of the time is spent for patient positioning and the proton beam position verification.

It should be noted that the proton accelerator (photon), devices generating the therapeutic proton beam, and the therapeutic chair were manufactured in Russia, which is currently a rarity when it comes to high-tech treatments.

The main objective of stereotactic proton radiosurgery of the AVM is complete obliteration of malformation pathological vessels. Criteria for evaluation of the treatment results are as follows:

- complete obliteration of malformation pathological vessels: no abnormal vessels;
- partial obliteration: reducing a malformation percentage by 10–99%;
- lack of obliteration: retaining the previous size or increasing the malformation tangle.

Excel 2010 and Statistica 7.0 software packages were applied for statistical data analysis, descriptive statistics, comparing groups of patients, using the Student’s criteria (t-test) and Fisher’s exact test, as well as for curve plotting and charting.

**Results**

In 56 patients who received the treatment, the follow-up ranged from 24 to 109 months, with the median value of 74 months, and with the mean value of 66.7±2.9 months. Of them, only 46 patients came personally for the follow-up examination or provided the necessary data by mail. We contacted the missing patients by mail or phone. It turned out that two patients had died from comorbidities, one had died from hemorrhage in the latent period, in one patient non-fatal hemorrhage had developed (also in the latent period). The other 6 patients could not be reached. Of the remaining 46 people, complete obliteration of AVM vessels was obtained in 23 (50%). An example of complete obliteration of the AVM with the volume of 28.8 cm³ is shown in Fig. 2. In one female patient, obliteration was achieved only after re-irradiation performed 38 months after the first radiosurgical treatment. Complete obliteration occurred 48 months after the re-irradiation.

Partial obliteration was obtained in 21 patients, among which it was 95–80% in 10, 79–50% in 6, and less than 49% in 5 patients. An example of partial obliteration of the AVM with the volume of 27.2 cm³ is shown in Fig. 3. No effect was obtained in 2 patients.

Over the entire follow-up period, repetitive hemorrhage from a partially obliterated AVM developed only in one female patient 60 months after the PRS. Of 12 patients with epileptic seizures, attacks ceased in 6 patients; besides, 100% obliteration of the AVM occurred in 5 of them, and 95% obliteration occurred in one patient.

Except one case, radiation reactions after PRS were mild or moderate. In our trial early reactions, several hours after irradiation, were observed in 2 patients: in one female patient with symptomatic epilepsy in the past medical history, repetitive epileptic seizure developed (sub-
sequently reversed by treatment with Relanium); in another patient with AVM in the brainstem, moderate toxicity manifested as qualms and vomiting spells that required prescription of steroids. Five patients developed late radiation reactions 12 months after radiosurgery, with 4 patients being grade II on the RTOG (Radiation Therapy Oncology Group – International Group for Study on the Use of Radiation Therapy in Oncology) toxicity scale. The reactions were accompanied by the emergence of edema slightly extending beyond the irradiation field determined from the MRI data. The symptoms regressed following steroid therapy within 1 month. One female patient developed radiation necrosis corresponding to grade 4 on the RTOG toxicity scale. This was the only serious sequela that was completely resolved within 12 months after the appointment of several courses of steroid therapy and dehydration. According to the control MRI, asymptomatic edema developed in 14 patients 12 months, on average, after irradiation. In these cases no steroid treatment was required. Upon further follow-up, the independent reduction or disappearance of edema occurred in all cases after 24–36 months (Fig. 4).

**Discussion**

The annual risk of hemorrhage in patients with AVM belonging to grade IV and V according to the Spetzler–Martin grading system is 10.4% [29, 44]. In 1986, R. Spetzler and N. Martin [50] proposed a classification that has become popular among neurosurgeons and neuroradiologists. It reflects the AVM size, the relation to functionally important areas of the brain, and features of blood drainage from an AVM. According to the Spetzler–Martin grading system, AVMs are grouped to give a score between I and V. The group number increase corresponds to an increase in the extent of risk for surgical AVM resection. Although we initially did not plan to irradiate medium and large size AVMs, in the course of
work it became clear that our patients belonged to the high risk group to undergo direct surgical intervention. Only 3 of the treated 56 patients were grade I, and 8 were grade II according to the Spetzler–Martin grading system. The vast majority (44 patients) was grade III and IV, and 1 patient was grade V according to this classification. An attempt of surgical removal of the malformation was undertaken in 3 patients only. In all cases, resection was partial and the AVM remained. An attempt of endovascular embolization was undertaken in 10 patients, with embolization repeated 4 times in one patient. In no patient was it possible to achieve complete exclusion of the AVM using the endovascular technique.

However, the Spetzler–Martin grading system does not play a significant role in predicting the outcome of radiosurgical treatment [42, 43], which was just demonstrated in our work. In 17 cases of complete obliteration, the AVM was grade III and IV by Spetzler–Martin, 5 patients only had grade II. All of the above suggests that in the given group of patients, radiosurgery was the only possible radical treatment technique.

Due to the advance in technical capabilities of devices for irradiation and the emergence of 3D computer systems for planning in the mid-1980s, stereotactic radiosurgery has taken an important place in treatment of inoperable brain AVMs. The complete obliteration rate upon radiosurgery depends on the minimum prescribed dose and malformation volume.

Radiosurgery of small size (up to 10 cm³) AVMs using photon emitters (Gamma Knife and linear accelerator) has demonstrated excellent results: complete obliteration in 70–80% cases [17, 31, 35, 47, 52]. However, the photon radiosurgery results are getting worse as AVM size increases. For AVMs with the volume of more than 15 cm³, complete obliteration by 40 months can be achieved only in 20–36% cases [14, 28, 37, 40]. The results of various photonic series for AVMs of more than 10 cm³ are presented in Table 1.

It is reasonable to use photon irradiation of AVMs of medium and large size, as well as those of complex shapes [16, 32].

Researchers from the Stanford University, on the basis of the synchrocyclotron of Lawrence Berkeley Laboratory (USA), had treated more than 400 patients with AVMs using the Bragg peak of the helium ion beam within the period of 1980–1992. The target volume ranged from 0.3 to 70 cm³. Complete obliteration at 2 years was achieved in 94% of patients with malformations of less than 4 cm³, in 75% with malformations of 4 to 25 cm³, and in 39% with AVMs of more than 25 cm³ [18–21, 33, 34].

At the Proton Medical Research Center, University of Tsukuba (Japan), in 1990–2005, PRS had been performed in 12 patients with AVM size ranging from 30 to 60 mm. The mean dose at the target center was 25.3 GyE. One patient dropped out of the study. Of the remaining 11, complete obliteration was achieved in 9 (81%) patients; partial obliteration of the malformation was obtained in 1 (9.1%), and the malformation remained unchanged in 1 patient. In the study, PRS was conducted in conjunction with endovascular embolization of malformations [54].

Table 1. Efficiency of photon radiosurgery for AVM>10 cm³ according to the data of different authors

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Radiosurgery method</th>
<th>Number of patients</th>
<th>AVM volume, cm³</th>
<th>% of complete obliterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. Miyawaki et al., 1999 [37]</td>
<td>LINAC</td>
<td>37</td>
<td>&gt;10</td>
<td>23</td>
</tr>
<tr>
<td>D. Pan et al., 2000 [40]</td>
<td>Gamma Knife</td>
<td>48</td>
<td>&gt;15</td>
<td>25</td>
</tr>
<tr>
<td>A. Bois et al., 2006 [14]</td>
<td>LINAC</td>
<td>15</td>
<td>&gt;10</td>
<td>20</td>
</tr>
</tbody>
</table>
At Tygerberg Hospital (South Africa), treatment of 64 patients with cerebral AVMs had been performed in 1993–2005 using the horizontal proton beam with the energy of 200 MeV. The mean margin dose was 17.37 GyE (from 10.38 to 22.05 GyE) for 2–3 irradiation sessions. In patients with the AVM volume of ≤14 cm³, complete obliteration occurred in 67% of cases, and in patients with the AVM volume of more than 14 cm³ — in 43% of cases [51].

In our group of patients with the malformation volume of 10–24.9 cm³, complete obliteration was achieved in 46.6% of cases. Table 2 presents the distribution of the percentage of complete obliteration after PRS in our series, depending on the AVM volume.

The presented data demonstrate that irradiation of AVMs with the volume of more than 10 cm³ with protons has a definite advantage over photon radiation.

**Conclusion**

Proton stereotactic radiosurgery is becoming the method of choice when selecting a treatment method for inoperable AVMs localizing near the critical anatomical structures, or having a large (more than 10 cm³) volume. Due to their unique physical properties, proton beams offer an option to form an irradiation field with a sharp gradient of the dose at the field margin, allowing highly conformal irradiation of targets located in the close proximity to the critical structures, without damaging the latter. PRS has the advantage over photon radiosurgery upon irradiation of AVMs with the volume of more than 10 cm³, since it allows one to maintain a sharp gradient at the field margin even in the case of irradiation of large targets.

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**Table 2. Distribution of the percentage of complete obliterations depending on the AVM volume for treatment with PRS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>up to 4.9 cm³</th>
<th>5—9.9 cm³</th>
<th>10—24.9 cm³</th>
<th>&gt; 25 cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>9</td>
<td>16</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Number of complete obliterations, abs. (%)</td>
<td>8 (89)</td>
<td>7 (43.75)</td>
<td>7 (46.6)</td>
<td>1 (16.6)</td>
</tr>
</tbody>
</table>
In connection with the development of the stereotactic technique of ionizing radiation delivery, the experience in proton irradiation of patients with arteriovenous malformations (AVM) of the brain presented by the authors is relevant and interesting. The paper provides the comprehensive description of the irradiation technique and presents the results of the analysis for the treatment of 56 patients with brain AVMs: is treatment justified? Stroke 2007; 38: 325—329.

Despite the overall positive impression, I would like to give a few comments and suggestions that have arisen after reading. Authors’ argumentation of proton irradiation advantages is disputable and needs clarification. It would be interesting to compare these studies to the results presented by the authors and to perform an analysis with allowance for the dose determination mode and dose distribution. 

A.V. Golanov (Moscow)
Microsurgery is widely used today to treat compression of nerve rootlets in the lumbar spine. Despite the minimization of the methods for decompression of nerve rootlets, cicatricial adhesions are formed in all patients who had been operated on. Swelling of nerve rootlet, sponginess, infiltration, and thickening of the epidural fiber are manifestations of postoperative reactive changes in the area of resection of a herniated intervertebral disc. The stage of aseptic inflammation is replaced by the fibroblastic stage by the end of the third week. Soft or dense adhesions emerge between the rootlet and the underlying disc [1, 2]. Fibrosis development is the cause of up to 60% unfavorable outcomes in surgical resection of herniated intervertebral discs [5, 8, 9]. Fibrosis occurs in 100% of reoperations [3]. Many authors report an association between the severity of epidural cicatricial adhesion and pain in rootlets. R. Pawl [12] performed a literature analysis to conclude that epidural fibrosis has clinical manifestation in the case of severe cicatricial adhesion process. J. Ross et al. [10–14] performed a multicenter, randomized, blind study and showed that patients with severe peridural fibrosis suffer from relapsing pain in rootlets 3.2 times more often than patients with mild adhesion process.

The role of autoimmunity in the formation of secondary pain syndrome has been proved in the studies devoted to cicatricial adhesion [7, 9]. A number of methods for prevention and minimization of the sequelae of epidural fibrosis are known. Most of the materials used (both synthetic and natural ones) showed low efficiency for preventing cicatricial adhesion. Hence, it seems rather relevant to study this aspect of the problem.

Materials and Methods

Treatment results were analyzed in 90 patients operated on in 2007–2011 at the Department of Neurosurgery of the Russian Medical Academy of Postgraduate Education at the S.P. Botkin Municipal Hospital. Inclusion criteria were as follows: spinal disc herniation at the same level as the level of syndrome of lumboischialgia or radiculopathy. There were 58 men (64.4%) and 32 women (35.6%). The median age was 48.4±3.6 years (range: 23 to 60 years). All patients had monoradicular symptoms.

In test group 1 (30 patients), biodegradable membrane was used to isolate a nerve rootlet from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In group 2 (30 patients), autologous fat tissue harvested during the approach was used to isolate a nerve rootlet from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In the group 3 (control group) consisting of 30 patients, no prevention of cicatricial adhesions was performed after decompression surgery.

In the test group patients, the L5–S1 level was affected most frequently (18 patients (60.0%)); the L4–L5 was affected less frequently (12 patients (40.0%)). In group 2, the most frequent cases (56.1%) of discoradicular conflict were revealed at the L5–S1 level with compression of the S1 rootlet; the L4–L5 level was involved rarely (42.9%). In group 3, discoradicular conflict was most frequently found at the L5–S1 level (72.6%) with compression of the S1 rootlet. The patients were divided according to the side of affected nerve rootlet as follows: 45 (50%) patients had left-sided compression radiculopathy, while 42 (41%) patients had right-sided compres-
sion radiculopathy. Three (3.3%) patients had central compression with right accent. The differences in age, gender, clinical symptoms, disease duration, and damage severity were negligible between the patient groups. Before hospitalization all patients underwent conservative treatment, which turned out to be inefficient.

Routine examination was performed in all patients, including functional radiograms of the lumbosacral spine, MRI in dynamics before and after the intervention (usually 3 months after the surgery). All intervertebral disc herniations were conventionally classified as median, paramedian, posterolateral, and foraminal. Pain syndrome intensity was estimated according to the Visual Analogue Scale (VAS). The Oswestry Disability Index was used to estimate the quality of life.

Statistical analysis of the data was performed using Windows Statistica 6 software. The relative values, mean and standard deviations of the mean were calculated; the significance level was determined using Student’s tests.

ElastoPOB biodegradable membrane was used to prevent cicatrical adhesions in the test group. This membrane is manufactured from bacterial biopolymer having very low antigenic properties (technical specifications TU 9398-002-54969743-2006). In human body, collagen having this structure is relatively quickly resorbed and degraded to simpler compounds, which are subsequently excreted or used in cellular biosynthesis processes. This material also possesses hemostatic properties.

In order to improve visualization of the installed biodegradable membrane, T2-weighted MRI images (TR2500, TE 118) were supplemented with proton density-weighted images with reduction of the MR signal from fat tissue in addition to the conventional T1- and T2-weighted imaging. The scan mode is based on the inversion–recovery pulse sequence in TR1940, TE 31.3. The selected values of FOV 20/20 of 4 mm slice thickness with 1 mm scan step were the same in both scanning modes. Supplementation of the conventional T2-weighted images with PDFS-mode images allowed us to obtain additional information on interaction between the membrane and the surrounding structures by reducing the MR signal from fat tissue; thus, the membrane position could be determined more precisely (Fig. 1).

Results and Discussion

ElastoPOB biodegradable membrane was used to isolate the following structures in the test group after decompression of neural structures: neural rootlet and dura mater from the adjacent bone and ligament structures both at the anterior and posterior sides to completely isolate the neurovascular bundle from involvement in secondary fibrosis.

The ElastoPOB biopolymer has already been proved to be efficient in cardiac and abdominal surgery, where it reduced the severity of cicatrical adhesion changes in the area of membrane grafting [4, 6, 9]. In neurosurgery this material is being widely used in surgery of the peripheral nervous system [7]. The present study is based on assumptions of possible efficiency of using the membrane in prevention of post-discectomy cicatrical adhesions. Efficiency of using this material has been proved by animal experimental studies, as well as in clinical studies for the interventions for peripheral nerves [7].

The commonly used method for prevention of cicatrical adhesions— isolation of neural structures by autologous fat tissue— was implemented in group 2. Fat tissue was harvested at the approach stage, soaked in prednisolone solution (30 mg), and arranged around the neural structures. In group 3 (control), standard microdiscectomy was performed without any prevention of epidual fibrosis.

The mean period of the catamnesis was 1.8 years (from 6 months to 4 years). The Oswestry Disability Index was used to estimate the quality of life; the Visual Analogue Scale (VAS) was used to estimate the intensity of pain syndrome in postoperative period. Clinical manifestations of radiculopathy and dynamics of MRI data of the lumbosacral spine before and after the surgery were also assessed (Fig. 2).

MRI was performed after 10 days. T2-weighted images in the PDFS-mode allowed one to obtain additional information on interaction between the membrane and the adjacent structures by decreasing an MR signal from the fat tissue and to more precisely determine the membrane position. The S1 rootlet was isolated from the adjacent structures (anterior ones, including posterior longitudinal ligament; the entry site of hernia compression; posterior surfaces of the vertebral bodies; lateral structures, including facet joints and processes; posterior ones, including the muscles and ligament apparatus) by the membrane. Six months after microdiscectomy, post-
operative changes (isolation of the neurovascular bundle from the adjacent structures and cicatricial tissues) were visualized.

No unwanted sequelae of using the biodegradable membrane were found.

All patients had positive results of surgical treatment at the moment of hospital discharge. Postoperative catamnestic follow-up was performed. Patients’ condition was examined at the moment of discharge, 6 and 12 months after surgery, and then annually.

Regression of rootlet pain symptoms was found in 30 (100%) patients of the test group. Out of 16 patients with sensitivity disorders, complete regression was found in 12 (39.6%) patients; partial regression — in 6 (19.8%). The disorders remained at the same level as before the surgery in 2 (6.6%) patients after 6 months. Movement disorders detected in 7 (23.1%) patients had completely regressed by the moment when the long-term outcomes were assessed.

Regression of rootlet pain symptoms was found in 30 (100%) group 2 patients treated with autologous fat tissue. Out of 15 patients with sensitivity disorders, complete regression was found in 11 (36.3%) patients; partial regression — in 3 (9.9%). The disorders remained at the same level as before the surgery in 2 (6.6%) patients after 6 months. Movement disorders found in 5 (16.5%) patients had completely regressed in all patients by the when the long-term outcomes were assessed.

Significant differences in the VAS score before the surgery and after discharge ($p<0.00001$) were detected in all three groups. A significant improvement was subsequently revealed between values of the test group and both control groups at the discharge and 6 or 12 months later ($p=0.02$). The mean values of pain syndrome intensity (for the rootlet pain syndrome in a leg) as judged by VAS decreased from $7.07\pm1.62$ to $1.53\pm0.68$; after 6 months to $1.42\pm0.5$, and after 1 year — to $1.35\pm0.5$. The Oswestry Index values were $55.8\pm19.9$ before the surgery and $15.8\pm6.4$ 6 months after the surgery. The VAS data suggest a more significant decrease in the pain syndrome at the long-term period in the test group when compared to the control groups (test group — $1.23—0.9—0.8$; group $2—1.23—1.2—1.1$; group $3—1.53—1.4—1.3$) (Fig. 3).

In the test group, the Oswestry Index values before the surgery were $51.7\pm18.2$ ($m=3.3$), in group 2 — $51.3\pm16.6$ ($m=3.0$), in group 3 — $55.8\pm19.2$ ($m=3.5$) with significance $p<0.00001$. In the dynamic observation 6 or 12 months after the surgery, the Oswestry Index values were as follows: in the test group — $12.7\pm7.3$ ($m=1.3$), in group 2 — $15.1\pm10.0$ ($m=1.8$), in group 3 — $15.8\pm6.4$ ($m=1.2$). Therefore, significant differences in the Oswestry Index values were found before and after the surgery in the groups studied ($p<0.00001$). However, there were no significant differences 6 or 12 months after the surgery ($p>0.05$) (Fig. 4). A better tendency was observed in the test group; however, it was statistically insignificant (Fig. 4).

In 2 (2.2%) cases, a relapse of the rootlet pain syndrome was observed after 1.8—2.2 years after the primary surgery and was accompanied by recurrence of disc herniation (detected by MRI); reoperation was needed. One of these patients was from the test group, the other
one was from the control group. In both cases, fibrosis tissue samples from the peridural area were histologically studied.

A noteworthy feature of reoperation was that a patient who had undergone prevention of cicatricial adhesions using biodegradable membrane had a clear dissection plane when the dura mater and neural rootlets were detached from the fibrosis tissue despite the typical cicatricial process in interlaminar and intermuscular areas. This fibrosis tissue was thin, soft, and easily dissectible. No fragments or traces of the biodegradable membrane were found during the intervention 1.5 years after the primary surgery. Meanwhile, typical cicatricial adhesions with rigid fusion of the fibrosis tissue with dura mater and neural rootlet were found in a patient from the control group. Peridural fibrosis tissue samples were taken for histological studies (Fig. 5).

The results of in vivo histological studies of fibrosis tissue samples taken during the reoperation (secondary microdiscectomy) when biodegradable membrane was used were as follows: thin loose-fibrous hyalinized cicatricial connective tissue at the contacts with neural structures and traces of the adjacent fiber, in the periphery transition to the typical coarse-fibrous fibrosis tissue. The results of in vivo histological studies of fibrosis tissue samples taken during reoperation without epidural fibrosis prophylaxis were as follows: epidural fibrosis tissue and coarse-fibrous connective tissue with sclerosis and hyalinosis, degenerative changes in connective tissue.

Taken together, the results of the study and reoperation data suggest that severity of fibrotic changes in the area of discoradicular conflict after surgery decreases when neural rootlet and dura mater are isolated with the biodegradable membrane ElastoPOB, which creates favorable conditions for functioning of neural structures.

Fig. 3. Diagram of the pain syndrome intensity according to VAS in dynamics.

Fig. 4. Diagram of the Oswestry Index values.

Fig. 5. Histological view of periradicular cicatricial tissue samples taken during reoperation in patients of the test (a) and control (b) groups. Haematoxylin and eosin staining. ×100.
Conclusions

1. Our study and literature analysis indicate that cicatricial adhesions are found after microdiscectomy in all patients. In several patients, this problem becomes the first-priority one in worsening the quality of life and long-term results. The dynamics of the VAS data in short- and long-term results in the control group of patients without prevention was 0.13–0.23.

2. The catamnestic data collected over the period from 6 months to 4 years suggest the following: the Oswestry Index values were almost equal in all three groups: the VAS data suggest a more significant decrease in the pain syndrome at the long-term period in the test group as compared to the control groups (test group – 1.23–0.9–0.8; group 2 – 1.23–1.2–1.1; group 3 – 1.53–1.4–1.3).

3. A method suggested for prevention of epidural fibrosis after lumbar microdiscectomy provided barrier function without complications in the area of discocartilaginous conflict. The most significant changes were observed during the first 6 months after the surgery (VAS dynamics 0.33 compared to 0.03–0.13 in other groups). Therefore, the test group shows a trend to improvement of the results, which can be result from a decrease in periradicular cicatricial adhesions due to the use of biodegradable material.

4. MRI, VAS, and the data of reoperations prove efficiency of using the biodegradable material to manage periradicular cicatricial adhesions.

REFERENCES


Commentary

The relevance of the present study is beyond any doubt. Prevention of cicatricial adhesions in postoperative period could significantly improve the results of surgical treatment in patients with disc hernias in the lumbar spine by reducing the rootlet pain syndromes. Without any doubt, the key factor in preventing cicatricial adhesions is minimization of interventions: careful planning of the surgical approach, resection of only those structures (bones and ligaments) that are essential for hernia removal and complete decompression of neural structures. Magnifying equipment (such as an endoscope or a microscope) is required for such purposes. The second important factor is thorough hemostasis. Many authors have demonstrated that the presence of even clinically insignificant hematicoma in the postoperative wound leads to the formation of cicatrices between the dural sac, the rootlet, and the adjacent tissues. In almost all reoperations, cicatricial adhesions are found between the dura mater, rootlets, and the adjacent tissues. However, the presence of cicatricial adhesions does not necessarily have corresponding manifestations.

The authors have analyzed the results of treatment of lumbar microdiscectomy in 90 patients operated on in 2007–2011 at the Department of Neurosurgery of the Russian Medical Academy of Postgraduate Education within S.P. Botkin Municipal Hospital. In the test group (30 patients), biodegradable membrane was used to isolate a nerve rootlet from the adjacent tissues prevent cicatricial adhesions after decompression surgery. In group 2 consisting of 30 patients, autologous fat tissue harvested during approach was used to isolate the nerve rootlet.
from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In group 3 (control) consisting of 30 patients, no prevention of cicatricial adhesions was performed after decompression surgery.

Having analyzed all three groups, the authors obtained the data strongly suggesting that the use of autologous fat tissue or (which is more effective) biodegradable membrane is reasonable for prevention of cicatricial adhesions. However, the leading Russian hospitals of spine surgery lack experience with using this biodegradable membrane. Final conclusions can only be made after multicenter research involving large groups of patients is conducted.

N.A. Konovalov (Moscow)
Intraarterial Administration of Verapamil to Treat Cerebral Vasospasm in a Patient with Acute Subarachnoid Hemorrhage from an Aneurysm: Case Report

K.G. MIKELADZE, SH.SH. ELIAVA, O.D. SHEKHTMAN, A.YU. LUBNIN, T.F. TABASARANSKY, S.B. YAKOVLEV

N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow, Russia

Cerebral vasospasm is one of the major causes of cerebral ischemia and neurological deficits in patients after subarachnoid hemorrhage (SAH) from an aneurysm. According to the angiography data, vasospasm in the acute stage of the cerebral aneurysm rupture is detected in 50–70% of cases, and the risk of developing vasospasm-related delayed ischemia is 19–46%. One of the new trends in treating cerebral vasospasm is intraarterial administration of calcium channel blockers. The article presents a clinical case of selective intraarterial administration of verapamil for the treatment of cerebral vasospasm in a female patient after severe subarachnoid parenchymal hemorrhage from the internal carotid artery bifurcation aneurysm with a good clinical outcome. The prospects of endovascular treatment of cerebral vasospasm are discussed.

Keywords: cerebral vasospasm, intraarterial administration of verapamil.

Cerebral vasospasm is one of the major causes of cerebral ischemia and neurological deficit in patients after subarachnoid hemorrhage (SAH) from an aneurysm. According to angiography data, vasospasm in the acute phase after cerebral aneurysm rupture is detected in 50–70% of cases, and the risk of developing vasospasm-related delayed ischemia is 19–46% [3]. Prevention of complications caused by vasospasm is the major direction in treatment of patients with hemorrhage during the acute phase. Symptoms of cerebral ischemia may occur in the first 72 h after SAH [3, 6, 12].

Up to this point, hypertensive-hypervolaemic-haemodilution (triple-H) therapy or its modifications were the main treatment regimens for patients with vasospasm. However, as shown by subsequent clinical experience, this therapy has several drawbacks and was ineffective in more than 20% of patients [3]. Endovascular procedures (angioplasty and intraarterial administration of calcium channel blockers) are promising modern methods for treating cerebral vasospasm, which can reduce the risk of cerebral ischemia and the frequency of development of persistent neurological deficit. The published data show the effectiveness and relative safety of endovascular techniques. Development of the vasospasm management protocol in patients with the acute phase following aneurysmal hemorrhage with the use of endovascular techniques is the extremely important and urgent task. This paper describes a case of selective intraarterial administration of verapamil to treat cerebral vasospasm in patients, who had a severe subarachnoid and parenchymal hemorrhage resulting from rupture of an internal carotid artery (ICA) bifurcation aneurysm.

Clinical case

A 66-year-old patient Kh. was admitted to the N.N. Burdenko Neurosurgical Institute on the third day after intracranial hemorrhage from an aneurysm (Hunt and Hess grade V). Upon admission, the consciousness level corresponded to coma II, body temperature was 38.0°C. The patient received mechanical ventilation (IPPV). The hemodynamics was instable with a tendency to arterial hypotension. Arterial pressure was maintained 120–140/79–85 mmHg by intravenous administration of vasopressors. Computed tomography of the brain revealed an intracerebral hematoma in the right temporal lobe with subarachnoid hemorrhage and brain edema (Fig. 1). According to cerebral angiography, an arterial saccular aneurysm 4.2×3.7 mm in size was detected in the area of ICA bifurcation. Given the severity of the condition, a ventricular drainage system with an intracranial pressure (ICP) sensor (ICP at that time was 30–32 mmHg) was installed.

The next day (day 5 after SAH) after patient’s condition stabilized, she underwent surgery: endovascular occlusion of the right ICA bifurcation aneurysm with microcoils (Fig. 2). Patient’s postoperative condition was satisfactory; angiography showed moderate arterial stenosis.

The patient received intensive therapy in the intensive care unit. Predominant involvement of the left limbs caused by surface sedation was observed in the neuro-
logical status. ICP was 12–18 mmHg, with brief episodes of rising up to 30 mmHg, which were cured by administration of osmodiuretics. On day 2 after surgery (day 6 after SAH), transcranial Doppler ultrasound (TCD) examination revealed an increase in blood flow velocity (BFV) (Table 1).

Taking into account the progression of cerebral vasospasm and a high risk of ischemia in the right ICA system, a decision was made to perform a selective intraarterial administration of verapamil to the patient. During the procedure by the standard Seldinger technique, the ICA was catheterized distally from the ICA bifurcation on the spasm side (right) and verapamil was slowly administered during 30 min at a total dose of 25 mg. As the drug was injected, a transient increase in ICP to 30 mmHg was observed; ICP decreased to 12 mmHg by the end of the procedure (along with open ventricular drainage). No complications were observed. According to the control TCD, BFV in the middle cerebral artery decreased 60 min after the procedure (Table 2).

![Fig. 1. CT scan at admission to the hospital: intracerebral hematoma of the right temporal lobe is detected.](image1)

![Fig. 2. Carotid angiogram before surgery (a). ICA bifurcation aneurysm of posterior localization (shown with an arrow). Angiogram after occlusion of the aneurysm with microcoils (b).](image2)

### Table 1. TCD data (BFV, cm/s) on day 2 after surgery (day 6 after SAH).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Right</th>
<th></th>
<th></th>
<th>Left</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td>Systolic</td>
<td>Diastolic</td>
<td></td>
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<tr>
<td>MCA</td>
<td>223</td>
<td>72</td>
<td>160</td>
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<td>139</td>
<td>34</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ICA</td>
<td>61</td>
<td>22</td>
<td>61</td>
<td>18</td>
<td></td>
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<tr>
<td>MCA (average)</td>
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<td></td>
<td>86,7</td>
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<tr>
<td>ICA (average)</td>
<td>35</td>
<td></td>
<td>32,33</td>
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<tr>
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<td>1,27</td>
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<tr>
<td>Resistance index</td>
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<td></td>
<td>0,69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lindegaard index</td>
<td>3,5</td>
<td></td>
<td>2,68</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Here, in Tables 2 and 3: MCA – middle cerebral artery, ACA – anterior cerebral artery, VA – vertebral artery, ICA – internal carotid artery.
Sedation was gradually discontinued as stable ICP parameters and hemodynamics were attained on day 3 after surgery (day 4 after SAH); the patient became available for contacts. Symptomatic and restorative therapies were performed; the patient was gradually switched to spontaneous breathing. Regression of left-sided hemiparesis was observed in the patient’s neurological status. Postoperative increase in BFV was no longer observed by TCD (Table 3).

At the time of discharge, the patient’s general condition was relatively satisfactory. Neurological condition: the patient was in clear consciousness, answered questions, executed commands, could orient well in time, space, and her own identity. Pupils D=S, photoreaction was alive, face was symmetrical, swallowing and phonation were not disturbed. No focal motor or sensory loss was observed. The patient was discharged in a relatively satisfactory condition. The total length of hospital stay was 30 days.

Discussion

Verapamil has been used long enough in patients with coronary vessel spasm. According to many authors, it is a relatively safe and effective treatment for refractory vasospasm of coronary vessels. Availability and low price are also the advantages of this drug [1–3, 12].

The data that intraarterial administration of verapamil improves the angiographic presentation of vasospasm were published earlier [3, 8, 12]. Verapamil has the most favorable profile among all the drugs used, although there have been reports on using other drugs from the group of calcium channel blockers (nicardipine, diltiazem) and papaverine [8] for the same purpose [3, 6, 11]. According to the literature, papaverine is characterized by a fairly high rate of complications.

The technique employed in our report was similar to one described in the study by P. Jun et al. [3]. The authors analyzed the results of endovascular treatment in 189 patients with refractory vasospasm in the acute phase after aneurysm rupture. 286 intraarterial injections of verapamil and 59 combined treatment procedures (administration of verapamil in combination with angioplasty) were performed in this series of patients. Verapamil dosage depended on vasospasm severity and was 2–30 mg per vessel and 3–55 mg per procedure. Repeated administration was conducted in 102 (54%) patients in cases of refractory vasospasm. Complications directly caused by endovascular procedure developed in 6 patients and led to neurological deterioration in two of them. Favorable and adverse treatment outcomes were observed in 115 (61%) and 55 (29%) patients, respectively; 16 patients died due to cerebral causes, 3 patients died of associated complications.

Our report provides the first in Russian scientific literature description of the clinical case of successful endovascular treatment of cerebral vasospasm (developed after a severe SAH in a patient with a right ICA bifurcation aneurysm) using intraarterial verapamil administration.

| Table 2. TCD data (BFV, cm/s) 60 min after selective intraarterial verapamil administration in the right internal carotid artery |
| --- | --- | --- | --- |
| Parameters | Right | Left |
| MCA | 185 | 61 | 140 | 50 |
| ACA | 140 | 72 | 146 | 70 |
| VA | 52 | 17 | 52 | 19 |
| ICA (average) | 102,33 | 80 |
| ICA (average) | 28,67 | 30 |
| Pulsatility index | 1,21 | 1,12 |
| Resistance index | 0,67 | 0,64 |
| Lindegaard index | 3,57 | 2,67 |

| Table 3. TCD data (BFV, cm/s) on day 6 after the surgery (day 10 after SAH) |
| --- | --- | --- | --- |
| Parameters | Right | Left |
| MCA | 200 | 100 | 120 | 40 |
| ACA | 120 | 60 | 130 | 60 |
| VA |  |  |  |  |
| ICA | 60 | 30 | 60 | 35 |
| MCA (average) | 133,33 | 66,67 |
| ICA (average) | 40 | 43,33 |
| Pulsatility index | 0,75 | 1,2 |
| Resistance index | 0,5 | 0,67 |
| Lindegaard index | 3,33 | 1,54 |
Conclusion

Endovascular treatment methods play an important, sometimes unique, role in modern vascular neurosurgery, especially in surgery of giant aneurysms and aneurysms of the posterior parts of the circle of Willis. Experience accumulated in the literature demonstrates that endovascular treatment of vasospasm is a relatively safe method with a low rate of complications both using angioplasty and intraarterial verapamil infusion. The publications of the leading foreign endovascular surgeons focused on this issue need further research and need to be adapted to Russian clinical practice. Preliminary results give grounds for concluding that the endovascular technique, in contrast to other methods for treating vasospasm, can be an effective means of reducing the lethality and disability in patients who underwent hemorrhage from an aneurysm.

REFERENCES


Commentary

Vasospasm caused by subarachnoid hemorrhage (SAH) develops in 70—100% of patients with cerebral aneurysm rupture. Symptomatic spasm occurs in 20—30% of patients and is accompanied by a 2–3-fold increase in lethality. In this connection, the subject matter of the article is extremely topical.

The authors presented a very interesting observation of vasospasm treatment by selective intraarterial verapamil administration. The treatment allowed the surgeons to bring the patient admitted to the hospital in a deep coma to her normal life. The clinical case is described in the traditional manner and is well illustrated with tables and figures. The study is very interesting, relevant, and essential to improve the quality of intensive care in patients with vasospasm due to the cerebral aneurysm rupture and can be published.

S.S. Petrikov (Moscow)
Radical Removal of a Malignant Mediastinal Hemangioendothelioma with Restoration of the Main Blood Supply to the Brain


1N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow; 2Blokhin Russian Cancer Research Center, Moscow, Russia

A 46-year-old man with unverified anterior superior mediastinal tumor, which was diagnosed in 2010, sought medical care at the Cancer Research Center of the Russian Academy of Medical Sciences in October 2012. Progressive compartment syndrome of the superior vena cava was observed. CT, MRI, angiography, histological and cytological examination of biopsy material failed to confirm the morphological structure of the tumor. Removal of the tumor with bifurcation of the brachiocephalic trunk prosthetics was performed. Immunohistochemical (IHC) study verified malignant hemangioendothelioma.

Keywords: tumors of the mediastinum, hemangioendothelioma, neurophysiological monitoring.

Mesenchymal tumors may have various histological forms. Vascular tumors (32.6%), adipose tissue tumors (28.8%), fibroblastic and fibrohistiocytic neoplasms (15.3%) comprise a relatively large group, while only sporadic cases have been reported for the other types of tumors [3]. Hemangioendothelioma is a tumor originating from the vascular tissue with different degrees of differentiation: from benign (hemangiomas) [17, 19] to malignant ones (angiosarcomas). Hemangioendothelioma develops in various organs: lungs, liver, spleen, bones; mediastinal hemangioendotheliomas are rather rare.

Clinical manifestations of the tumor are accompanied by non-specific symptoms or the absence of symptoms. Mediastinal hemangioendothelioma is rarely discussed in light of differential diagnosis of mediastinal tumors.

The international experience in treatment of these tumors is rather scant and mostly represented by sporadic clinical cases. Retrospective reviews describe small patient groups [17–19, 22, 23, 25].

Clinical case

A 46-year-old patient received outpatient care at the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences, over the period from October 22, 2012 until January 10, 2013.

The patient was admitted to the hospital with preliminary diagnosis of malignant schwannoma of the anterior superior mediastinum. His condition was assessed after biopsy of the tumor performed on November 3, 2013. The patient underwent 10 courses of polychemotherapy, beam therapy (TBD 50 Gy; December 8, 2012) at place of residence. Compartment syndrome of the superior vena cava (SVC), right-sided thrombosis of the internal jugular vein, and subcompensation of cerebral blood flow were observed.

When admitted, the patient complained of bursting sensation in his head under insignificant physical activity, hoarse voice, dysphagia, vision impairment, headache, and dizziness.

Past medical history. In November 2010, the patient started to have a bursting sensation in head and eyes when bending his body. He was examined at the place of residence. CT revealed an anterior mediastinal tumor. In February 2011, the patient underwent left-side thoracotomy and tumor biopsy. After re-examination of histological specimens at the Regional Oncology Clinics, the patient was diagnosed with malignant schwannoma. He was given two courses of polychemotherapy with vincristine, doxorubicin, cyclophosphamid, and dacarbazine, which showed no effect. The chemotherapy regimen was changed. Over the period from July 2011 till April 2012, the patient received 8 courses of polychemotherapy with doxorubicin, mesna, and dacarbazine phosphamide, which also showed no effect. Since June 2012, the patient noted the symptoms of dysphagia, hoarse voice, and vision impairment. Over the period between July 13, 2012 and August 17, 2012 he received a course of gamma therapy (TBD of 50 Gy, SBD of 2 Gy) for the mediastinal tumor at the Republican Oncology Clinics; the CT data showed the minimal clinical effect. The patient was referred to the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences, to receive consultation and determine the further treatment strategy.

Patient’s condition upon admission was relatively satisfactory. Height 170 cm; body weight 67 kg.

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e-mail: Wlukshin@nsi.ru
Examination revealed swelling of the face and neck (Fig. 1a) and pronounced neck vein swelling (Fig. 1b), which became stronger under physical activity; reddening of the face and neck areas under physical activity and when bending forward (compartment syndrome of the SVC), occasional pulse deficit of the right radial artery. The veins of the anterior thoracic wall both on the left and right sides were dilated.

CT scan obtained on October 15, 2012 (Fig. 2) showed a 3×4.5 cm tumor node visualized in the superior mediastinum along the right common carotid artery (CCA) and the right subclavian artery, as well as in the starting portions of the brachiocephalic trunk. The arterial vessels ran along the posterior surface of the node; only the CCA ran in the bulk for 2 cm; the SVC was stenosed (affected) and ran along the anterolateral surface. The subcutaneous veins and the thoracic vein were dilated. The left brachiocephalic vein was stenosed; no blood circulation was detected in it. Sporadic foci-like nodularities up to 0.3 cm in size (fibrosis?) were detected in the parenchyma of both lungs. Bronchial lumina were unchanged. Conclusion: a tumor node along the mediastinal vessels (a primary tumor? a metastasis?).

Histological conclusion made on October 11, 2012: small fragments of fibrous connective tissue with myxomatosis foci containing cells with oblong nuclei and thin collagen fibers, hemorrhage spots, and hemosiderophages were detected in the specimens. Such regions may occur in case of secondary (degenerative) changes in peripheral nerve sheath tumor (e.g., schwannoma). However, the data were rather scant, making the judgments of the tumor nature hypothetical. The immunohistochemical test did not refine the diagnosis (providing a positive response only to anti-vimentin antibodies).

Endoscopic examination included fibrobronchoscopy (October 29, 2012); the right side of the larynx was immobilized during the phonation. The mucous membrane...
of the larynx was hyperemic. The tracheal lumen was wide; the tracheal rings were well-differentiated. The vascular pattern was enhanced. The carina was straight; its base was non-dilated. Examination of the both halves of the bronchial tree revealed no tumor pathologies. The bronchial lumina accessible for examination were unobstructed. The mucous membrane was pink, smooth, and shiny. There was a small amount of mucous contents in the bronchial lumen. Conclusion: paresis of the right half of the larynx. No tumor pathology was revealed in the tracheobronchial tree.

Fibroesophagogastroduodenoscopy was performed on October 29, 2012. No changes were detected in the esophagus lumen; the walls were flexible; the mucous membrane in the upper and medium thirds of the esophagus was paste-like. The mucosal rosette at the cardiac orifice was flexible and closed completely. The stomach contained a moderate amount of mucus. The lumen was unchanged; the walls were flexible; the mucous membrane was pale pink. The strongly curved folds were soft and mobile. The bulb and postbulbar portions of the duodenum were unchanged. No biopsy was performed. Conclusion: visual signs of venous stasis at the levels of the upper and medium thirds of the esophagus. No pathological changes were observed in the stomach and duodenum.

MRI was performed on October 24, 2012: no accumulation of a contrast agent in the brain was reported. No reliable data on disturbance of the architecture of cerebral arteries were obtained. The ventricular system was neither dilated nor displaced. During the examination of the neck arteries were obtained. The ventricular system was neither reliable data on disturbance of the architecture of cerebral circulation of a contrast agent in the brain was reported. No changes were observed in the stomach and duodenum.

Ultrasonographic examination performed on October 9, 2012: no signs of distant metastases were revealed.

Ultrasonographic examination performed on October 26, 2012: the common carotid arteries were linear. The intima–media complex thickness was 0.5 mm. No signs of stenosis or occlusion were revealed. The blood stream was symmetrical. The vertebral arteries were passable, without any signs of stenosis or occlusion. Thrombotic masses (0.4×0.4 in size; up to 3.0 cm long) were visualized on the right side of the lumen of the internal jugular vein; the blood flow was mapped above. The superficial and deep veins of the lower extremities were passable on both sides over the entire length and compressible; their lumen was unobstructed; the blood flow was mapped. Conclusion: local right-sided thrombosis of the internal jugular vein. No data on thrombosis of the veins of the lower extremities were obtained.

Magnetic resonance angiography of cerebral vessels in the reformation mode revealed signs of anterior communicating artery and right-side posterior communicating artery. Tentative clamping of the right CCA under control of duplex scanning and simultaneous monitoring of the linear velocity of blood flow (LVBF) in the middle cerebral artery (MCA) at the right side resulted in a decrease in LVBF in the right MCA from 75 to 40 cm/s followed by an increase in LVBF to 45–50 cm/s 1 min after the clamping. No focal symptoms emerged during the 2–3 min of clamping. Thus, signs of subcompensation of the cerebral blood flow were caused by clamping the right CCA according to the data of clinical and instrumental examination. Decision regarding temporary shunt placement when performing reconstruction of the CCA should be made intraoperatively according to the data of neurophysiologic ultrasound monitoring. Patient’s condition was discussed at the clinical conference at the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences. Surgical treatment was recommended. During the preoperative preparation, the patient received several consultations from Academician M.I. Davydov and vascular neurosurgeons working at the N.N. Burdenko Neurosurgical Institute.

The surgical treatment was carried out on November 8, 2012 by surgeons M.I. Davydov, V.A. Sobolevsky, L.A. Nikulichev, D.Yu. Usachev, S.S. Gerasimov, V.A. Lukshin, and anesthesiologist V.E. Gruzdev.

Radicality of surgical intervention: resection of the anterior mediastinal tumor and prosthetics of the brachiocephalic arterial trunk, CCA, and the subclavian artery was performed. Resection of SVC and the right clavicle was carried out through a combined transternal approach.

Surgery course: partial manubrio-sternotomy along the 3rd right intercostal space in combination with the “collar” approach. The sternocleidomastoid muscle was isolated and transected. Resection of two thirds of the right clavicle was performed followed by pericardiotomy.

A 5×6 cm tumor node infiltrating in the mediastinal pleura was visualized during the revision in the upper mediastinum along the right CCA and right subclavian artery, as well as in the initial portions of the brachiocephalic trunk. Arterial vessels ran in the nodular bulk, while the SVC was stenosed (affected) and ran along the anterolateral surface. The subcutaneous veins and the thoracic vein were dilated. The left brachiocephalic vein was narrowed; no blood flow was detected in it. Mediastinal adipose tissue was dense. The left brachiocephalic vein was isolated and ligated.

The SVC was mobilized by being resected in its distal potion and at the level of the jugular vein in the proximal portion using an US30 surgical stapling instrument.

The tumor with the great vessels (the brachiocephalic trunk, the right CCA, and the right vagus nerve) was
mobilized. The vessels were isolated and a tourniquet was applied (Figs. 3, 4).

The right vertebral artery was visualized and a tourniquet was applied.

The tumor was resected together with the mobilized vessels.

Arterial vessels were reconstructed using a Gore-Tex bifurcation graft (Figs. 5a, b).

Radical surgery was performed. The total duration of the surgery was 5 h 30 min. The vascular grafting stage included multimodal neurophysiological monitoring (transcranial ultrasound dopplerography with detection of the MCA on the right side and cerebral oxymetry (CO) [6, 14]. Taking into account the pattern of compensation for cerebral circulation under conditions of moderate arterial hypertension (reduction of LVBF from 80 to 60 cm/s after the CCA was clamped, while the CO indicators remained unchanged), a decision was made to perform the main stage of reconstruction without using a temporary intraluminal shunt. The stage of clamping the right CCA took 26 min. The stage of clamping the right subclavian artery took 40 min. The total blood loss was 2500 ml; 1000 ml of autoblood was replaced using a Cell Saver system. The patient was awakened and extubated while lying on the operating room table; no signs of neurological deficit were revealed.

Features of the anesthetic support

The main task of an anesthetist during the surgeries involving interventions for the great cerebral vessels is to maintain adequate cerebral perfusion pressure. It is extremely important to prevent increased levels of brain metabolism and increased myocardial load [9].

The procedure of combined multimodal anesthesia, which is commonly used in most European clinics and in the Russian Cancer Research Center, was selected. This procedure allows one to perform well-controlled anesthetic support of various trauma surgeries of different duration and localization [1, 8].

To ensure perioperative anesthesia, an epidural catheter was placed at the Th2—Th3 level [24]. A ropivacaine (Naropin), fentanyl, and adrenaline mixture was infused through the catheter.

After anesthetic induction with barbiturates, the anesthesia was maintained by sevoflurane inhalation. This inhaled anesthetic agent allows easy, prompt, and safe control of anesthetic depth within a wide range at any stage of the surgery [5].
There are special requirements to vital function monitoring when performing such complex surgeries. The standard set of parameters (12-lead ECG, SpO₂, HBR, and complete blood gas analysis) was supplemented with invasive monitoring of blood pressure (BP) and controlling the EEG parameters according to the entropy values. Neurophysiological monitoring prevented the development of cerebral ischemia at the stages of clamping and replacing the right CCA. With allowance for the international recommendations, the normal or slightly elevated level of BP was maintained [15, 16, 20].

The adequate and continuous venous approach was ensured by a femoral vein catheter. Blood from the surgical wound was collected by a reinfusion device. The combination of these measures ensured the smooth intraoperative course and possibility of early extubation of the patient on the operating room table without any signs of neurological disorders.

Fig. 6 shows the indicators of cerebral oximetry measured separately for each hemisphere.

Fig. 7 shows the stability of the main (“non-specific”) indicators of monitoring.

Morphological examination of the surgical material (November 19, 2012)

The neoplasm mostly consists of dense fibrous tissue with thin collagen fibers, fibroblast- and histiocyte-like cells spreading to the arterial walls (mainly near the outer tunic — the adventitial tunic) (Fig. 8) and propagating to the venous wall and obliterating its lumen. Cell aggregates with round-shaped and oblong nuclei localize in some spots of the fibrous tissue; the periphery of these aggregates is characterized by hematomas of various prescription, lymphohistiocytic infiltration, and deposition of calcium salts. A fragment of adipose tissue contained lymphatic nodules without tumor growth signs. Conclusion: tumor histogenesis could not be verified based on the light microscopy data only. An immunohistochemical examination was required to determine the tumor type.

An immunohistochemical examination was performed on November 27, 2012 to refine the diagnosis (blocks...
39014/12 — paraffin blocks obtained before radiosurgery) using a broad panel of antibodies against vimentin, desmin, Ki-67, S100, CD34, CD31, β-catenin, CD57, GFAP, CD68, CD117, CD99, bcl2, α-antitrypsin, FAP, type IV collagen, chromogranin, synaptophysin, HMB-45, SMA, and caldesmon. Expression of CD34, CD31, type IV collagen was detected in the tumor cells. No expression of vimentin, desmin, S100, β-catenin, CD57, GFAP, CD68, CD117, CD99, bcl2, α-antitrypsin, FAP, chromogranin, synaptophysin, HMB-45, SMA, and caldesmon was detected. Conclusion: with allowance for the morphological and immunohistochemical patterns (extended sclerotic fields in the tumor, which are associated with the previous treatment), the clinical examination data, and features of the disease course, this tumor should be regarded as a transitional epithelioid hemangioendothelioma (Ki-67 labeling index was 5%).

Postoperative period

The patient stayed at the intensive care unit for 4 days and was subsequently transferred to the thoracic department. Abundant serous discharge (up to 600 ml per day) via the mediastinal drainage was observed up to December 1, 2012, when the amount of the discharge started to decrease. The drainage was removed on December 4, 2012. Hyperthermia developed on December 6, 2012; the mediastinal cavity was redrained. The material obtained was referred to bacteriological examination; antibiotic treatment was prescribed. Despite the therapy, the hyperthermia persisted and the patient’s condition deteriorated. On December 11, 2012, significant amount of fluid in the pericardial cavity was detected during echocardiography. The patient underwent pericardiocentesis in the operating room; 500 ml of turbid yellow/pink fluid was isolated. On December 12, 2012, ultrasonographic examination revealed a significant amount of fluid in the right pleural cavity; the patient was subjected to pleurocentesis; up to 100 ml of chyloous fluid (chylothorax); a drain was placed. On December 18, 2012, the patient complained of dyspnea and sensation as if the sternum was compressed. CT scanning and ultrasonography showed a significant amount of liquid in the pericardial cavity. The patient underwent pericardiocentesis in the operating room; 670 ml of turbid yellow/pink fluid was isolated; the drain was placed into the pericardial cavity. On December 19, 2012, additional 520 ml of chyloous fluid was evacuated from the pericardial cavity (the chyloous nature of the fluid was verified by biochemical examination).

According to the data of cytological examination performed on December 19, 2012, the fluid obtained by draining the pleural and the pericardial cavities contained mesothelial, plasma, and lymphoid cells. No tumor cells were detected.

A bacteriological examination of the fluids isolated on December 17, 2012 from the pleural and pericardial...
cavities, of venous blood and wound discharge provided a negative result (no growth on culture media).

Patient’s condition considerably improved after massive antibacterial therapy, infusion therapy with parenteral nutrition, and fat-free diet. The drains were removed on January 1, 2013 after the X-ray control. With allowance for the histological subtype and low mitotic activity, the adjuvant therapy was not indicated. Dynamic follow-up every three months was recommended.

The recovered patient was discharged from the hospital. Patient’s condition at discharge was satisfactory.

**Discussion**

Hemangioendotheliomas are attributed to the group of soft-tissue sarcomas, subgroup of vascular tumors, and subtype of endotheliocytic tumors. The total incidence rate of soft-tissue sarcomas is 1.4 per 100,000 population (in individuals older than 80 years, 8.0 per 100,000 population). The WHO classification of soft-tissue and bone tumors is commonly used [10].

When determining the biological potential of a tumor, WHO recommends subdividing the soft-tissue tumors into the four categories as follows: benign, locally aggressive, rarely metastasizing, and malignant ones [3]. These categories should not be confused with the degree of malignancy. The degree of malignancy of soft-tissue sarcomas is currently evaluated using three indicators (the FNCLCC grading system): tumor differentiation, proliferative activity of tumor cells, presence and intensity of tumor tissue necrosis [4, 11, 12].

**I. Tumor differentiation:** score 1 – sarcomas closely resembling normal, adult soft tissue; score 2 – sarcomas with signs of slight resemblance with the normal adult soft tissue; score 3 – embryonal sarcomas, undifferentiated sarcomas, and sarcomas of doubtful tumor type.

**II. Mitotic activity** (mitosis count in 10 successive high-power fields under x400 magnification): score 1 – 0 to 9 mitoses; score 2 – 10 to 19 mitoses; score 3 – 20 or more mitoses.

**III. Tumor necrosis:** score 0 – no tumor necrosis; score 1 – less than or equal to 50% tumor necrosis; score 2 – more than 50% tumor necrosis.

The total score of all three micromorphological indicators determines three degrees of malignancy of soft-tissue sarcomas: grade I – score 2–3, grade II – score 4–5, and grade III – score 6–8.

Hemangioendotheliomas are tumors originating from the vascular tissue and can be subdivided into three types: epithelioid hemangioendothelioma [25], endovascular papillary angioendothelioma (or Dabska tumor) [21], and spindle cell hemangioendothelioma [18]. Hemangioendotheliomas may affect any organ (lungs, liver, spleen, bones). It is a rare type of tumor and can be accompanied by clinical symptoms induced by other oncological processes occurring in the mediastinum (dyspnea, glottic spasm, cough, thoracic pain, dysphagia, etc.) or can be asymptomatic (in this case, it is radiologists who detect them). Hemangioendotheliomas occur equally often in adult males and females and almost do not occur in children [13].

S. Weiss et al. were the first to describe hemangioendotheliomas as a separate subtype of vascular tumors [25]. The authors performed a follow-up of 46 patients after surgical treatment for epithelioid hemangioendotheliomas for 48 months. Local relapses were detected in 13% of cases; metastases were observed in 31% of cases; the lethality rate was 13% in patients with soft-tissue epithelioid hemangioendotheliomas and 40 and 65% in patients with epithelioid hemangioendotheliomas of the lungs and liver, respectively.

Mytosis count per high-power field, the presence of necrosis and metaplasia of bone, as well as increased cellular pleomorphism are the key histological prognostic parameters.

Epithelioid hemangioendotheliomas are tumors with boundary malignancy and are regarded as low-malignancy angiosarcomas. Most cases are characterized by low lethality; however, in some cases fatal metastases were revealed. A. Deyrup et al. [7] in their observation of 51 patients with hemangioendotheliomas in 1989–2005 reported a 81% five-year survival rate. Among 11 (21%) patients, metastases to the lungs were detected in 6 patients; to the lymph nodes (in 4 patients); to the liver (in 2 patients); and to bones, soft tissues, and the retroperitoneal space (in 1 patient in each case). When performing a univariate analysis, the mitotic activity and tumor size were associated with high lethality ($p=0.007$ and $p=0.004$, respectively). Tumor localization, degree of cellular atypia, presence of necrosis is not statistically significant. Patients with the verified high risk of metastasis survive more than 5 years in 59% of cases; the patients with the low risk of metastasis survive more than 5 years in 100% of cases.

Biopsy is not recommended because of the risk of massive hemorrhage. The objective of the treatment is to perform radical excision of the tumor masses. With allowance for the possible infiltration of the brachiocephalic arteries (as it was reported in this clinical case), the possibility of radical surgery followed by reconstruction of branchiocephalic arteries depends on patient’s tolerance to temporary occlusion of the CCA. The choice of the tactics for brain protection in these cases is determined according to the results of multimodal neurophysiological monitoring when planning the surgical intervention and intraoperatively.

Surgical intervention is the only radical therapy. Radiation therapy does not ensure satisfactory results; nevertheless, many authors recommend irradiating to reduce tumor growth and the risk of metastasis in case of inoperable vascular tumor [2].

If a tumor with high degree of malignancy was verified, radiation or chemotherapy can be proposed as an adjuvant treatment [22].
REFERENCES


Commentary

There are two aspects why the aforesaided clinical case is of interest. On one hand, a rare tumor (malignant mediastinal hemangioendothelioma) has been resected. On the other hand, an up-to-date vascular procedure has been used, which made it possible to radically remove the tumor together with the brachiocephalic trunk involved in the oncological process and to recover blood flow along the vital arteries. The favorable outcome of this surgery was possible only provided that oncologists and vascular surgeons worked together. At the current stage of development of surgery it is only cooperation, close collaboration, and mutual understanding between surgeons of various specializations, anesthetists, and resuscitation specialists that can allow them to achieve good results of treatment in patients with combined polyfactor pathologies.

E.V. Kungurtsev, V.L. Lemenev (Moscow)
Topics to be covered in our next issue:

- Diagnosis and principles of surgical treatment for tumors of the skull base
- fMRI studies of the dominant hemisphere
- Anesthesiological management in transnasal surgery
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Radical Removal of a Malignant Mediastinal Hemangioendothelioma with Restoration
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In accordance with the resolution of the Higher Attestation Commission of the Ministry of Education and Science of the
Russian Federation, the N.N. Burdenko Journal of Neurosurgery was included in the List of Leading Peer-Reviewed Journals
and Periodicals issued in the Russian Federation where the main results of Candidate and Doctor Theses are recommended
to be published.

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Brain tumors in infants were believed to be uncommon and made only 3% of the overall number of brain tumors diagnosed in children under 15. Since the early 1980s, literature has been demonstrating higher numbers, 8–15%, which have been corrected due to the new techniques of visualization [7, 8, 24, 25, 27, 28]. Wide application of computed tomography (CT) and magnetic resonance imaging (MRI) of the brain along with neurosonography (NSG) made it possible to diagnose brain tumors in infants during the first twelve months of life.

Early diagnosis of brain tumors in infants has stimulated the enhancement of surgical activity. However, functional immaturity of all organs and systems and high risk of complications, the most serious ones being massive blood loss and severe disorders of hemostasis, became an important constraint for neurosurgery [23]. Perioperative mortality in these infants varies from 13 to 33% in the present series of observations [12, 16, 17, 23, 27, 28].

The purpose of this study was: a) to determine groups of blood loss risk in surgery of infants with brain tumors according to topography and morphology of tumors, and the features of surgeries and b) to propose the optimal surgical strategies.

Material and Methods

Eighty surgeries for tumors in 1–12 months old infants were performed in the N.N. Burdenko Neurosurgical Institute during 2000–2010. Seventy eight of them were radical or partial removal of tumors; 2 surgeries were biopsies.

The study was retrospective-prospective in design: retrospective analysis reviewed the seven-year data, from 2000 through 2007, (n=39); prospective – three-year data, from 2008 through 2010 (n=41).

The same team of neurosurgeons and anesthesiologists performed neurosurgeries in all infants using the facilities of the Burdenko Neurosurgical Institute.

The infants were distributed into three groups according to the volume of intraoperative blood loss: less than 100% of the calculated total blood volume (CBV) – 55 (69%) of infants; 100 – 200% of CBV – 11 (14%); more than 200% of CBV – 14 (17%).

Diagnostics. All patients were diagnosed using CT and/or MRI of the brain with or without contrast enhancement. Neoplasms with cross-over diameter more than 4 cm, according to the CT or MRI results, were referred to as large tumors – 47 (59%). The degree of tumor vascularization was determined by the results of preoperative contrast-enhanced MRI of the brain, HCT angiography, and total cerebral angiography. The conclusive analysis of the intensity of tumor blood supply was performed after a surgery with allowance for the intraoperative blood loss.

Surgical techniques. Total cerebral angiography was performed in seven observations according to the standard technique. Selective catheterization and embolization of afferents feeding a tumor was successfully performed in three observations only.

Rigid fixation of the infant’s head with a Mayfield headrest was used in 17 observations, 13 of them – in a sitting infant. Circular fitting of the head with a frame was used in 44 observations (55%).
made of adhesive tape was used to prevent calvarial bones from being punched with pins. In other observations, the infant’s head was fixed on a soft head support with pressure-reducing support surface.

The transfontanellar-transcallosal approach was used in 17 observations, while various transcortical approaches were used in 36 other cases. The following basal approaches were used: subfrontal — in 6 cases; pterional — in 2 cases; combined transcallosal-pterional — in 3 cases, and subtemporal or transtemporal — in 2 cases. In 12 observations, we used the suboccipital approach to posterior fossa.

Tumor was removed under microscope control. The removal technique was chosen according to tumor histology and topography. The endoscopic assistance was used to control radicality of removal when a tumor was spread beyond the microscopic view region, and to visualize a vascular pedicle feeding the tumor (n=9). The angled optics with 0°, 30° and 45° view angle was used.

The radicality of a surgery was subjectively assessed by the surgeons performing the surgery and after the operation according to the results of postoperative CT and MRI of the brain. The patients were distributed into three groups according to the radicality of surgery: radical (resection of over 85% of a tumor, according to the CT or MRI results), partial (<85%), and biopsy.

Anesthesia techniques. One of the peripheral veins was catheterized immediately after taking a patient into the operation room; two or more central veins (subclavian, femoral or jugular veins) were catheterized as well. Body temperature was maintained with heated blankets and heat guns from the beginning of the surgery through its end.

Over the recent years, we have visually estimated the volume of blood loss: the volume of liquid used for on-table lavage was subtracted from the content of disposable plastic graduated reservoirs; this technique was considered to be reasonably accurate.

The lungs were ventilated artificially with the oxygen—air mixture through a semi-closed circuit at the stages of massive operative blood loss. FiO₂ was increased up to 1.0 in the regimen of moderate hyperventilation (EtCO₂=34–35 mm Hg).

In all infants, anesthesia was maintained with intravenous Propofol infusions and bolus fentanyl injections in age-related doses corrected by the traumatizing effect of a certain stage. In case of massive operative blood loss and unstable systemic hemodynamics, anesthesia was maintained as follows: both propofol infusions and fentanyl injections were discontinued and displaced with bolus intravenous injection of 25–50 mg ketamine, the only intravenous anesthetic having no depression effect on systemic hemodynamics. Rapid blood replacement could be achieved by supplementing with colloid infuse solutions. All infants whose tumors were removed (n=78) received transfusions of donor blood components. Infusion of fresh frozen plasma (FFP) (n=78) and donor erythrocyte concentrate (n=69) started at the stage of approach or at the beginning of the main surgery stage. Hemoglobin contents, hematocrit volume, and erythrocyte and platelet counts were determined before and during the surgery: immediately after induction, several times (about once an hour) at the peak of blood loss, and during its compensation, at the end of the surgery, and further at the intensive care unit — every 6–12 hours.

Blood-saving techniques. In 8 cases of surgery of large highly-vascularized tumors, hemostasis disorders were corrected and prevented at the stage of approach with the recombinant activated coagulation factor VII (rFVII, Coagil, Russia, 70–90 μg/kg) along with the conventional FFP infusion. Efficiency of the product was monitored mainly by the clinical observation of clots forming in a surgical wound.

In addition to donor blood components, a system blood reinfusion was used to compensate for operative blood loss in five cases. A cell-saver was used mainly in a High quality wash mode. The procedure was applied only when the cardiotomy reservoir contained a sufficient volume of blood, 300 mL or more. The resulting autoreythrocyte concentrate with 65% hematocrit was diluted and filtered through leukocyte filters to remove potential tumor cell impurities.

Statistical analysis. The data were processed with the Statistica 7.0 software. It included ANOVA dispersion analysis in addition to the standard methods of sample uniformity evaluation (retrospective and prospective data). Significant influence of a number of factors [infant’s age (months), body mass/initial CBV, duration of the tumor resection procedure, and volume of intraoperative blood loss] on surgery outcome was evaluated with the Kruskal-Wallis non-parametric test.

Results

Our material contains the data of both prospective and retrospective observations; therefore, the uniformity of the sample parts was urgent for the further analysis. We compared the observations by three parameters: tumor topography, tumor histology, and infant’s age/body mass ratio (for different months); the analysis revealed no significant differences in any parameter. Therefore, we could consider both, the retrospective and prospective, groups to be relatively uniform and combine the data into a single sample. The further analysis of the material depended on tumor size (over or under 4 cm in the maximal transverse section according to CT or MRI data) and volume of intraoperative blood loss (see above).

Group of low risk for intraoperative blood loss

This group includes 55 (69%) patients with intraoperative blood loss less than 100% of the calculated CBV.

1. Almost a half of observations, 24 (44%), included large (over 4 cm in size) brain tumors, optic tract gliomas predominating, 6 (25%). Due to low blood supply of the tumors and in spite of their large size, the intraoperative...
blood loss in this group did not exceed 100% CBV. Histological distribution of tumors and their dimensions are presented in Table 1.

2. Papillomas of vascular plexus were the most common ones: they were observed in 11 (45%) cases among the tumors under 4 cm in size (31 (56%). Three observations included large choroid plexus papillomas of lateral and the III ventricles.

3. In posterior fossa, the tumors were presented by anaplastic ependymomas and ATRT. Blood loss in the posterior fossa tumors did not exceed 100% of the calculated CBV, although the tumors were large and highly malignant.

Some cases were presented by the histological forms uncommon in infants: glioblastoma, craniopharyngioma, and hamartoma.

Thus, the group of low risk for intraoperative blood loss includes mainly tumors of the following topographical and histological forms (regardless of tumor size): chiasm glioma, choroid papilloma, all tumors of posterior fossa. All of them have typical CT and MRI patterns and can be easily diagnosed in the preoperative period.

**Group of medium risk for intraoperative blood loss**

This group includes 11 (14%) patients with intraoperative blood loss ranging from 100 to 200% of the calculated CBV.

This group includes mainly (90%) large malignant tumors of supratentorial localization, anaplastic astrocytomomas and ependymomas, often with cystic components, facilitating surgical removal and reducing blood loss.

Some observations included pineoblastomas, malignant teratomas, and malignant schwannomas.

Distribution of these tumors according to their size, histology, and topography is presented in Table 2.

**Group of high risk for intraoperative blood loss**

This group includes 14 (17%) patients with intraoperative blood loss higher than 200% of the calculated CBV.

This group includes only large supratentorial tumors; more than a half of them, 8 (60%), are plexus carcinomas. In all cases, tumors had large size and high vascularization, and localized in the lateral and/or III ventricles.

The following tumors were mentioned in some observations: anaplastic astrocytoma, glioblastoma, malignant teratoma, and ATRT.

Histological distribution of tumors with blood loss over 200% of the calculated CBV with respect to their size and topography is presented in Table 3.

Thus, the group of high risk for intraoperative blood loss includes mainly plexus carcinomas, reaching large size (over 4 cm) and intensively supplied with blood.

**Surgical treatment**

Techniques and volume of tumor resection depended on the degree of tumor malignancy, localization and size.

---

**Table 1.** Tumors with blood loss less than 100% of calculated CBV, n=55 (69%)  

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Less than 4 cm (n=31)</th>
<th>More than 4 cm (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>subtentorial localization</td>
<td>supratentorial localization</td>
</tr>
<tr>
<td>Grade I—II (n=38)</td>
<td>Papillomas of plexus — 11</td>
<td>Astrocytoma — 1</td>
</tr>
<tr>
<td></td>
<td>Astrocytoma — 4</td>
<td>Ganglioglioma — 1</td>
</tr>
<tr>
<td></td>
<td>Glioma of CSR — 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hamartoma — 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myxofibroma — 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ganglioglioma — 1</td>
<td></td>
</tr>
<tr>
<td>Grade III—IV (n=17)</td>
<td>Anaplastic ependymoma — 2</td>
<td>Medulloblastoma — 4</td>
</tr>
<tr>
<td></td>
<td>Pineoblastoma — 1</td>
<td>ATRT — 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

*Note. CSR — the chiasm-sellar region; ATRT — atypical teratoid rhabdoid tumor; PNET — primitive neuroectodermal tumor.*

**Table 2.** Tumors with blood loss 100–200% of the calculated CBV, n=11 (14%)  

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Less than 4 cm (n=1)</th>
<th>More than 4 cm (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supratentorial localization</td>
<td>subtentorial localization</td>
</tr>
<tr>
<td>Grade I—II</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Grade III—IV</td>
<td>Malignant teratoma — 1</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>—</td>
<td></td>
</tr>
<tr>
<td></td>
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</tbody>
</table>
Low risk group

**Plexus papillomas (PP)** \( (n=11, \text{ Fig. 1}) \). The approach was planned on the basis of preoperative CT and MRI of the brain, where a vessel pedicle feeding the tumor was verified. The best strategy minimizing the risk of intraoperative blood loss in PP surgery was coagulation of the vascular pedicle, which prevented severe bleeding during tumor removal.

Indications for surgical treatment of chiasm glioma in infants include progressing growth of a tumor with occlusion of cerebrospinal fluid pathways, diencephalic syndrome, and/or inefficient chemotherapy \( (\text{Fig. 2}) \).

The purpose of chiasm glioma surgery is to remove the exophytic part of a tumor, since the removal of its diffuse part is dangerous and unreasonable. The tumor localization (optic tracts, diencephalic region), required the attenuated techniques of its removal, that is, slow stage-wise removal with the use of ultrasound suction system, and with resection of the exophytic part of a tumor in small fragments. This surgical technique reduced the risk of damaging safe optic nerves and traumatizing of hypothalamic structures.

Vascularization of chiasm-sellar gliomas was poor in most infants \( (90\%) \). According to preoperative MRI or HCT angiography, tumor vasculature could not be con-
dymomas and astrocytomas, often with the cystic component. Although the cystic component was large, the solid parts were less than 4 cm. Puncturing and drainage of the tumor cyst were the first stages in three observations. This procedure not only improved the clinical condition of the infant but also allowed for better visualization of the solid part of the tumor in the course of its unfolding, thus facilitating the further more radical surgery. The second stage was the main surgery for resecting the solid component and macroscopically visible cyst walls.

The resection was performed according to the general surgical principles: debulking of the central part, then mobilization and removal of the peripheral portions up to the infiltration zone of healthy brain tissues.

No complications related to coagulation hemostasis disorder and no lethal outcomes were registered.

**High risk group**

Large plexus carcinomas along with other malignant tumors with the solid part over 4 cm in size provoked the highest risk of fatal blood loss. The carcinomas of the lateral ventricle plexus are blood supplied from the anterior choroid artery, and medial and lateral branches of the posterior choroid artery. Far not all feeding arteries could be coagulated at the beginning of the surgery due to the large size of the tumor. In all retrospective observations in this group, inner decompression of a tumor caused high acute blood loss, and a minimal tumor injury was followed by excessive bleeding.

The retrospective analysis of this group showed that rapid aggressive resection caused rapid massive blood loss and a critical decrease in arterial blood pressure. Slower resection with intermediate stops for hemostasis increased the surgery duration but allowed the anesthesiologist to replenish the blood loss and prevent acute disorders in hemodynamics. Meanwhile, an undue delaying of tumor resection in small fragments caused exceeding of the 300% threshold of the calculated CBV and stable disorders of coagulation hemostasis: CBV was replenished but coagulation factors never restored. This was manifested by uncontrolled bleeding in the surgical wound, and the lethal outcome could happen on an operating table, independently from the rate of tumor removal. Lethality in the retrospective group was as high as 57%.

The best compromise had to be achieved between the tumor resection technique and new blood saving methods, including angiography with embolization of tumor feeding afferents and the use of the recombinant activated factor (rFVIIa).

Angiography with an attempt to embolize the tumor feeding afferents had its disadvantages: problems of selective catheterization of an infant’s anterior or posterior artery (these arteries usually being a site where a tumor feeding pedicle originated) and the high risk of embolization of terminating branches of the choroid artery [6, 14, 15]. We managed to apply the selective catheterization and embolization of tumor feeding afferents in three infants with plexus carcinomas (Fig. 3).

Partial excluding of a tumor from the blood circulation allowed a surgeon to remove the embolized part of the tu-

---

**Fig. 3. Large choroid carcinoma of the right lateral ventricle.**

a — contrast-enhanced MRI; b — angiography before embolization; c — angiography after embolization of choroid carcinoma feeding afferents (medial and lateral posterior choroid arteries).
Injection of rFVIIa \((n=8)\) was most efficient when started at the approach stage \((n=3)\), and repeated every 15–20 minutes. When tumor resection was accompanied with rFVIIa injection, clinical (decrease in wound bleeding) and thromboelastographic normalization of coagulation was registered.

Two-stage tumor resections in the presence of rFVIIa injection and absence of visually available tumor afferents were performed in two cases until the critical threshold of intraoperative blood loss (300% of the calculated CBV) was reached (Fig. 4).

Under conditions of rapid intraoperative blood loss, blood replenishment and blood saving were performed mainly without control blood analyses, first of all, because the anesthesia care team was busy with life support. Therefore, the laboratory parameters were estimated at the stage of stabilizing infant’s condition. Table 4 presents the summarized data on blood loss and its replenishment in the groups of low, medium and high risk.

Perfecting the surgery technique along with efficient implementation of transfusion techniques improved surgical outcomes in the prospective group and decreased mortality rate from 57 to 28%.

No relation between the outcome and the degree of blood loss was revealed when analyzing the duration of tumor resection in the high risk group (Fig. 5).

**Radicality**

The highest radicality was achieved in the groups of tumors in: lateral and the third ventricles (85%), cerebral hemispheres (81%) and posterior fossa (83%). The lowest radicality (15%) corresponded to the tumors in the chiasm-sellar region, mainly large gliomas in the optic tract (Table 5).
Table 4. Characteristics of blood loss and its replenishment in infants with brain tumors in groups of of low (A), moderate (B) and high (C) risk

<table>
<thead>
<tr>
<th>Group (blood loss in % of the calculated CBV)</th>
<th>Duration of tumor resection, min</th>
<th>Maximal decrease in hematocrit level, % (normal level 33—45%)</th>
<th>Maximal decrease in platelet level, % (normal level 150—400 • 10^9/mL)</th>
<th>Transfusion support, % of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A, n=55 (5 — 91%)</td>
<td>30—240</td>
<td>28</td>
<td>200</td>
<td>FFP, er. concentrate — 80%</td>
</tr>
<tr>
<td>Group B, n=11 (105 — 160%)</td>
<td>80—280</td>
<td>15</td>
<td>176</td>
<td>FFP — 100%, er. concentrate — 100% Coagil (rFVIIa) — 9%</td>
</tr>
<tr>
<td>Group C, n=14 (200 — 650%)</td>
<td>35—300</td>
<td>14</td>
<td>77</td>
<td>FFP — 100%, er. concentrate — 100%, IOMR — 36%, Coagil (rFVIIa) — 50%</td>
</tr>
</tbody>
</table>

Note. er. concentrate — erythrocyte concentrate; IOMR — intraoperative mechanical reinfusion of auto-erythrocyte concentrate.


<table>
<thead>
<tr>
<th>Topographic group</th>
<th>Tumor resection, abs. (%)</th>
<th>Intraoperative lethality</th>
<th>Postoperative lethality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>radical resection (&gt;85%)</td>
<td>partial resection (&lt;85%)</td>
<td>biopsy</td>
</tr>
<tr>
<td>Tumors of lateral and III ventricles (n=34)</td>
<td>29 (85)</td>
<td>5 (15)</td>
<td>0</td>
</tr>
<tr>
<td>Tumors of hemispheres (n=21)</td>
<td>17 (81)</td>
<td>4 (19)</td>
<td>0</td>
</tr>
<tr>
<td>Tumors of the chiasm-sellar region (n=13)</td>
<td>2 (15)</td>
<td>9 (70)</td>
<td>2 (15)</td>
</tr>
<tr>
<td>Tumors of posterior fossa (n=12)</td>
<td>10 (83)</td>
<td>2 (17)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>58 (72)</td>
<td>20 (25)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

Note: abs — absolute; CBV — cerebral blood volume; FFP — fresh frozen plasma; er. concentrate — erythrocyte concentrate; IOMR — intraoperative mechanical reinfusion of auto-erythrocyte concentrate; rFVIIa — recombinant activated factor VII; % — percentage; regression — regressed.
Lethality

In all observations, the lethal outcomes, 7 (9%), were caused by the factors listed in Table 6.

In three cases, death occurred during the surgery as a result of rapid blood loss, lack of time for replenishment of CBV, which caused a decrease in arterial blood pressure and failure of cardiac activity.

In four cases, lethal outcomes were registered on day 2, 3, 14, and 16 after the surgery, due to the following reasons: blood stroke into the tumor remnants (n=1), hematoma formation in the tumor bed (n=2), and developed syndrome of disseminated intravascular coagulation (n=1).

In these observations, the CBV was replenished but massive blood loss exceeding 300% of the calculated CBV disrupted coagulation hemostasis. In one of these observations, the situation was complicated by the initial thrombocytopenia that followed the preceding chemotherapy.

Surgery duration (speed of tumor resection) in the prospective group was the same as earlier; therefore, improvement of the surgery outcomes was related, in particular, to perfecting the blood saving methods, which decreased the rate of blood loss at the stage of tumor debulking and hence the total blood loss became not higher than 300% of CBV.

The use of up-to-date blood saving techniques combined with details of the surgery strategy (preoperative embolization of afferent vessels; meticulous planning of the approach; deep coagulation of the tumor stroma during debulking; time-urgent coagulation of the vessels feeding the tumor; two-stage surgery, and optimization of the speed of tumor resection) when removing large highly vascularized malignant tumors allowed one to reduce the intra- and postoperative lethality from 31 to 16%, in the groups of medium and high risks, and from 57 to 28%, in the highest risk group.

Discussion

In our series comprising 80 infant patients with brain tumors who had been operated on, large tumors were diagnosed in more than a half of observations (59%), and large grade III—IV tumors — in 41%.

The main surgical problems in our series of observations were caused by massive intraoperative blood loss during the resection of grade III—IV tumors in the high risk group (17%): mainly plexus carcinomas and anaplastic ependymomas, and less common ATRTs, PNETs, anaplastic astrocytomas, glioblastoma, and pineoblastoma.

The tumors included into the group of high risk of intraoperative bleeding topographically localized in the lateral and third ventricles, and in the cerebral hemispheres. The hemostatic disorders occurred concomitantly with the massive blood loss and corresponding infusion therapy. Several problems should be taken into account: small CBV in infants, high percentage of head-directed cardiac output, and immaturity of some coagulation factors, which are formed by the sixth months of life in healthy infants [4]. The large size of the tumors, their good vascularization, and high malignancy complicated surgery to a significant extent.

In a similar series of studies by foreign researchers, many surgeries of such tumors were also followed by massive blood loss, which in some cases several-fold exceeded the initial CBV causing the intraoperative lethal outcome [6, 19]. Thus, according to B. Due-Tonnesen et al. [10], intraoperative blood loss varied from 5 to 524% of the calculated CBV, and in two observations lethal outcomes were caused by uncontrolled intraoperative bleeding. In our series, the range of intraoperative blood loss was 30 – 650% of the due CBV. The intraoperative lethal outcomes caused by uncontrolled bleeding were registered in three observations. Lethality in the early postoperative period was registered in four observations.

In modern series of studies focused on surgery of brain tumors in infants, operative lethality varies from 13 to 26% and is related mostly to the intensive blood loss during surgery of highly malignant tumors, whose share is as high as 50% [14, 16, 23].

C. Rickert et al. [26] and R. Rivera-Luna et al. [23] recommended the multistage surgery, preoperative chemotherapy or selective embolization as preventive massive blood loss measures. And this is the case: in our series the large tumors (histological diagnosis: choroid carcinoma and anaplastic ependymoma) were removed in two patients using the two-stage surgery due to intensive uncontrolled bleeding and acute hypocoagulation (in one patient with choroid carcinoma and preliminary embolization).

H. Do et al. [9] reported successful catheterization and embolization of afferents of choroid papilloma in the third ventricle; however, publications of such sort are few, and their authors mention technical difficulties associated with selective catheterization in infants [10, 18, 19]. In seven observations of our work, angiography of cerebral vessels was performed in infants with tumors in hemispheres, and in lateral and third ventricles. Successful embolization was performed in three observations, Table 6. Lethality in various groups of risk, abs. (%)/total

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total</th>
<th>Retrospective</th>
<th>Prospective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall number of patients</td>
<td>7 (9)/80</td>
<td>5 (13)/39</td>
<td>2 (5)/41</td>
</tr>
<tr>
<td>Low risk group</td>
<td>1 (2)/55</td>
<td>1 (4)/26</td>
<td>0 (0)/29</td>
</tr>
<tr>
<td>Moderate risk group</td>
<td>0 (0)/11</td>
<td>0 (0)/6</td>
<td>0 (0)/5</td>
</tr>
<tr>
<td>High risk group</td>
<td>6 (43)/14</td>
<td>4 (57)/7</td>
<td>2 (28)/7</td>
</tr>
</tbody>
</table>

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while in four observations it failed due to the lack of factors accessible for embolization and diffuse blood supply of tumors.

Degree and type of coagulopathy are mainly assessed by intraoperative changes in the platelet level, hematocrit value, and volume of intraoperative blood loss. According to N.V. Lemeneva et al. [2], when blood loss is equal to one CBV, only a slight increase in prothrombin index (PI) and activated partial thromboplastin time (APTT) occurs. In our observations, the minimal blood loss had already occurred at the stages of vein puncture and catheterization, and blood sampling for the cross-match test and other analyses, thus reducing the hemoglobin content, hematocrit value, and platelet count on the background of the infusion therapy. Unfortunately, in practice, laboratory analyses take much longer than anesthesiologist taking a decision on transfusion under conditions of intramassive operative blood loss. No method allowing for rapid and maximally accurate assessment of a patient’s blood loss volume is available up to now. Some authors [21] use the calculation methods, including serial determination of both the hemoglobin and hematocrit levels in blood samples followed by the calculation. However, these methods cannot provide even approximately accurate figures, the more so, for an infant receiving the infusion therapy at the moment. Our method of determining the intraoperative blood loss based on the evaluation of aspiration reservoir content is simple and, as we can see, rather correct.

According to the Guidelines issued by the British Committee for Standards in Hematology in 2004 [5], introduction of FFP for replenishment of coagulation factors under conditions of intraoperative bleeding must be justified with the results of coagulation test and performed only when both PI and APTT are at least 1.5-fold higher than the standard values. On opinion of M. Piasstra et al. [20–22], when we deal with the infants with large highly vascularized tumors and rapid intraoperative blood loss, erythrocyte mass and FFP should be injected earlier than the results of coagulation test are available. In our series, injection of the blood products in infants with highly malignant tumors was started at the approach stage and continued at the tumor removal stage before laboratory confirmation of the progressing coagulopathy. Intraoperative system reinfusion of erythrocytes was applied in five patients from our series of observations (the initially low CBV level in infants was a limitation factor for extensive use of the method). According to E.S. Gorobets et al. [1], the use of this method in neuro oncology allows one to significantly reduce the volume of transfused donor erythrocytes and, being combined with leukocyte filters when the infusion is returned into the circulation, is a safe procedure.

At the N.N. Burdenko Neurosurgical Institute, since 2003, the recombinant activated factor VII (rFVIIa) is used in infants to activate the hemostasis system immediately at the injury site by forming the complex between the tissue factor (TF) and factor VIIa. According to N.V. Lemeneva et al. [2], injection of rFVIIa was efficient in six out of nine patients included in the series of 6 month – 15 year-old children operated on for brain tumors [1]. M. Heisel et al. [11] reported successful use of rFVIIa in eight children with brain tumors, two of which were 3 month-old infants.

In our series, rFVIIa was used in eight observations. In four cases, the product was injected when blood loss volume had already reached 2 CBV, and standard neurosurgical methods of hemostasis and infusion-transfusion therapy failed; in three cases, rFVIIa injection preceded the surgery due to high vascularization and large size of a tumor. In all cases but two (a 7 month-old infant with giant choroid carcinoma and a 7 month-old infant with anaplastic ependymoma), injection of rFVIIa promoted bleeding arrest and surgery success. In five cases, repeated injection of rFVIIa was necessary: with 15–20-min intervals (at the absence of the effect) or 1.5 hours later. Identically to the literature [2, 11], the early use of the product in our series (before the laboratory confirmed hypocoagulation had developed) at the early stage of tumor resection was maximally efficient. It is most likely conditioned by the mechanism of action of rFVIIa, that is, activation of the hemostasis system immediately at the injury site by forming the TF–rFVIIa complex. When high doses of the product are injected, this process does not depend on the availability of coagulation factors VIII and IX [15]. When exposed to the TF – rFVIIa complex, thromboocytes are activated, and thrombin formed on their surface compensates for its deficiency in patients with thrombocytopenia and thrombocytopenia [15]. Early introduction of rFVIIa is absolutely reasonable, since coagulation factors are formed not earlier than by the 6th month of life [4].

No unequivocal recommendations on the techniques of resecting highly malignant tumors are available in the foreign literature. For example, A. Albright et al. [3] mentioned that the use of blood saving methods does not ensure the absence of a potentially adverse outcome. The authors recommend the following measures to reduce blood loss volume: coagulation of the tumor surface before its debulking and planning of such an approach that would ensure control of the tumor feeding vessels. However, when dealing with large highly vascularized grade III—IV tumors (plexus carcinomas, anaplastic ependymomas, ATRT), such a surgery may be unavailable due to the large size of a tumor and its topography. In our study, resection of an infant’s tumor before the level of intraoperative blood loss reaches its critical threshold exceeding 300% of the calculated CBV resulted in favorable outcomes. A. Albright et al. [3] mentioned that the recognition of the small CBV (80 mL/kg) in infants is an indication for early, as soon as blood loss reaches 100% of a calculated CBV, injection of plasma and platelet concentrate. We started to inject plasma at the approach stage; in addition, recognition of immaturity of coagulation fac-
tors in infants was an indication for the early injection of rFVIIa. Tumor debulking was performed intensively and was controlled by the blood loss volume. When the volume of removed tumor comprised \( \frac{1}{2} \) of the initial and intraoperative blood loss approached 300% of the calculated CBV, the surgery was stopped, and the tumor remnants were removed at the second stage, 10–14 days later. When the volume of the removed tumor approached 100%, before the blood loss reached 300% of the calculated CBV, the tumor was removed completely, and the external drainage was left in the tumor bed, since slight postoperative bleeding was inevitable in 100% of observations. The blood saving methods (early injection of plasma and blood products, and use of rFVIIa) were applied alongside with the tumor removal.

The comparison of surgery outcomes is complicated by the ratio between malignant and benign tumors in different series of observations and by the lack of differentiation according to tumor topography and degree of its malignancy. The data available from the literature are generalized. The outcomes of infant surgery from various series of observations compared with our own data are presented in Table 7.

In our series, lethal outcomes in the surgery of large highly malignant tumors of hemispheres (including lateral and III ventricles) were recorded in all observations with the volume of intraoperative blood loss over 300% of the calculated CBV. Under the conditions of rapid intraoperative blood loss, clinical signs of disturbance of coagulation hemostasis in form of diffuse bleeding from a tumor stroma started as soon as the volume of blood loss reached 200—250% of the calculated CBV. In all series with the volume of blood loss under 300% of the calculated CBV, the surgeries were completed and disturbance of coagulation hemostasis was corrected without lethal outcomes.

**Conclusion**

When performing surgeries of brain tumors in infants, allowance must be made for the immaturity of all organs and systems of the first year of life. The following parameters should be considered when determining the risk criteria: 1) initial blood parameters (CBV, presence of thrombocytopenia, etc.); 2) tumor size (tumor over 4 cm is a high risk); 3) tumor localization (hemispheres, lateral and third ventricles are high risk); 4) grade of tumor malignancy (grade III—IV are high risk).

The following topographical and histological criteria could be formulated for generalization.

The group of low risk of intraoperative blood loss includes tumors of the following topographical and histological forms regardless of a tumor size: chiasm gliomas, choroid papillomas, all tumors of cerebellum and the fourth ventricle.

The group of moderate risk of intraoperative blood loss includes large (>4 cm) malignant tumors of supratentorial localization (mainly anaplastic astrocytomas and ependymomas) with a cyst component.

The group of high risk of intraoperative blood loss includes large (>4 cm) solid malignant tumors (mainly choroid carcinomas, less commonly ependymoblastomas, pineoblastomas, ATRT).

All the aforementioned topographical and histological forms have typical signs that are shown by MRI and CT data and can be with high probability suspected before a surgery. Description of the X-ray pattern is beyond this publication.

When the intraoperative blood loss exceeds 300% of the calculated CBV, chronic disturbance of coagulation hemostasis occurs, leading either to uncontrolled bleeding and death on the operating table or to postoperative bleeding. The intraoperative blood loss volume can be decreased by mastering both the surgical technique and anesthetic support. The former includes preoperative embolization of the afferent vessels; meticulous planning the approach, including the use of neuronavigation; deep coagulation of a tumor stroma during its debulking; primary debulking of the tumor feeding vessels; two-stage surgery, and optimization of the speed of tumor removal.

Our analysis demonstrated that rapid resection in an aggressive manner causes rapid massive blood loss and critical decrease in arterial blood pressure. A slower resection with the intermediate hemostasis-related stops increases the surgery time but allows an anesthetist to replenish the blood loss and prevent the acute hemodynamic disorders. Meanwhile, an unreasonable
delaying of tumor removal in small fragments causes exceeding of the 300% threshold of the calculated CBV and chronic disturbance of coagulation hemostasis: CBV can be replenished but coagulation factors are not restored, thus resulting in uncontrolled bleeding in the surgical wound.

Preventive measures against disorders of coagulation hemostasis should be started as early as possible in addition to the conventional blood saving methods. It is reasonable to use early injection of plasma and platelet concentrates, early injection of rFVIIa, and intraoperative system reinfusion of autologous blood.

REFERENCES


Commentary

The study focuses on the relevant problem of pediatric neurosurgery: neurosurgical assistance in the first-year life infants with brain tumors. The authors’ team includes both neurosurgeons and anesthesiologists; which is quite reasonable, since the main problems of surgery in these patients are intraoperative blood losses requiring correction by both groups of specialists. Bleeding during the resection of brain tumors in infants is primarily related to the giant size of the tumors in this age group, their high blood supply, and malignant nature of the most tumors. On the other hand, the circulating blood volume in infants is so small (80 mL/kg) that a blood loss that is insignificant and often needs no correction in adults and in older children becomes critical in infants.

The authors distinguish three groups of patients according to the blood loss risk: low (less than 100% of the calculated CBV), moderate (from 100 to 200% of CBV), and high (more than 200% of CBV). These criteria are the basis for further review of the findings on tumor localization, its size, and histological structure. It allowed the authors to predict the degree of blood loss before a surgery and to start the preventive measures
from the very beginning of surgical intervention. These mea-
sures included the changes in surgical strategy and technique
of blood loss replenishment along with injection of plasma,
and erythrocyte and platelet concentrates before a hemorrhage
began; the use of the recombinant activated factor VII, and
autohemotransfusion. All these measures reduced the perio-
perative lethality from 57 to 28%. The proposed anesthetic
techniques of blood loss replenishment and maintenance of
blood coagulation properties can be approved unequivocally.
Evaluation of the surgical technologies is not so simple. Preo-
perative embolization of tumor feeding vessels should un-
doubtedly be welcomed, although it is successful fairly rare in
children of the analyzed age, even with plexus papillomas.

The wide use of electrocoagulation techniques for hemo-
stasis is sound. Optimization of the speed of tumor resection
remains a very controversial issue. On the one hand, the au-
thors argue against rapid (aggressive) regimen of tumor remov-
al and propose slower resection with intermediate stops; on the
other hand, resection of small fragments of the tumor causes
exceeding of the 300% of calculated CBV threshold and
chronic disruption of coagulation hemostasis: CBV can be re-
plenished but coagulation factors do not restore, leading to
uncontrolled bleeding in a surgical wound. There is no com-
prehensive answer yet.

Our material has much in common with the authors’ data
concerning the histological structure and localization of tu-
mors, and approaches to managing of bleeding and blood loss
in this age group. It includes 82 observations with 36.7% le-
thality for the period of 1980—2004 [Yu.A. Orlov, A.V. Shaver-
sky. Intracranial tumors in infants (review of our own and lite-
rature material). Ukr Neurokhirurg Zh 2005; 1]. The only
parameter not confirmed in our material was the effect of the
malignancy degree on blood loss intensity and postoperative
lethality. This could be related to the high percentage of plexus
carcinomas in the authors’ material (60% in patients of high
risk).

In general, the work is very relevant and will be interesting
both for neurosurgeons and anaesthesists.

Yu.A. Orlov (Kyiv)
Deep-seated tumors, such as tumors of the midbrain and thalamus, have a different growth direction and can deform the adjacent deep structures, including spreading into the ambient cisterns. Surgical approach depends on the tumors’ preferential localization. The goal of a surgeon is to use the least traumatic approach to deep-seated tumors with the possibility of complete resection of the tumor and minimizing the risk of development of neurological symptoms.

The main surgical approaches for the removal of midbrain and thalamus tumors that extend to the ambient and interpeduncular cisterns include the pterional, infratemporal, occipital interhemispheric, and infratentorial supracerebellar approaches.

Some tumors of the midbrain and basal parts of the thalamus spread to the ambient cistern and can deform the medial regions of the temporal lobe. In these cases, infratemporal and pterional surgical approaches are usually performed. The advantage of these approaches is the possibility to access the tumor without brain dissection. The main drawback of these approaches is the narrowness of the surgical field, possible risk of damaging the vein of Labbé and veins of the basal surface of the temporal lobe during the brain traction, and the presence of branches of perforating vessels in the field of view of a surgeon during the pterional approach [8, 11].

The temporal transchoroidal approach can be used as an alternative approach for deep-seated brain tumors that spread to the ambient cistern [2, 3, 5, 8, 9, 13].

This article describes the use of temporal transchoroidal access for resection of the midbrain and thalamus tumors and assesses its advantages and disadvantages.

Materials and Methods

During the past 4 years, 12 surgeries for resection of deep-seated tumors were performed using the temporal transchoroidal approach at the N.N. Burdenko Neurosurgical Institute. Four illustrative examples (three female patients and one male patient; 3, 4, 7 and 18 years old) on removal of piloid astrocytomas of the midbrain and thalamus using this approach are described in this article. In two cases, the tumor localized within the cerebral peduncle, in the other two cases it localized in the cerebral peduncle and basal parts of the thalamus.

In all cases, the tumor was accessed through the temporal transchoroidal approach. Two cases resulted in total tumor resection, and the other two resulted in subtotal resection. In all cases, a decrease in the neurological symptoms severity was observed during the postoperative period. No speech disorders after the tumor removal from the dominant hemisphere were observed.

Approach description and the clinical cases

In 1988, S. Nagata et al. [9] published a description of the microsurgical anatomy of the choroidal fissure and approaches to the medial temporal lobe and ambient cistern through the temporal horn of the lateral ventricle. The temporal transchoroidal approach described in the literature [1, 3, 4, 7, 10, 11, 14, 18] as a low-traumatic approach to access the vascular aneurysms of the P2 segment of the posterior cerebral artery (PCA), arteriovenous malformations in the field of vascular slits and ambient cistern, to the bulk tumors of supracellular retrochiasmal localization, to diencephalic area and the midbrain.

The patient was positioned on the operating table lying on his back with head turned sideways at 90° angle. Arcuate malacotomy within the frontotemporal region of the scalp was conducted. The temporal muscle was displaced as a single flap with skin and subcutaneous tissue. The supraorbital region and temporal bone scales were skeletonized. Osteoplastic pterional craniotomy was performed, inclu-

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Ding temporal bone scales up to its foundation. The dura mater was dissected by arch-like path, with its base facing the greater wing of the sphenoid bone. The lateral brain slit and the pole of the temporal lobe are exposed.

Corticotomy was performed in the lower regions of medial temporal gyrus; it was 1.5–2.5 cm long and located 3—4 cm posterior to the anterior edge of the temporal lobe pole. Its projection was aligned with the lower section of the lateral ventricle temporal horn and lower choroidal point (inferior choroidal point) — the terminal part of the choroidal fissure (Fig. 1). The approach direction was perpendicular to the temporal lobe plane. The entrance into the temporal horn localized at a depth of 2—3 cm. The depth of entry into the temporal horn depended on the expansion of the ventricular system in the cases of occlusive hydrocephalus. For slit ventricles, ultrasound examination or neuronavigation was performed to determine the lumen of the temporal horn. Fig. 1 schematically shows the approach to reach the choroidal fissure of the lateral ventricle temporal horn and the ambient cistern.

After temporal horn had been opened, it was important to identify anatomical structures in its lumen for easier navigation in the wound. The main anatomical landmarks on the medial surface are the choroid plexus and the hippocampus (Fig. 2). The choroid plexus is a mark for the choroidal fissure. In the temporal horn, the choroid plexus is attached to the walls of the choroidal fissure between the thalamus in the upper medial sections and fimbria of the hippocampus in the lower-lateral sections (Fig. 2).

During the displacement of the choroid plexus medially and upward, the choroidal fissure became exposed. During the choroidal fissure dissection, the tenia fimbria hippocampi was dissected starting from the bottom of the choroidal point. The hippocampus was moved downward and laterally. During widening of the choroidal fissure, the upper sections of the ambient cistern became exposed. In the medial part of the cistern, the lateral surface of the midbrain was visualized. The optic tract with the oculomotor nerve were located in the anterior direction; the lateral geniculate bodies and the thalamus localized in the posterior direction. Vascular structures localized in the lumen of the ambient cistern are P2 segment of the PCA, the posterior communicating artery (PIA), and the anterior ciliary artery (ACA).

Depending on their size, tumors of the midbrain, the thalamus and the optic tract, may expand to the ambient cistern area and deform the hippocampus, the choroidal fissure, and the lower horn of the lateral ventricle. Therefore, a thorough study of the MRI data may contribute to the selection of not the standard subtemporal pterional approach, but the temporal transchoroidal approach instead, which in these cases is less traumatic and allows for greater surgery radicality.

The examples of resection of deep-seated tumors (pilocytic astrocytomas) through the temporal transchoroidal approach are presented below.
the hand developed and began to propagate. The brain MRI revealed a tumor in the right side of the midbrain and the thalamus (Fig. 3a). A slight hydrocephalic expansion of the ventricular system was noted.

The clinical picture during the examination in the N.N. Burdenko Neurosurgical Institute revealed the left-sided pyramidal syndrome in form of hemiparesis that was most distinct in the hand (score of 3), along with the central type paresis of facial muscles and the failure of third nerve on the right.

Taking into account the preferential tumor location within the right cerebral peduncle and basal parts of the thalamus, the spread of the tumor into the lumen of the ambient cistern, choroidal fissure and medial temporal lobe deformation, it was decided to remove the tumor through the temporal transchoroidal approach.

Description of the surgery: the patient’s head was turned 90° to the left. Arcuate malacotomy in the right frontotemporal region within the scalp was performed. The pterional osteoplastic craniotomy was carried out. The dura mater was opened in an arcuate manner, with the base facing the wing of the sphenoid bone. Corticotomy of the anterior parts of middle temporal gyrus was performed (Fig. 3b). At a depth of 2.5 cm, the right inferior horn of lateral ventricle was revealed. The choroid plexus and choroidal fissure with extended original parts were revealed. In the lumen, the tumor of gray-yellow color was exposed (Fig. 3b). A tumor tissue sample was taken for histological examination. Tumor removal was performed using bipolar coagulation of the conventional and ultrasonic suction devices. The tumor was large, localized within the cerebral peduncle of the thalamus basal parts, and occupied the ambient cistern. Upon removal of the upper part of the tumor, the tumor cyst was revealed. The tumor had clear boundaries with the brain, except the areas of infiltration in the medial part. Gradually, the entire tumor volume was resected till the border with visually unaffected brain. During the tumor removal, the optic tract in the anterior part of surgical field was detected and PIA and PCA were visualized above. After the tumor removal, a large cavity was formed. Hemostasis using bipolar coagulation and hemostatic cotton was carried out. The dura mater was sewn up tight. The bone was laid in place and fixed. Soft tissues were sutured up. Urgent biopsy revealed astrocytoma with mitosis tumor type.

By the time of discharge from the hospital, in the neurological score there was an increase in the strength and range of motion in the left hand. Field of view was not examined due to the low age of the child.

Morphological diagnosis (after immunohistochemistry) revealed piloid astrocytoma; the treatment index of the Ki-67 proliferative marker was less than 5%.

The contrast-enhanced control MR images of the brain 2 months after the surgery revealed a small tumor remnant within the right cerebral peduncle. Narrow wound path was observed in the right temporal lobe (Fig. 3c).

The stereotactic surgical tumor irradiation was planned.

Case 2.

Patient D., 7 years old. Ten months prior to admission to the N.N. Burdenko Neurosurgical Institute, inconstant strabismus in the left eyeball was developed. The headache appeared simultaneously. The periodic nausea and vomiting gradually developed. In the dynamics, the gait disturbance was observed, along with tremor in the right hand. Brain MRI revealed a lesion of the left cerebral peduncle with a formed cyst.

During the examination at the N.N. Burdenko Neurosurgical Institute, the neurologic score detected the hypertension syndrome (headache, nausea, vomiting, initial stagnation in the fundus), right-sided pyramidal syndrome (central type of the right facial nerve paresis, right hemiparesis, most pronounced in the hand, score of 3–4), extrapyramidal syndrome (intention tremor in her right hand amplified in purposeful movements); mesencephalic symptoms (mild anisocoria d’s, convergence disorder, nystagmus). Field of view was found to be without blind spots.

According to the brain MRI data, a cystic tumor of the left cerebral peduncle was found. The solid portion of the tumor had a clear border with the adjacent brain and was homogeneously and rapidly accumulating the contrast agent. The ventricular system was hydrocephalically expanded (Fig. 4a).

Tumor resection was performed through the temporal transchoroidal approach. The choice of the approach was based on the tumor presence in the dominant hemisphere cerebral peduncle, hydrocephalic enlargement of lateral ventricles, and deformation of the medial temporal lobe and choroidal fissure.

After the osteoplastic pterional craniotomy and dura mater opening, the enlarged inferior horn of the left lateral ventricle was visualized using an ultrasonic scanner at a depth of 2.5 cm. The top layer of the inferior temporal gyrus was coagulated and resected at the length of 1–1.5 cm in middle sections. The lower horn of the lateral ventricle was accessed; the wound began to produce clear cerebrospinal fluid decreasing the brain tension. During the examination of the lower horn, the choroid plexus was found. The choroidal fissure was opened and the cistern of the cerebral peduncle side surface was exposed; ACA at its entry into the choroidal fissure and ICA were visualized. Below, the protrusion of the medullary substance was noted; it was perforated using the microsurgical forceps. A tumor cyst was revealed, and the cyst contents of yellow color were extracted. In the anteromedial parts of the cyst, the tumor tissue of gray-pink color was detected. The tumor was removed using bipolar coagulation and using the conventional and ultrasonic suction devices.

A tumor tissue sample was taken for histological examination. The tumor was located within the cerebral peduncle, had clear boundaries, which allowed its com-
Fig. 3. Contrast-enhanced MR images of the brain in the axial and frontal projections (a, c) and the intraoperative photograph (b). Case 1. Patient O., 3 years old.

a — prior to surgery: revealed delimited tumor of the right cerebral peduncle and basal parts of the thalamus with a cystic component. Tumor node intensively and homogeneously accumulates the contrast agent. Tumor extends to the interpeduncular and ambient cisterns, deforms the hippocampus and choroidal fissure. Lateral ventricles are widened; b — intraoperative photos. An extended vascular fissure and the tumor tissue in the area of ambient cistern and the cerebral peduncle are visualized in the depth of the wound. Defect of the brain in the region of the middle temporal gyrus after tumor resection is observed; c — 2 months after surgery. Small residual tumor fragment in the cerebral peduncle is observed. Deformations of the midbrain and thalamus regressed.

Case 3. Patient B., 18 years old. Six months prior to admission to the N.N. Burdenko Neurosurgical Institute, the patient developed a headache with increasing frequency and intensity, nausea, vomiting. Diplopia and weakness in the right extremities developed over time. At the time of headache, an episode of convulsive paroxysm was observed. MRI of the brain revealed a tumor of the midbrain and thalamus on the left side with noticeable occlusive hydrocephalus. Torkildsen’s ventriculostomy was performed at the patient’s home residence. Postoperative period was complicated by liquorrea development. The liquorrea regressed during the treatment.
At the time of examination in the N.N. Burdenko Neurosurgical Institute the following symptoms were revealed in the clinical picture: 1) rough mesencephalic symptoms, such as the lack of pupillary response to light, the lack of spontaneous upward gaze, upward gaze palsy; 2) right-sided pyramidal syndrome in the form of central type facial nerve paresis, right-sided hemiparesis with a decrease in muscle strength up to 4 points. Field of view was without distinct blind spots.

MR images of the brain revealed the cyst tumor of the left half of the midbrain and basal parts of the thalamus. Tumor had deformed the adjacent brain structures, including the choroidal fissure in the temporal horn of the lateral ventricle. The ventricular system was expanded and hydrocephalic (Fig. 5a).

Taking into account the localization of the tumor in the dominant hemisphere and the existing risk of speech disorders during the temporal lobe traction through the infratemporal approach, spreading of the tumor into the ambient cistern, the deformation of choroidal fissure and medial temporal lobe, and hydrocephalic expansion of the ventricular system, it was decided to access the tumor through the temporal transchoroidal approach.

Pterional osteoplastic craniotomy was carried out. The dura mater was very tense. In this regard, the inferior horn of the left lateral ventricle was punctured. After the excessive cerebrospinal fluid had been removed, the tension of the brain regressed. The dura mater was opened using a semi-oval incision, with its base facing the wing of the sphenoid bone. Corticotomy in the anterior middle temporal gyrus for about 1.5 cm in length was performed; the access to the lower horn of the lateral ventricle was carried out. The choroid plexus, deformed hippocampus and parahippocampal gyrus were visualized. Choroid plexus was allocated upwards. Arachnoid adhesions were separated and primary parts of the choroidal fissure were stretched. A tumor of gray-yellow color was discovered. A tumor tissue sample was taken for histological examination. The tumor had a heterogeneous structure, sometimes it was soft and removed by suction device; in some places it was denser, where it was resected using the ultrasonic suction device. The tumor localized within the cerebral peduncle and the basal parts of the thalamus. During the removal of the tumor, a large cyst was revealed. The tumor had compact structure; however, it had infiltrated the brain in the peripheral regions. The entire volume of the tumor to the borders with externally unaltered brain was resected. The cerebellum tentorium edge, ICA, PCA, and the basal vein were visualized. Hemostasis was done using bipolar coagulation and hemostatic cotton pads. Urgent biopsy revealed astrocytic glioma tumor.

Fig. 4. Contrast-enhanced MR images of the brain in the axial and frontal projections. Case 2. Patient D., 7 years old.

a — prior to the surgery: the tumor localizes within the cerebral peduncle and is distributed in intrapeduncular and ambient cisterns, deforms Uncus and the choroidal fissure. Lateral ventricles are hydrocephalically dilated; b — 6 months after the surgery. Tumor remnants are not visualized. Postoperative defect in the left cerebral peduncle after the tumor removal and the operational path in the left temporal lobe are present.
Fig. 5. MR images of the brain in FLAIR and T1-weighted modes in the axial and frontal projections (a); contrast-enhanced CT scan of the brain on the 2nd day after the surgery (b). Case 3. Patient B., 18 years old.

a — large tumor in the left half of the midbrain and the left thalamus with cystic component is detected. The tumor deforms the third ventricle, the internal capsule, temporal lobe, and the choroidal fissure. Hydrocephalic expansion of the ventricular system is revealed; b — tumor remnants are not visualized. Postoperative changes in the midbrain and the left thalamus are observed after tumor removal. The ventricular system is reduced in size. Operating path in the anterior left temporal lobe is visualized.

Postoperatively, the mesencephalic syndrome regressed, the strength in right extremities increased. No speech disorders were observed.

The control contrast-enhanced CT scan of the brain (Fig. 5b) revealed postoperative changes in the bed of the removed tumor. No evidence of residual tumor was revealed. The wound path in the left temporal lobe was observed.

The histological diagnosis data revealed the piloid astrocytoma with noticeable polymorphism of the nuclei and cells and a large number of eosinophilic granule cells. Immunohistochemical study revealed positive expression of glial fibrillary acidic protein (GFAP), synaptophysin expression in some single cells, and CD34 expression in the vascular wall. The labeling index of proliferative marker Ki-67 was less than 5%.

Case 4.

Patient V., 4 years old. Five months prior to the examination and treatment, weaknesses developed in the left hand (the patient stopped using hand while playing, in the self-care), and in the leg: the patient often stumbled when walking, was running awkwardly. Weakness in the left extremities was slowly increasing. In the overall dynamics periodic vomiting in the morning, headache, weakness, and fatigue appeared. Contrast-enhanced MRI of the brain revealed a large tumor in the right midbrain. The tumor was resected through the temporal tranchoroidal approach. Osteoplastic pterional craniotomy. The dura mater was opened in an arcuate manner, with base facing the wing of the sphenoid bone. Corticotomy in the anterior middle temporal gyrus was performed; the access to the lower horn of the right lateral ventricle at a depth of 3 cm was performed. Deformed choroidal fissure was visualized. It was extended and a gray-pink color tumor was discovered (Fig. 6a).

The tumor was resected up to the borders with visually unaltered brain, the floor of the third ventri-
The removal of the tumor formed a large cavity. Hemostasis using bipolar coagulation and hemostatic gauze was carried out. The brain sharply sunk down. The dura was sutured tightly. The bone was laid in its place and fixed. Soft tissues were sutured up. Urgent biopsy revealed astrocytoma tumor.

Postoperatively, the hypertension syndrome regressed, left-sided hemiparesis significantly regressed, and fine motor skills appeared in the palm. At the time of discharge, the motor skills deficit was minimal and central facial nerve paresis has regressed. Field of view examination revealed no major defects.

Histological diagnosis revealed piloid astrocytoma tumor. The labeling index of proliferative marker Ki-67 was less than 5%.

Contrast-enhanced control brain MRI revealed a small residual tumor within the right cerebral peduncle (Fig. 6c). Deformation of the adjacent structures has regressed.

Due to the small volume of the residual deep-seated tumor, stereotactic radiosurgery was planned after patient had been examined by a radiologist.

Discussion

Tumors of the midbrain and thalamus are the most challenging ones for surgical removal. Choice of surgical approach to these tumors depends on the preferential localization and direction of tumor growth. Main surgical approaches to tumors spreading into the ambient cistern...
are pterional, infratemporal and occipital interhemispheric transtentorial approaches. The advantage of the above approaches is the ability to reach the tumor without brain dissection. The disadvantage of these approaches is the narrowness of the surgical field, the risk of damaging the temporal lobe, the vein of Labbé, and veins of the temporal lobe basal surface with the excessive brain traction, which can result in venous infarction in the temporal lobe and can also lead to speech disorders upon the dominant hemisphere damage.

The temporal transchoroidal approach is an alternative access for tumors of the midbrain and thalamus, extending into the ambient cistern [3, 6, 9, 10, 13, 15–17].

This approach was described in literature [1, 3, 4, 7, 10, 11, 14, 18] during the access to vascular malformations in the area of ambient cistern and basal-medial temporal lobes, aneurysms of P2 segment of PCA, tumors of the midbrain, tumors of retrochiasmal and diencephalic localization during amygdala–hippocampal ectomy.

During this approach, the corticotomy has to be performed in the lower regions of the medial temporal gyrus, on the border with the inferior temporal gyrus 3 cm posterior from the temporal lobe pole. This allows the access into the temporal horn of the lateral ventricle without damaging the optic radiation that passes in the top part of the temporal horn. Some authors [5] prefer approach in the temporal horn through the inferior temporal gyrus, fusiform gyrus, and collateral gyrus in order to preserve the optic tract. Corticotomy in this field allows one to preserve the sensory speech center located in the upper and middle temporal gyrus of the dominant hemisphere 5–6 cm posterior from the edge of the temporal lobe pole.

The difficulty of the access to the temporal horn could be its lumen narrowness in the absence of hydrocephalus. In these cases, the use of neuronavigation and an ultrasound scanner can be helpful.

During the approach to a deep-seated tumor through the temporal transchoroidal approach, it is important to know the anatomical landmarks in the temporal horn lumen and the anatomical structures and vessels in the ambient cistern. The choroid plexus, choroidal fissure, and lower choroidal point are the main landmarks in the temporal horn. It is important to identify them in the ventricular lumen, especially in cases of deformation of the midbrain and the thalamus medial temporal lobes by the tumor.

A. Hamlat et al. [3] proposed partial resection of the hippocampus and amygdala to widen the access during the resection of retrochiasmal craniopharyngiomas and tumors with diencephalic localization, including hypothalamic hamartomas.

During the resection of the midbrain and thalamus tumor in the ambient cistern area, depending on the length of the cistern, it is necessary to identify PIA, PCA, AVA, oculomotor nerve, and the optic tract.

Advantages of the temporal transchoroidal approach include the greater angle of attack during the deep-seated tumor resection with less brain traction compared to the subtemporal approach and the lack of risk of damaging the vein of Labbé and veins of the temporal lobe basal surface (Fig. 7). This approach, unlike the subtemporal one, allows inspection of both the lower and the upper parts of the ambient cistern (Fig. 7). The disadvantage is the need for dissection of the medullary substance, the risk of damaging the optic radiation in the top part of the lateral ventricle temporal horn. However, with a good anatomy knowledge, the proper choice of corticotomy in the lower middle temporal gyus, and the selection of correct path to access the temporal horn, the risk of damaging the visual pathway is minimal.

Conclusions

Temporal transchoroidal approach is less traumatic during access and removal of delineated tumors of cerebral peduncle, basal parts of the thalamus, or the optic tract. This approach, in contrast to the infratemporal and pterional, allows one to visualize the lower and upper sections of ambient cistern with less traction of the brain. This is important during the resection of deep-seated tumors in the dominant hemisphere, where there is a risk of speech disorders with excessive traction of the temporal lobe. With a good knowledge of anatomy of the ventricu-
lar system and the ambient cistern, the selection of the optimal path when approaching the tumor, the risk of damaging the optic radiation during the temporal tran-
chordoid access is minimal.

The approach described above seems to be optimal and low-invasive for resection of deep-seated tumors that extend into the ambient cistern and deform the choroidal fissure.

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Commentary

Hard-to-reach deep-seated brain tumors still represent a complex microsurgical problem. Attempts are being made to optimize the minimally traumatic surgical approach options when using the optimal angle of the surgery for the maximum possible resection of these tumors and therefore to obtain favor-
able postoperative results. These issues are addressed in the present work: to improve microsurgical opportunities for re-
section of tumors localized in the midbrain, thalamus, extend-
ing into the ambient cistern, and superior and interpeduncular 
cistern, which ultimately will have a positive impact on the 
results of treatment of this serious category of cancer patients.

The article analyzes the data obtained in the N.N. Bur-
denko Neurorsurgical Institute, RAMS, over the past 4 years. A total of 12 patients with cystic tumors of the midbrain and 
thalamus were operated on through the temporal tranchoriod-
al approach; its advantages and disadvantages were assessed.

A total of 4 detailed clinical cases are described in the article to clearly demonstrate the benefits of the microneurors-
urgical approach used to remove two piloid astrocytomas locali-
zed in the cerebral peduncle, and two other tumors localized in 
the cerebral peduncle and the basal parts of the thalamus. In 
all cases, the positive dynamics in neurological score was ob-
served after the surgical procedure, and more importantly no 
voice disorders developed after the removal of the tumors in 
the dominant hemisphere.

A very brief historical experience of using this method is 
provided; the method was developed mostly for removing an-
aplastic astrocytomas of the posterior cerebral artery and ar-
teriovenous malformations in the area of ambient cistern, tu-
ors of retrochiasmal localization, and some tumors of the 
diencephalic area. Nuances of the present approach are de-
scribed in detail, starting from the position of the patient on 
the operating table, planning of the skin incision and bone 
flap formation, incision of the dura mater, and corticotomy 
performance in the lower middle temporal gyrus. The impor-
tance of internal landmarks identification (the choroid plex-
us, choroidal fissure and lower choroidal point) during the 
surgical access is emphasized. Options for accessing to the 
hydrocephalic temporal horn are discussed. All these steps 
are vividly illustrated with diagrams, intraoperative photo-
graphs, and correlative comparison of preoperative and post-
operative MRT studies.

The conducted studies allowed the authors to clarify the 
benefits of the approach: a greater angle of attack during resec-

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tion of deep-seated tumors; less brain traction compared to the subtemporal approach; virtually no risk of damaging the vein of Labbé and basal surface veins; the possibility of visual evaluation of the top parts of the ambient cistern.

The drawbacks of the approach include necessity of brain tissue dissection, with some risk of damaging the optic radiations in the roof of the temporal horn of the lateral ventricle.

There is no doubt that the accumulation of clinical cases can be even more convincing for evaluation of the role of this interesting and important approach in the arsenal of possible microneurosurgical interventions.

The article is rather interesting, informative, especially for the practicing neurosurgeons, and reflects the latest trends in the determination of the best ways to improve the microneurosurgical procedure and to develop various versions of approaches for the treatment of deep-seated brain tumors.

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Surgical Aspects of Endoscopic Treatment of Sagittal Craniosynostosis (Scaphocephaly) in Children

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The article focuses on surgical treatment of sagittal craniosynostosis in children. Sagittal craniosynostosis (scaphocephaly) is the most common nonsyndromic monosynostosis. Treatment of children with craniosynostosis should be started as early as possible. Endoscopic method is a low-invasive technique in surgical correction of craniosynostosis. This article describes the features of surgical treatment at all stages of the endoscopic cranioplasty. The data presented are based on the experience of treating 20 children with primary sagittal craniosynostosis. Treatment was performed using endoscopic techniques and special tools designed for endoscopic cranioplasty.

Keywords: nonsyndromic craniosynostosis, scaphocephaly, endoscopic cranioplasty.

Material and Methods

Endoscopic cranioplasty was performed in 20 children with primarily detected sagittal craniosynostosis. All children were routinely examined following the standard procedures approved for craniosynostosis in our clinic, comorbidities were analyzed, and the neurological status was estimated in accordance to child’s age. CT followed by 3D skull reconstruction was performed in all patients; its results were used to detect abnormalities typical of scaphocephaly; craniometric measurements were made. Treatment was performed using endoscopic technique; special tools designed for endoscopic cranioplasty were used: endoscopic retractor (Dura-Scalp Retractor acc. to JIMENEZ, Karl Storz) with a rigid 4 mm endoscope (Forward–Oblique Telescope Hopkins II, Karl Storz) 0° and 30° and two 5 and 10 mm wide exchangeable extendable plates (Fig. 1). The endoscopic retractor was fixed in

Fig. 1. Endoscopic retractor (Dura-Scalp Retractor acc. to JIMENEZ, Karl Storz).

a – 4 mm endoscope (Forward–Oblique Telescope Hopkins II, Karl Storz) 30°; b – assembled retractor (ready to be used).
the chosen position with a special rigid mounting system equipped with an adapter (KS-Lock, Karl Storz) (Fig. 2a). A kit of curved raspatories of different curvature and shape of the operating unit and a bone cutting kit were used to dissect soft tissues and resect bones (Fig. 2b). A multifunctional endoscopic unit (Karl Storz) equipped with a H3-Z Full HD camera (Karl Storz) to transmit the image was used for imaging (Fig. 3a). Gel head supports of different shapes were used for convenient positioning of child’s head (Fig. 3b). Comprehensive photo- and video-recording of the key moments of intervention was performed at all stages of surgery in accordance with ethic principles.

Results and Discussion

Cranial deformities have always attracted scientists’ attention. Hippocrates has mentioned the tower-like shape of the head in his manuscripts; he regarded it as a constitutive abnormality and presumed that there was an association between this abnormality and the cranial sutures [6]. In 1791, S. Soemmering, a German physiologist, anatomist, and anthropologist, admitted that premature fusion of the cranial suture played a significant role in pathogenesis of craniosynostosis. It was Rudolf Virchow who further advanced the fundamentals of modern knowledge of craniosynostosis development in 1851. He postulated that stricture formation of the cranial suture causes restriction of cranial growth in the direction perpendicular to the axis of the damaged suture (the Virchow’s rule) [6]. Notably, craniosynostosis was earlier considered to be an incurable disease and was not of no interest for surgeons. Currently, taking into account the modern methods for diagnostics and treatment, the tactics for this pathology have been significantly changed. There is a clear trend for early diagnosis; earliest possible correction of craniosynostosis is considered to be crucial. Over than a century of surgical treatment of this pathology, multiple surgical techniques have been proposed for different types of craniosynostosis; some of them have been proposed by Russian surgeons. Several of these methods are still used in clinics. Surgery of sagittal craniosynostosis has a long history. The first surgeries of this type (linear craniotomies) were performed by Lanne-
2) facilitation of the formation of skull shape by rapidly growing brain: residual bone defects are healed easier in younger children. In our opinion, craniosynostosis should also be corrected as early as possible. Endoscopic cranioplasty is the method for removing open surgery artifacts. It was proposed in 1998 by D. Jimenez and C. Barone [5]. It is noteworthy that the first treatment of craniosynostosis was performed in a patient with sagittal craniosynostosis in a same manner as over 100 years ago. Other advantages are reduction of the blood loss caused by conventional reconstruction, reduction of the incision size, surgery duration, and hospital length of stay.

In the present study, scaphocephaly was detected in 20 children (18 boys and 2 girls) out of 40 children with craniosynostoses. The mean age of patients was 10.05 months. There were 16 (80%) of patients under 1 year of age (mean age was 5.81±3.02 months); this age was considered to be optimal for endoscopic treatment. CT followed by 3D reconstruction of the skull was used to perform craniometric measurements and to analyze the cephalic index, which was 67.84±7.45 on average. This value is a criterion of dolichocephaly, one of the manifestations of sagittal craniosynostosis. Endotracheal anesthesia was used to fix a child on the operating table. In all cases, the supine position with the head flexed forward to a maximum possible angle. It is most convenient to use the main endoscopic instrumentation for a patient lying in this position. The artificial lung ventilation data were used to monitor the adequacy of head position. Moreover, child’s body position was adjusted using surgical table handles. No special tools were used for head fixation; C-shaped silica gel head supports were used to ensure convenient head positioning. This provided a sufficient level of head fixation in the proper position. An important issue is prevention of bed sores and injuries from surgical electrodes. For this purpose, disposable sticky electrodes that ensure the maximal contact surface area with child’s skin and isolation were used. Another important thing is to control of child’s body temperature. Various body warming systems (WarmTouch WT-5900, Covidien AG, USA; Thermomatress Bioterm 5-U, Russia) were used to maintain the normal body temperature.

An important step in preparing for the surgery is to mark the surgical site. A median cranial line (a projection of the sagittal sinus), the coronal suture, anterior fontanel (if it is present), and external occipital protuberance were used as the main landmarks. In all cases, the surgical site was treated with iodopyrone and alcohol. Proper fixation of the surgical clothing is needed to prevent overlying and traction of the soft tissues in the projection of intervention, to prevent restriction of freedom of surgeon’s actions. We fixed the surgical clothing along the border between the facial and cerebral head sections, leaving the cranial vault uncovered.

The next step of the surgery was the installation of a special mounting system with adapters (KS-Lock, Karl Storz) for an endoscopic retractor. This system allows...
one to fix the retractor in the selected position and easily adjust it, thus changing the view angle in the wound. Skin incision is made 1.5–2 cm posterior from the coronal suture or anterior fontanel (if it is not closed). The possible damage to the large terminal branches of the superficial temporal artery should be avoided to prevent intense bleeding. In our study, the anterior fontanel was opened in 6 children with verified scaphocephaly. The median line of the incision coincided with the sagittal suture. An additional incision was made in the projection of the point at the intersection of the lambdoid suture and median (sagittal) line. S-shaped incisions were made instead of linear incisions due to fact that they are more cosmetic and can be better hidden under hair; incisions were no longer than 4–5 cm. Bone resection was performed by the subperiosteal method. The periosteum was stripped with a common raspary in the incision projection by 1.5–2 cm in the anterior direction to visualize the coronal suture, which is a jagged line in front of the pathological sagittal suture. It can also be projected as a diagonal of the rhombus of the anterior fontanel perpendicular to the sagittal line and can be used as an additional landmark. It is extremely important to avoid damaging skin when using raspatories. The periosteum was detached in the projection of the sagittal suture and at 3–4 cm to the sides, as well as in the projections of the coronal and lambdoid sutures on both sides (3–4 cm wide). No large-scale detachment of the periosteum is needed (it may cause additional hemorrhage). The stenosed sagittal suture is defined as an area with bone hyperostosis; its relief can be palpated; there is no broken line typical of the serrate suture at the conjunction of two bones (Fig. 4). A trephination aperture 0.5 cm in diameter was made by 1.5–2 cm in the posterior direction from the coronal suture and 1.5–2 cm in the lateral direction from the sagittal line using a high-speed drill (Midas Rex Legend EHS Surgical Drill, Medtronic) equipped with a special burr (Match Head Fluted, Medtronic). The cutting edge of the burr in proper position prevents damage to the scleromeninx.

After making the trephination aperture, the bone was punched using bone forceps in the incision projection. If the anterior fontanel is present, there is no need in perforating the trephination aperture. In this case the scleromeninx can be dissected from the bone in the projection of the anterior fontanel. An important action during the surgery is detachment of the dura mater from inner surface of bones in the craniotomy area. The dura mater is often rigidly attached near the cranial suture; quite large emissary veins are sometimes present. There is a risk of damaging the sagittal sinus when detaching the dura mater from the bone. Under endoscopic visualization, the sagittal sinus always has a medial position and appears as a long dome-like formation. Sometimes a low blood flota- tion can be observed due to pulsation of brain vessels. Under inner-side visualization, the surfaces of parietal bones in its projection protrude into the skull cavity. One should also bear in mind that in 76% cases the sinus has lateral protrusions (lacunas 2–4 cm and 1.5–2.5 cm wide). The most typical lacuna localizes in the parietal area near the medial edge of the central gyrus [1]. Additional difficulties when the dura mater is dissected emerge when ante-
rior fontanel is present. In this case, fontanel tissues participate in fixation of the dura mater to bone edges. A Polenov guidewire and a Penfield dissector were used to detach the dura mater from bone. These tools were used in all cases to perform dissection at the area required for resection without damaging the dura mater. The dura mater was detached along all the sagittal, coronal and lambdoid sutures. Detachment of the dura mater near the skull base was performed using a raspatory with wide cutting edge under endoscopic control, since the dura mater here is rigidly attached to the bones.

The subsequent manipulations were performed under endoscopic control (Fig. 5). Scalp structures in the projection of the resected suture were moved upward. It is important to control the child’s head position. The most convenient is the endoscope position in a plane parallel to the bone suture and moving the operating unit along the suture during bone resection. Osteotomy was performed along the sagittal suture from its intersection with the coronal suture to the lambdoid suture; the average resection width was 3.57±1.38 cm. In order to obtain additional mobilization, paracoronal osteotomy was performed in several cases in a posterior direction from the coronal suture until the skull base with resection of a part of the greater wing of sphenoid bone and paralambdoid osteotomy anterior to the lambdoid suture until its intersection with the parietotemporal suture at both sides. The resection volume was 1.45±0.12 and 1.69±0.63 cm, respectively.

Notably, there are no known landmarks today to define osteotomy borders. The sagittal sinus is used as a landmark to dissect the sagittal suture, but there are no clear landmarks for additional osteotomies. A special landmark to define the borders of additional bone resection was the greater wing of sphenoid bone. It was partially removed using a high-speed drill and a diamond burr. The osteotomy area here was limited by posterolateral (temporal) surface of the greater wing of sphenoid bone. It is slightly concaved and is involved in the formation of a wall of the temporal fossa. The lower part of this surface is limited by the infratemporal crest. One needs to keep in mind that in 51% of cases, arteries localize in the osteal canal in the anteroinferior part of the sphenoid bone [1]. The hemorrhage is stopped by bipolar coagulation and applying bone wax. At this stage, an important advantage of rigid fixation and endoscopic control can be seen: the possibility to perform manipulations with both hands (bimanually). A point before the intersection with the parietotemporal suture was used as a landmark of the border when conducting paralambdoid osteotomy (Fig. 6).

Hemostasis is another important problem. Hemostasis should be performed at each stage during the surgery. Bones of the cranial base and vault are characterized by a sponge structure and intense blood supply. Large

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**Fig. 5. Dissection of the dura mater and resection of a bone portion.**

emissary veins often lead to the dura mater; coagulation is needed if they are revealed. Another important feature of venous component of the cranial vault is the presence of intraostal venous system localized in the spongy bone layer together with the external (intracutaneous) venous system. These systems are tightly interconnected and interact with the deep venous system localized between the dura mater layers [1]. Bone wax and treatment of the bone edge using a high-speed drill with a diamond tip can be used to stop bone bleeding. Another well-known technique is the use of an aspirator with bipolar coagulation. The use of this tool allows one to stop bone bleeding. However, when using it in hemostasis it is extremely important not to damage and not to coagulate the dura mater; a brain spatula is used to protect it. This method is of best choice in the youngest children, when bones are thin. It is also possible to use such hemostatic agents as SURGIFLO Hemostatic Matrix (Ethicon LLC). Hemostasis is performed under the endoscopic control. An endoscopic retractor is removed after the hemostasis was thoroughly performed. Only resorbable material is used for sealing due to the small size of incision, low tissue mobility in this area, and good healing. The wound is sealed with intracutaneous sutures; the surface is treated with sterile medical glue Dermabond Pro Pen (Ethicon LLC, USA) (Fig. 7). Wound condition is monitored during the hospitalization period.

The mean duration of surgery for sagittal craniosynostosis was 163.3±43.25 min. Blood loss was 103.46±58.43 ml and increased with child’s age. Patients stayed in the Resuscitation Department for less than 1 day. Control CT followed by 3D reconstruction of skull was performed 1–2 day after surgery. In all cases, no damage to the dura mater, sagittal sinus, air embolism were detected. Neither inflam-

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Fig. 6. Schematic and endoscopic views of osteotomy.
a, b – scheme for bone resection: 1 – coronal suture, 2 – area of medial resection removal, 3 – coronal suture, area for paracoronal resection is indicated, 4 – greater wing of sphenoid bone, 5 – lambdoid suture, area for paralambdoid resection is indicated, 6 – squamosal suture; c – endoscopic view after medial resection: 7 – periostium, 8 – parietal bone, 9 – sagittal sinus; d – endoscopic view after paracoronal resection, anterior and medial cranial fossae are indicated: 10 – crest of the greater wing of sphenoid bone from the inner side, 11 – parietal bone, 12 – burr, 13 – frontal bone (a part of the lateral surface).
Fig. 7. Types and methods of hemostasis in endoscopic cranioplasty.

a – the use of SURGIFLO Hemostatic Matrix (Ethicon LLC): 1 – view after applying the matrix; b – hemostasis with bone wax: 2 – spatula; c – the use of an aspirator with bipolar coagulation: 3 – aspirator coagulator; d – view of the postoperative wound treated with sterile medical glue Dermabond Pro Pen (Ethicon LLC, USA): 4 – incision area.

mation, nor infection complications, nor postoperative wound inconsistency were observed. There was no need for puncture in the intervention area. The length of a hospital stay after endoscopic cranioplasty was 3.1±0.5 days.

Therefore, endoscopic surgical treatment of scaphocephaly was performed in 20 children. Treatment results were estimated after 1, 3 and 6 months in dynamic follow-up according to the CT scanning followed by 3D reconstruction of the skull and anthropometric measurements. An orthotic helmet (“helmet therapy”) was used after regression of postoperative swelling of soft tissues in order to ensure additional correction of the head shape and for protection. The CT and 3D reconstruction data were used to calculate the cranial (cephalic) index for unbiased estimation of treatment results. In the dynamic follow-up after 6 months, the cephalic index was 77.29±4.17 (being 67.84±7.45 at hospitalization), which was considered to be an efficient outcome of intervention. These values, as well as the CT and 3D reconstruction data were used to determine the duration of wearing a helmet. The com-
Comparison of the preoperative cephalic index with the data from control examination revealed significant differences (U-test, \( p<0.01 \)) (Fig. 8).

**Conclusion**

The possibilities of modern endoscopic tools and instrumentation allow one to perform successful surgical treatment for scaphocephaly.

Endoscopic cranioplasty for correction of scaphocephaly is a low-invasion method to treat patients with this pathology.

In contrast to the conventional approaches, this method lowers the risks of complications connected with the volume of surgical interventions due to its low-invasiveness.

Since the method is low-invasive, there is no need for long hospital stay.

**Fig. 8.** Change in the cephalic index (CI) before and after the endoscopic surgery in children with scaphocephaly after 6 months (U-test, \( p<0.01 \)).

**REFERENCES**


**Commentary**

The article is devoted to the relevant problem of surgical treatment for sagittal craniosynostosis in children. The purpose of the study was to analyze the features of endoscopic surgical treatment in children with scaphocephaly.

A total of 20 patients with sagittal craniosynostosis were analyzed. The stages and technical features of the surgery, as well as the anatomical landmarks, were precisely described.

The method proposed by D. Jimenez and C. Barone and described in the study has been widely used over the past 16 years. The method consists in performing craniotomy with endoscopic assistance through small incisions of soft tissues. During the surgery, the cranial vault is resected in projection of the synostosed suture with formation of a linear bone defect. Similar surgeries were performed without endoscopic tools in the early XX century and were considered to be low-efficient. Hence, there was a demand for developing reconstructive surgical techniques to be used in patients with craniosynostoses. Development of the methods for orthopedic correction of skull deformities using cranial orthoses (helmets) allowed one to return to using the craniectomy methods.

Therefore, treatment of patients with craniosynostoses yields good results neither when using the conventional craniectomy nor when using the endoscopic assistance modification. This was also proved by an analysis of the unsuccessful results by D. Jimenez and C. Barone who had developed this technique. The main reason for bad results was the lack of orthopedic treatment. Thus, it is more correct to talk about complex surgical and orthopedic treatment of patients with craniosynostoses.

The radiography protocol (in particular, CT) was used in the study; 3D anthropometric measurements were performed. The evidential basis of the study relies on measurements performed using 3D CT reconstruction images. The use of X-ray computed tomography causes significant radiation exposure of young child’s brain and should not be used as a routine control technique; it is used only in the presence of indications.

Craniometric parameter (the cranial index) was used to evaluate the intervention efficiency. The results were statistically analyzed. Statistically significant differences were found in patient groups before and after the treatment, which led to a conclusion about sufficient efficiency of the surgeries. The
cranial index should be used beyond any doubt to assess the treatment results in patients with scaphocephaly, which was also proved by the literature data.

The features of surgical technique that differs from the previously described one are of especial interest: the use of the rigid fixation system for an endoscope with a retractor, which would enable bimanual performing of the surgery; subperiosteal bone resection in the area of the synostosed suture with forceps. Hemostasis methods that are of high importance when performing such surgeries have been described.

Future research should address long-term results of craniectomy with endoscopic assistance. This will allow one to specify indications for treatment and efficiency of the method for treating patients with craniosynostoses.

L.A. Satanin (Moscow)
Carotid Endarterectomy in Patients with High Surgical Risk

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N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow, Russia

The aim of the work was to examine risk factors for carotid endarterectomy (CEA) and their impact on the results of surgical treatment in patients with chronic cerebral ischemia. The study included 340 patients operated on at the Institute from 2007 to 2011. All patients underwent CEA in various modifications. The patients were divided into four groups, based on the classification of surgical risks of CEA proposed by T. Sundt. In the course of the subsequent analysis, perioperative outcomes of surgical treatment in the 3rd and 4th groups were evaluated; the rate of intraoperative placement of temporary intraluminal shunt (TIS) was compared, depending on the severity of angiographic risk factors and neurological anamnesis. The rate of perioperative ischemic complications in the 3rd group was 4.2%; in the 4th group – 6.4%. In both groups, TIS placement was required in 15% of operations. In patients operated on under regional anesthesia, shunts were used 2 times less often than in patients under general anesthesia (8.8% vs. 19.8%). A correlation between the severity of angiographic risk factors and tolerance of the brain to hypoperfusion, caused by temporary clamping of the internal carotid artery (ICA), was observed. In patients with contralateral ICA occlusions, shunts were required in 40% of cases; in patients with contralateral stenoses – in 15%, and in patients without angiographic risk factors – in 8% of cases. These findings coincide with the results of similar studies published in the literature.

Taking into account our and foreign data, it should be noted that CEA in patients with high surgical risk by Sundt is accompanied by the increased rate of perioperative ischemic complications and requires a more differentiated approach to the tactics of surgical treatment and to the choice of a the method for neurophysiological monitoring during surgery.

**Keywords:** carotid endarterectomy, surgical treatment, surgical risk, perioperative ischemia, temporary intraluminal shunt.

In the developed countries, stroke is the third leading cause of mortality, giving place only to cardiac and cancer diseases, as well as is the number one cause of disability in the working age population. In Russia, about 500,000 cases of acute cerebrovascular accident are reported each year; in the United States, 700,000 (of which 200,000 cases are recurrent), and in Europe, about 1.3 million [2, 4]. Up to 45% of patients who had stroke die in the acute phase, and the mortality rate is 50% during the first year. Among patients who survived the acute phase of stroke, about 60% have remained severely disabled and only 20% of them are able to return to work [3, 5].

To prevent the development of ischemic cerebral diseases caused by atherosclerotic carotid artery stenosis, carotid endarterectomy (CEA) has been applied since the 1950s. Since the 1990s, after the results of several large studies had been published, CEA has been recognized as an effective method of surgical treatment for hemodynamically significant carotid artery stenosis [1, 4, 6, 7]. According to the NASCET, ECST, and ACST data, CEA allows one to reduce the risk of stroke development in patients with subcritical and critical stenosis of the internal carotid artery (ICA) within the subsequent 2 years in 3 times. The permissible mean perioperative ischemic complication rate for symptomatic patients should not exceed 6%, and for asymptomatic patients – 3% [10, 12].

To predict surgical risks when performing CEA, a surgical risk scale developed by T. Sundt in 1975 [9] has been widely used (Table 1).

Patients with acute cerebrovascular disorders (ACD) of the ischemic type or with past medical history of transient ischemic attacks (TIAs) of not more than 1 month before hospitalization belong to neurologically unstable patients (the 4th group of surgical risks). According to T. Sundt as well as several other authors [8, 11, 13], the real complication rate after CEA varies from 1 to 15%. The highest probability for the development of perioperative ischemic complications is observed in patients with past medical history of stroke (duration < 6 months) and with TIA immediately before surgery [8, 11, 12]. According to T. Sundt, the risk of perioperative ischemic complications in the 1st group is 1%, in the 2nd – 2%, in the 3rd – 7%, in the 4th – 10%. NYCASS (New York Carotid Atherosclerosis Surgery Study) is one of the recent major studies on CEA, which has reported the results of perioperative ischemic complications [8]. In this paper, the large dispersion in the complication rate, depending on the severity of chronic cerebral ischemia, has been marked: perioperative strokes occurred in 3% of asymptomatic patients, in 6.5% of patients with TIA in anamnesis, and in 14.5% of patients with previous stroke. Despite a high risk for stroke development during the perioperative period, it is these patients who are mostly in need of endarterectomy, because the risk of recurrent

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Table 1
strokes in the natural course of the disease reaches 10% in the first year and 45–50% over the next 5 years [9, 11].

The modern methods for preoperative examination and intraoperative monitoring of the basic brain functions, a differentiated approach to the choice of an endarterectomy method, the choice of an anesthesia method, as well as dynamic monitoring in the immediate postoperative period, allow the safer use of surgical techniques for correction of stenotic carotid artery lesions in patients with a high surgical risk.

The aim of this work is to evaluate the possibility of improving the results of perioperative surgical treatment in patients from the 3rd and 4th groups of the Sundt surgical risk scale by means of a differentiated approach to the choice of a method for intraoperative neuromonitoring, anesthesia during surgery, and methods for intraoperative cerebral protection from ischemia caused by temporary clamping of the ICA, depending on risk factors identified prior to operation.

**Material and Methods**

A total of 340 patients (240 males) with atherosclerotic carotid artery stenosis had been operated on at the N.N. Burdenko Neurosurgical Institute between 2007 and 2011. The mean age of the patients was 63.6 years (43–88 years). The mean number of perioperative ischemic complications was 4.07%, mortality – 1.17%. More detailed information about complications that occurred in our patients from different surgical risk groups is presented in Table 2.

All patients, depending on the degree of manifestation of perioperative risks for the stroke/myocardial infarction/mortality development, were divided into four groups according to the Sundt surgical risk classification. The 3rd group consisted of 156 patients (178 surgeries), the 4th consisted of 91 (92). The mean age of patients was 66.5 (49–88) and 65.8 years (49–86 years) in the 3rd and 4th groups, respectively. Detailed information on the patients is presented in Table 3.

Making a diagnosis was performed on the basis of ultrasound (US) duplex scanning of the brachiocephalic arteries. Depending on the patient’s condition, spiral computed angiography, magnetic resonance angiography of the brachiocephalic and intracranial arteries, as well as direct angiography, were performed. Additional examinations, if required, were conducted on the individual basis. In the absence of contraindications, antiplatelet agents were canceled a week before surgery.

Transcranial Doppler ultrasound (TCD US) was performed in all patients before surgery to determine the fea-

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**Table 1. Classification of surgical risks for CEA according to Sundt**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st group</td>
<td>Neurologically stable, somatically unburdened patients without angiographic risks</td>
</tr>
<tr>
<td>2nd group</td>
<td>Neurologically stable, somatically unburdened patients with verified angiographic risks</td>
</tr>
<tr>
<td>3rd group</td>
<td>Neurologically stable, somatically burdened patients regardless of the presence of angiographic risks</td>
</tr>
<tr>
<td>4th group</td>
<td>Neurologically unstable patients regardless of the presence of somatic or angiographic risks</td>
</tr>
<tr>
<td>Somatic</td>
<td>Angina pectoris, myocardial infarction in anamnesis, congestive heart failure, severe obesity, chronic obstructive pulmonary disease, biological age over 70 years</td>
</tr>
<tr>
<td>Angiographic</td>
<td>Occlusion of the contralateral ICA, ICA siphon stenosis, the presence of a soft plaque or ulceration on the plaque surface</td>
</tr>
<tr>
<td>Neurological</td>
<td>Progressive neurological deficit, multiple transient ischemic attacks, stroke in anamnesis</td>
</tr>
</tbody>
</table>

*Source: © Lippincott Williams & Wilkins*

**Table 2. The rate of complications (in%) in the different groups of surgical risk**

<table>
<thead>
<tr>
<th>Complication</th>
<th>1st group</th>
<th>2nd group</th>
<th>3rd group</th>
<th>4th group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/mortality</td>
<td>—</td>
<td>2,1</td>
<td>4,8*</td>
<td>6,4*</td>
</tr>
<tr>
<td>Stroke</td>
<td>—</td>
<td>2,1</td>
<td>3,03</td>
<td>4,3</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>—</td>
<td>—</td>
<td>1,2</td>
<td>2,1</td>
</tr>
<tr>
<td>Intracerebral hematoma</td>
<td>—</td>
<td>—</td>
<td>0,6</td>
<td>2,1</td>
</tr>
</tbody>
</table>

*Source: * — p<0.05.
sibility of intraoperative US-monitoring of the linear velocity of blood flow (LVBF) in the middle cerebral artery (MCA) on the ipsilateral side. In the absence of “temporal US window” (about 10% of the population) or because of impossibility of TCD US for technical reasons, endarterectomy was performed under regional anesthesia (RA). Direct contact with the patient during surgery allows direct dynamic neuromonitoring (DNM) and thus assessing the degree of compensation of the collateral blood flow during cross-clamping of the ICA, which is a major factor in the choice of intraoperative brain protection methods. RA was also used in patients with burdened somatic pathology, embolic unstable plaque, in patients older than 70 years, as well as in accordance with individual patient’s preferences. RA was not used in patients with gross neurological deficit, apparent encephalopathy (inability to communicate adequately with the patient), aphasic disorders, language barrier with the patient, the anatomical features [distal ICA tortuosity, prolonged stenoses, high bifurcation of the common carotid artery (at the C2 vertebral body level), “short thick neck”].

The temporary intraluminal shunts (TIS) at the time of ICA clamping were placed on the basis of the intraoperative neuromonitoring data. When operating under RA, an indication for shunt placement was the patient’s depressed consciousness or the emergence of focal neurologic deficit: paresis of the limbs, aphasic disorders (the examination was conducted at the moment of clamping, on the 2nd, 3rd, 5th minutes after application of vascular clamps and then every 3 min until the start of blood flow in the ICA). In patients operated on under general anesthesia (GA), intraoperative multimodal neuromonitoring, comprising TCD US and bifrontal cerebral oximetry (CO), was carried out. Relative indication for shunt placement in patients operated on under GA was the reduction of LVBF in the ipsilateral MCA during clamping by more than 50% of the initial values. The reduction of the parameters by more than 10% of their initial values served as a CO threshold, demonstrating subcompensation for the cerebral blood flow. The decision on TIS placement during ICA clamping was made upon the emergence of subcompensation symptoms, based on the outputs of both methods or upon reducing LVBF, according to TCD US, to less than 30–35 cm/s. T-shaped shunts manufactured by Le Maitre Vascular company were used in the work.

Treatment outcomes were evaluated by the day of discharge, on the 6th–7th day after surgery. Control US of the brachiocephalic arteries was performed 3 months after surgery.

Results

Patient samples in the 3rd and 4th groups did not differ significantly by gender, age, and the affected side of the artery. Among comorbid somatic diseases, the high incidence rate for diabetes and chronic obstructive pulmonary disease (COPD) has been revealed among the patients of the 3rd surgical risk group (Table 3). In both groups, RA was required in about half of the patients (47% of operations in the 3rd group and 55% of operations in the 4th group). It is noteworthy that the main indications for RA in the 3rd group were the somatic risks: past medical history of angina pectoris, heart attack, heart failure, grade III-IV obesity, COPD, and biological age over 70 years. In the 4th group, RA was mainly conducted in patients with stroke or TIA, which had occurred less than 1 month before surgery, embolic atherosclerotic plaques, and gross atherosclerotic lesions of the contralateral ICA. TIS placement in both groups was required in 15% of cases (the average frequency of placement among all analyzed patients was 14.6%). In patients operated on under RA, shunts were reliably used 2 times less often than in patients under general endotracheal anesthesia (8.8% vs. 19.8%, \( p < 0.05 \)). The analysis of the material showed that up to 40% of patients with contralateral ICA occlusion did not tolerate ICA clamping and needed intraoperative TIS placement. Patients with contralateral stenosis needed shunt placement in 15% of cases, and patients without angiographic risk factors needed TIS placement not more than in 8% of cases. Regarding patients operated on under RA, TIS placement was mostly often required in the 4th group: 17.6% (in the 3rd group – 5.9%, in the 2nd and 1st groups no such cases were detected).

The total rate of perioperative ischemic complications was 4.15%. No sequelae were observed in the 1st group of the surgical risk, and the incidence of ischemic disorders of varying severity during the perioperative period was 2.1% (\( p < 0.05 \)) in the 2nd group. In groups of the increased surgical risk, the greater rate of complications was significantly noted: 4.2% in the 3rd group and 6.4% (\( p < 0.05 \)) in the 4th group. The mortality/stroke parameter was 4.57% overall, it was 0% in the 1st group, 2.1% in the 2nd, 4.8% in the 3rd, and 6.4% in the 4th group.

Discussion

In our work, we tried to implement a differentiated approach to the tactics of perioperative treatment for patients with hemodynamically significant atherosclerotic stenoses of the carotid arteries. The main starting points were the clinical picture of the disease, the patient’s neurological status at admission, angiographic risks, accompanying somatic anamnesis, and possibility to perform intraoperative neuromonitoring. The comparative outcome analysis for treatment in patients operated on at the N.N. Burdenko Neurosurgical Institute in 2007–2011 and patients treated in the earlier period (2000–2007) was performed. Implementation of the RA methodology and direct DNM upon CEA (2006) has greatly expanded indications for surgical treatment of patients with severe comorbidities and high neurological risks. Thus, the proportion of patients with the third and fourth groups of surgical risks in the clinical material of our study was 72%; it did not exceed 50% in the earlier period [7]. Periopera-
tive complications in patients of the 3rd group occurred in 4.8% of cases; in patients of the 4th group – 6.4%, which was less than in studies published by T. Sundt, NASCET, et al. [8, 10].

As mentioned above, in our patients during CEA under GA, TIS placement was required 2 times more often than in surgeries under RA. This difference was due to the difficulties arising from the interpretation of the multimodal neuromonitoring data in some patients operated on under GA. In particular, a reduction of LVBF according to the TCD US data and a decrease in SpO2 according to the CO data are the indicators reflecting the development of subcompensation of cerebral circulation and brain metabolism during ICA clamping, which may either go by without affecting the patient or may turn into irreversible brain ischemia. Direct DNM enables diagnosing the onset for decompensation of the cerebral circulation. Therefore, its diagnostic accuracy is significantly higher.

### Table 3. Comparative characteristics of patients from the 3rd and 4th groups of surgical risks

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>3rd group</th>
<th>4th group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>165</td>
<td>92</td>
</tr>
<tr>
<td>Number of performed operations</td>
<td>178</td>
<td>92</td>
</tr>
<tr>
<td>Males/females</td>
<td>120/45 (72/28)</td>
<td>69/23 (75/25)</td>
</tr>
<tr>
<td>Mean age (min–max), years</td>
<td>66.5 (49—88)</td>
<td>65.8 (49—86)</td>
</tr>
</tbody>
</table>

**Somatic anamnesis**

- Hypertension: 137 (83) vs. 78 (84.7)
- Ischemic heart disease: 71 (43) vs. 36 (39.1)
- Myocardial infarction in anamnesis: 22 (13.7) vs. 18 (19.5)
- Angina pectoris: 49 (30.6) vs. 26 (28.2)
- Coronary artery stenting/coronary artery bypass grafting in anamnesis: 14 (8.75) vs. 11 (11.9)
- Arrhythmia: 25 (15.6) vs. 8 (8.6)
- Diabetes: 35 (21.8) vs. 15 (16.3)
- Chronic obstructive pulmonary disease: 23 (13.9) vs. 9 (9.7)
- Renal factors: 5 (3) vs. 3 (3.2)

**Degree of manifestation of chronic cerebral ischemia according to A.V. Pokrovsky**

- Asymptomatic: 16 (9,6) vs. 0
- Discirculatory encephalopathy: 45 (27,2) vs. 0
- Stroke in anamnesis: 77 (46.6) vs. 44 (47.2)
- TIA: 27 (16.3) vs. 65 (70.6)

**Angiographic risk factors**

- Contralateral ICA stenoses: 33 (20) vs. 14 (15,2)

  **Including:**
  - Severe: 10 (6) vs. 4 (4.3)
  - Subcritical: 22 (13) vs. 9 (9.7)
  - Critical: 1 (0,6) vs. 1 (1.08)

- Contralateral ICA occlusion: 14 (8,4) vs. 12 (13.04)

- Vertebral artery stenoses:
  - contralateral: 2 (1,2) vs. 0
  - ipsilateral: 1 (0,6) vs. 0

- Vertebral artery occlusion:
  - contralateral: 2 (1,2) vs. 0
  - ipsilateral: 1 (0,6) vs. 4 (4.3)

- Extra-, intracranial microvascular anastomosis in anamnesis: 2 (1,2) vs. 0

- Contralateral CEA in anamnesis: 9 (5,4) vs. 1 (1.08)
and, respectively, TIS placement in patients operated on using DNM is required significantly less often.

In the world literature [11, 14], indications for TIS placement upon performing CEA have still been discussed. On one hand, the use of TIS upon performing CEA is accompanied by an increased risk for the development of embolic complications and early ICA thrombosis due to intimal dissection in the distal ICA. On the other hand, some patients are not able in principle to undergo even short-term ICA clamping, which is usually associated with an open circle of Willis and the deficiency of cortical collaterals. We have observed several cases when clamping the ICA for 2 min [the average time required for TIS placement (operation under RA)] caused neurological deficit regressing immediately after the shunt placement. At the same time, in 2 cases focal neurological symptoms appeared on the 10th and 18th minutes of ICA clamping, which evidenced for cerebrovascular reserve exhaustion and transition of the cerebral blood flow from the subcompensation stage to that the decompensation stage.

According to our experience, upon a differentiated approach to the choice of neuromonitoring and anesthesia in patients with high surgical risks, CEA is the effective method of surgical treatment if surgical activity of our center is not less than 50 CEAs per year [8]. Application of the neurosurgical methods, as well as opportunities of neuroanesthesiology and neuroresuscitation in these patients allow one to achieve the better results of surgical treatment, as well as to increase the efficiency of the control for possible ischemic complications during the perioperative period. Intraoperative direct DNM, the use of RA, selective TIS placement, and cerebroprotective treatment during the perioperative period allowed us to expand the spectrum of patients undergoing surgery due to the patients who had previously been refused for surgical treatment because of the extremely high risk of neurological and systemic complications. At that, the rate of perioperative complications did not get higher.

Conclusions

1. The combination of biological age (over 70 years) with angiographic and somatic risk is a factor increasing the level of perioperative ischemic complications, which explains the higher stroke/mortality rate in patients: in the 3rd group – 4.8%, in the 4th group – 6.4%.

2. CEA during the early period after stroke (up to 1 month) as well as upon TIA in the ipsilateral hemisphere leads to the increased level of perioperative ischemic complications in patients in the 4th group of surgical risk compared with those in other groups.

3. RA, using direct DNM, is the method of choice in patients with high anesthetic and surgical risk, since it allows diagnosing intraoperative complications at the very early stages and is an indicator for a timely and optimal choice of intraoperative cerebral protection methods. It also expands the range of indications for surgical treatment in somatic burdened patients without significant exceeding the permissible level of perioperative complications.

REFERENCES


Commentary

The work, presented by a team of authors from the leading neurosurgical institution of our country, is extremely topical and timely. Despite significant progress in basic and applied research in the field of cerebrovascular pathology, acute cerebrovascular accidents remain the most important medical and social problem in all developed countries at the turn of the
XXth and XXIst centuries. Moreover, due to the unprecedented increase in the number of senior people in the general population of the Earth, stroke forges ahead among the leading causes of death. In Russia, mortality in the acute phase of stroke is 35%, increasing by almost 15% by the end of the first year of the disease. Post-stroke disability ranks first among all the possible causes of disability. Only about 20% of patients who had stroke return to their previous jobs, while one-third of the patients are people of socially active age. Operative interventions of the revascularization type on the major arteries of the head (MAH) occupy an important and, in some cases, leading position in the complex treatment of ischemic cerebrovascular accidents as well as their residuals, successfully performing the task of restoring the impaired cerebral function and optimizing the parameters of cerebral circulation.

Twenty years ago, MAH surgery was the issue of exclusive competence of vascular surgeons. In this regard, it is encouraging that the presented research and application work is written by a neurosurgical team. Perhaps, of the 16,000 surgeries for MAH annually performed in Russia today, only one thousand is performed by neurosurgeons. It is just 6.25%, but this number has been steadily increasing from year to year. And taking into account the need for such surgeries (up to 60–70 thousands), the question of any competition among professionals is not relevant, but can be seen as mutually beneficial cooperation among different specialists: neurologists, vascular surgeons, neurosurgeons, and X-ray endovascular surgeons.

According to the existing international standards, complications in MAH surgery (which, unfortunately, occur in any surgical practice) are permissible within the following limits: mortality — less than 2%, with general complications less than 5%. In the early 1990s, after the unprecedented international co-operative research (NASCET) had been completed, these figures were as follows: mortality not more than 3%, with 7.5% of common complications. It is possible to speak with confidence that the quality requirements for surgery on MAH were toughened due to the direct participation of neurosurgeons in the development of the diagnostic arsenal and operational tactics. Moreover, this situation allowed improving the immediate results of surgical treatment in patients with pathology of the brachocephalic arteries.

In this paper, the risk factors for carotid endarterectomy (CEA) directly affecting outcomes of surgical treatment in patients with chronic cerebral ischemia, especially in groups of high surgical risk, have been comprehensively determined.

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In this paper, the risk factors for carotid endarterectomy (CEA) directly affecting outcomes of surgical treatment in patients with chronic cerebral ischemia, especially in groups of high surgical risk, have been comprehensively determined.

I am convinced that this work will be extremely useful and interesting for professionals engaged in the surgical prevention of brain stroke.

G. I. Antonov (Moscow)
Arteriovenous malformations (AVMs) are abnormal vascular lesions arising from impaired angiogenesis during the stage of transformation of primary embryonic arteriovenous anastomoses to capillaries [7, 36]. AVMs most often manifest themselves as spontaneous hemorrhages, less often as epileptic seizures, headache, or focal neurological symptoms. A combination of several symptoms is possible. AVM significantly shortens the longevity. The annual risk of hemorrhage is approximately 2–3% [13, 15]. Each episode of repetitive hemorrhage is associated with an increased risk of death. Most often, the first hemorrhage occurs at the age of 20–40 years. If a malformation localizes in the posterior fossa, the risk of death after the first hemorrhage is up to 67% [25].

Currently, the main techniques for AVM treatment include malformation resection, endovascular occlusion, radiosurgery, and a combination of the above three [22]. Cortical AVMs with the volume less than 10 cm³ can be cured by surgery [26, 27, 41, 49]. Resection of malformations located in the deep and functionally important parts of the brain, even if they are small, carries a high risk of persistent neurological defects and is rarely radical [26, 38, 48]. In these cases, radiosurgery becomes the method of choice [39].

Stereotactic radiosurgery is the method for accurate conformal irradiation of relatively small size targets in one or two fractions. The purpose of AVM irradiation radiosurgery is achieving complete obliteration of its vessels. A disadvantage of the method is the presence of a latent period of 2–3 years, during which obliteration of malformation vessels occurs and a risk of hemorrhage development still remains.

Stereotactic radiosurgery can be performed using a variety of devices and radiations, including narrow photon beams of the Gamma Knife and linear electron accelerators, beams of high energy heavy charged particles, such as protons.

Compared with photon radiation, protons have several beneficial properties regarding the spatial dose distribution, which enables one to significantly increase the total focal dose and simultaneously reduce the integrated dose to the surrounding normal tissues by 2–3 times [3, 4, 11, 12, 45, 46].

In the Soviet Union and later in Russia, proton radiosurgery (PRS) had been developed in the 1970s in the Laboratory of Nuclear Problems of the Joint Institute for Nuclear Research (JINR), Dubna [8], at the Institute of Theoretical and Experimental Physics, Moscow [10], and at the Institute of Nuclear Physics, Gatchina [6].
However, these techniques had significant limitations: they allowed one to form the dose field of small size and confined shape only (round or oval) as well as to irradiate AVMs located at a short distance from the midsagittal plane of the head. For these reasons, it was not possible to provide optimal irradiation of complex shape and large size AVMs. The emergence of three-dimensional computer systems for irradiation planning in the mid-1980s made it possible to obtain irradiation plans for targets of any shape, size and localization [23, 24].

Cerebral angiography had long remained the primary method for the pre-irradiation diagnostics, as well as for the anatomical and dosimetric planning of “stereotactic radiosurgery” of AVM. The development of computed tomography and magnetic resonance imaging using CT and MRI features in angiography over the past 25 years has allowed conducting pre-irradiation diagnostics by non-invasive methods [9, 30, 53].

In Russia, the new stage in the development of proton therapy came in 1999 when a specialized radiology department was opened at the Laboratory of Nuclear Problems of JINR, where the technique of three-dimensional conformal proton radiotherapy based on CT and MRI diagnosis and three-dimensional conformal irradiation planning has been developed and successfully applied for the first time in Russia [1, 5].

Material and methods

Selection of patients had been conducted between December 2001 and February 2012. PRS was performed in 65 patients with brain AVM. Of them, 56 patients, including 26 (45.5%) females and 30 (54.5%) males, aged from 7 to 55 years (mean age 30.7±1.5 years); the follow-up was more than 24 months. Clinical manifestations were as follows: hemorrhage (in 31 patients), epileptic seizures (in 14), headache (in 5), neurological deficit (in 5), incidental finding (in 1). Location was as follows: cerebral hemispheres (in 35), corpus callosum (in 5), basal ganglia (in 7), cerebellum (in 5), and cerebral trunk (in 4). The distribution of malformations according to the Spetzler–Martin grading system [50] was as follows: grade I in 3 (5.3%) patients, grade II in 8 (14.3%), grade III in 29 (51.8%), grade IV in 15 (26.8%), and grade V in 1 (1.8%). The vascular tangle volume varied from 1 to 82 cm³. The mean volume was 14.22±2.14 cm³. To evaluate the effect of the AVM volume on the treatment results, all malformations were arbitrarily divided into four groups: up to 4.9 cm³ in 13 (23%) patients, from 5 to 9.9 cm³ in 18 (32%), from 10 to 24.9 cm³ in 17 (30%), and from 25 to 82 cm³ in 8 (14%). Among 56 patients, 20 received surgical treatment before PRS (decompression trepanation to remove intracerebral hematoma was performed in 3 patients, an attempt to partially remove AVM simultaneously with the evacuation of hematoma was performed in 3 patients; endovascular embolization of AVM vessels with a partial effect of malformation size reduction was conducted in 10 patients; the shunt system for eliminating hydrocephalus was placed in 4 patients); and proton stereotactic radiosurgery was performed in 36 patients as the only treatment.

Upon selection of the irradiation parameters, the dose standardization was performed at the isocenter and was equal to 100%. The isocenter dose for small (volume up to 5 cm³) and medium (volume up to 25 cm³) malformations localized outside of the critical brain structures was 25 GyE (1 GyE is equal to 1 physical Gy multiplied by the relative biological effectiveness of protons, which is 1.1 [2–4]). The isocenter dose for small and medium malformations located in the critical areas of the brain was 24 GyE, and it was 20–23 GyE for large AVMs (volume greater than 25 cm³). The mean dose was 24.61±0.12 GyE. The target margin was included in the 70–90% isodose, 79.46±0.7% on average, and it received 16–22.5 GyE, 19.56±0.22 GyE on average. In most patients irradiation was carried out in two sessions on two consecutive days.

Irradiation was carried out in the treatment box, to which a horizontal proton beam with the energy of 155 MeV was delivered (Fig. 1). The penetration depth for protons of the given beam in water was 160 mm at the 90% isodose. The maximum beam cross-section was 80 mm wide and 77 mm high. A set of comb filters allows one to extend the Bragg peak in depth from 2 to 5 cm. The unmodulated peak was 8 mm. The beam dose rate at the Bragg peak was about 1 Gy per minute.

Fig. 1. Comparison of dose distributions for single 6 MeV photon (left figure) and 155 MeV proton beams.
A therapeutic chair having four degrees of freedom of movement was placed in the box to accommodate a patient. Opposite to the proton beam and along its axis, the X-ray tube was set at a distance of 1.8 m from the isocenter. The centration laser system determined three mutually perpendicular planes that intersect at the isocenter and the central axis of the beam. Thus, all elements of the stereotactic technology for dose delivery to the pathological focus were implemented in the treatment box.

A mask made of perforated thermoplastic immobilized the patient’s head both during the diagnostic procedures and during irradiation. CT of the head was performed using a GE Hi-Speed CT scanner, to obtain 96 to 200 slices of 1–2 mm thickness, which were used in irradiation planning. A brain MRI with slice orientation same as that in CT scanning was also used for matching images upon the irradiation planning (image fusion).

The three-dimensional conformal computer planning of irradiation was conducted using an OptiRad-3D planning system developed at the world’s first Medical Proton Therapy Center of Loma Linda University Medical Center (Loma Linda, California, USA). The system was adapted at JINR to be used with proton beams. The irradiation plan consisted of 3–8 irradiation fields arranged in the axial plane of the head. The cross-section shape of the proton beam was set by the target projection at a certain angle (beam’s-eye-view), which was formed, upon real irradiation, with an individual collimator made of Wood’s alloy. To provide conformity to the dose distribution in depth, bolus compensators of complex shapes were calculated and were subsequently made of special wax with the density of 0.98. The irradiation plan quality was assessed using the dose–volume histograms for the irradiation target and critical structures.

After completion of irradiation plan preparation, reconstructed digital craniograms for each irradiation field scaled to the real skull images were printed. The digital craniograms provided the following images: the irradiation target, coordinate axis with the isocenter, and reference bone structures and, if available, artificial structures. Craniogram-based stencils were prepared, to which the bone structures of the skull, the centration point with the coordinate axes, and the proton beam contours were transferred.

During PRS a patient is sitting in the therapeutic chair. The patient’s head is initially positioned in the immobilizing mask using laser centralizers, and the final centration of the proton beam on the target is then carried out under the X-ray control. An X-ray skull image from each irradiation field is exposed with a reduced therapeutic proton beam. This image is compared to a digital reconstructed craniogram by overlapping the above described stencil. The accuracy of proton beam pointing at the target is about 1 mm. An irradiation session takes 30 to 50 min on average. In this case, most of the time is spent for patient positioning and the proton beam position verification.

It should be noted that the proton accelerator (phasotron), devices generating the therapeutic proton beam, and the therapeutic chair were manufactured in Russia, which is currently a rarity when it comes to high-tech treatments.

The main objective of stereotactic proton radiosurgery of the AVM is complete obliteration pathological vessels. Criteria for evaluation of the treatment results are as follows:
- complete obliteration of malformation pathological vessels: no abnormal vessels;
- partial obliteration: reducing a malformation tangle by 10–99%
- lack of obliteration: retaining the previous size or increasing the malformation tangle.

Excel 2010 and Statistica 7.0 software packages were applied for statistical data analysis, descriptive statistics, comparing groups of patients, using the Student’s criteria (t-test) and Fisher’s exact test, as well as for curve plotting and charting.

**Results**

In 56 patients who received the treatment, the follow-up ranged from 24 to 109 months, with the median value of 74 months, and with the mean value of 66.7±2.9 months. Of them, only 46 patients came personally for the follow-up examination or provided the necessary data by mail. We contacted the missing patients by mail or phone. It turned out that two patients had died from comorbidities, one had died from hemorrhage in the latent period, in one patient non-fatal hemorrhage had developed (also in the latent period). The other 6 patients could not be reached. Of the remaining 46 people, complete obliteration of AVM vessels was obtained in 23 (50%). An example of complete obliteration of the AVM with the volume of 28.8 cm³ is shown in Fig. 2. In one female patient, obliteration was achieved only after re-irradiation performed 38 months after the first radiosurgical treatment. Complete obliteration occurred 48 months after the re-irradiation.

Partial obliteration was obtained in 21 patients, among which it was 95–80% in 10, 79–50% in 6, and less than 49% in 5 patients. An example of partial obliteration of the AVM with the volume of 27.2 cm³ is shown in Fig. 3. No effect was obtained in 2 patients.

Over the entire follow-up period, repetitive hemorrhage from a partially obliterated AVM developed only in one female patient 60 months after the PRS. Of 12 patients with epileptic seizures, attacks ceased in 6 (50%) patients; besides, 100% obliteration of the AVM occurred in 5 of them, and 95% obliteration occurred in one patient.

Except one case, radiation reactions after PRS were mild or moderate. In our trial early reactions, several hours after irradiation, were observed in 2 patients: in one female patient with symptomatic epilepsy in the past medical history, repetitive epileptic seizure developed (sub-
sequently reversed by treatment with Relanium); in another patient with AVM in the brainstem, moderate toxicity manifested as qualms and vomiting spells that required prescription of steroids. Five patients developed late radiation reactions 12 months after radiosurgery, with 4 patients being grade II on the RTOG (Radiation Therapy Oncology Group – International Group for Study on the Use of Radiation Therapy in Oncology) toxicity scale. The reactions were accompanied by the emergence of edema slightly extending beyond the irradiation field determined from the MRI data. The symptoms regressed following steroid therapy within 1 month. One female patient developed radiation necrosis corresponding to grade 4 on the RTOG toxicity scale. This was the only serious sequela that was completely resolved within 12 months after the appointment of several courses of steroid therapy and dehydration. According to the control MRI, asymptomatic edema developed in 14 patients 12 months, on average, after irradiation. In these cases no steroid treatment was required. Upon further follow-up, the independent reduction or disappearance of edema occurred in all cases after 24—36 months (Fig. 4).

**Discussion**

The annual risk of hemorrhage in patients with AVM belonging to grade IV and V according to the Spetzler—Martin grading system is 10.4% [29, 44]. In 1986, R. Spetzler and N. Martin [50] proposed a classification that has become popular among neurosurgeons and neuroradiologists. It reflects the AVM size, the relation to functionally important areas of the brain, and features of blood drainage from an AVM. According to the Spetzler—Martin grading system, AVMs are grouped to give a score between I and V. The group number increase corresponds to an increase in the extent of risk for surgical AVM resection. Although we initially did not plan to irradiate medium and large size AVMs, in the course of

*Fig. 2. AVM of posterior parts of the corpus callosum (volume 28.8 cm³). A 30-year-old female patient G.*
Left – a PRS plan; middle – initial MRA; right – complete obliteration of the AVM 22 months after PRS.

*Fig. 3. AVM of the region of vein of Galen (volume 27.2 cm³), a 13-year-old male patient U.*
Left – an irradiation plan; middle – initial MRA; right – partial (90–95%) obliteration 40 months after PRS.
work it became clear that our patients belonged to the high risk group to undergo direct surgical intervention. Only 3 of the treated 56 patients were grade I, and 8 were grade II according to the Spetzler–Martin grading system. The vast majority (44 patients) was grade III and IV, and 1 patient was grade V according to this classification. An attempt of surgical removal of the malformation was undertaken in 3 patients only. In all cases, resection was partial and the AVM remained. An attempt of endovascular embolization was undertaken in 10 patients, with embolization repeated 4 times in one patient. In no patient was it possible to achieve complete exclusion of the AVM using the endovascular technique.

However, the Spetzler–Martin grading system does not play a significant role in predicting the outcome of radiosurgical treatment [42, 43], which was just demonstrated in our work. In 17 cases of complete obliteration, the AVM was grade III and IV by Spetzler–Martin, 5 patients only had grade II. All of the above suggests that in the given group of patients, radiosurgery was the only possible radical treatment technique.

Due to the advance in technical capabilities of devices for irradiation and the emergence of 3D computer systems for planning in the mid-1980s, stereotactic radiosurgery has taken an important place in treatment of inoperable brain AVMs. The complete obliteration rate upon radiosurgery depends on the minimum prescribed dose and malformation volume.

Radiosurgery of small size (up to 10 cm³) AVMs using photon emitters (Gamma Knife and linear accelerator) has demonstrated excellent results: complete obliteration in 70–80% cases [17, 31, 35, 47, 52]. However, the photon radiosurgery results are getting worse as AVM size increases. For AVMs with the volume of more than 15 cm³, complete obliteration by 40 months can be achieved only in 20–36% cases [14, 28, 37, 40]. The results of various photonic series for AVMs of more than 10 cm³ are presented in Table 1.

It is reasonable to use photon irradiation of AVMs of medium and large size, as well as those of complex shapes [16, 32].

Researchers from the Stanford University, on the basis of the synchrocyclotron of Lawrence Berkeley Laboratory (USA), had treated more than 400 patients with AVMs using the Bragg peak of the helium ion beam within the period of 1980–1992. The target volume ranged from 0.3 to 70 cm³. Complete obliteration at 2 years was achieved in 94% of patients with malformations of less than 4 cm³, in 75% with malformations of 4 to 25 cm³, and in 39% with AVMs of more than 25 cm³ [18–21, 33, 34].

At the Proton Medical Research Center, University of Tsukuba (Japan), in 1990–2005, PRS had been performed in 12 patients with AVM size ranging from 30 to 60 mm. The mean dose at the target center was 25.3 GyE. One patient dropped out of the study. Of the remaining 11, complete obliteration was achieved in 9 (81%) patients; partial obliteration of the malformation was obtained in 1 (9.1%), and the malformation remained unchanged in 1 patient. In the study, PRS was conducted in conjunction with endovascular embolization of malformations [54].

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Radiosurgery method</th>
<th>Number of patients</th>
<th>AVM volume, cm³</th>
<th>% of complete obliterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. Miyawaki et al., 1999 [37]</td>
<td>LINAC</td>
<td>37</td>
<td>&gt;10</td>
<td>23</td>
</tr>
<tr>
<td>D. Pan et al., 2000 [40]</td>
<td>Gamma Knife</td>
<td>48</td>
<td>&gt;15</td>
<td>25</td>
</tr>
<tr>
<td>H. Inou, C. Ohye, 2002 [28]</td>
<td>Gamma Knife</td>
<td>14</td>
<td>&gt;10</td>
<td>36.4</td>
</tr>
<tr>
<td>A. Bois et al., 2006 [14]</td>
<td>LINAC</td>
<td>15</td>
<td>&gt;10</td>
<td>20</td>
</tr>
</tbody>
</table>

Fig. 4. AVM of the pellucid and interventricular septum region, a 31-year-old female patient P. Left — a PRS plan; middle — initial MRI; right — MRI 14 months after PRS — edema spreading beyond the irradiation field, complete cease of the edema within 24 months.
The prospective application or a grading system for inoperable AVMs localizing near the critical anatomical structures, or having a large (more than 10 cm³) volume. Due to their unique physical properties, proton beams offer an opportunity to form an irradiation field with a sharp gradient of the dose at the field margin, allowing highly conformal irradiation of targets located in the close proximity to the critical structures, without damaging the latter. PRS has the advantage over photon radiotherapy upon irradiation of AVMs with the volume of more than 10 cm³, since it allows one to maintain a sharp gradient at the field margin even in the case of irradiation of large targets.

Conclusion

Proton stereotactic radiosurgery is becoming the method of choice when selecting a treatment method for inoperable AVMs localizing near the critical anatomical structures, or having a large (more than 10 cm³) volume. Due to their unique physical properties, proton beams offer an opportunity to form an irradiation field with a sharp gradient of the dose at the field margin, allowing highly conformal irradiation of targets located in the close proximity to the critical structures, without damaging the latter. PRS has the advantage over photon radiotherapy upon irradiation of AVMs with the volume of more than 10 cm³, since it allows one to maintain a sharp gradient at the field margin even in the case of irradiation of large targets.

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Table 2. Distribution of the percentage of complete obliterations depending on the AVM volume for treatment with PRS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>up to 4.9 cm³</th>
<th>5—9.9 cm³</th>
<th>10—24.9 cm³</th>
<th>&gt; 25 cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>9</td>
<td>16</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Number of complete obliterations, abs.(%)</td>
<td>8 (89)</td>
<td>7 (43.75)</td>
<td>7 (46.6)</td>
<td>1 (16.6)</td>
</tr>
</tbody>
</table>
In connection with the development of the stereotactic technique of ionizing radiation delivery, the experience in proton irradiation of patients with arteriovenous malformations (AVM) of the brain presented by the authors is relevant and interesting. The paper provides the comprehensive description of the irradiation technique and presents the results of the analysis for the treatment of 56 patients with brain AVMs ranging from 0.92 to 82 cm³. The authors' terminology, in particular the use of the term “radiotherapy” for the treatment typically performed “in two consecutive days” is the subject for extensive discussion in the literature. In particular, the experts who use the Gamma Knife system define this technique as “hypofractionated stereotactic radiotherapy”. A similar scheme with somewhat different parameters of irradiation with the temporal interval of 6 months between treatments is known as “staging radiotherapy”. It seems rather relevant to compare these studies to the results presented by the authors and to perform an analysis with allowance for the dose determination mode and dose distribution.

A.V. Golanov (Moscow)
Prevention of Cicatricial Adhesions Using Biodegradable Membrane in Lumbar Microdiscectomy

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Microsurgery is widely used today to treat compression of nerve rootlets in the lumbar spine. Despite the minimization of the methods for decompression of nerve rootlets, cicatricial adhesions are formed in all patients who had been operated on. Swelling of nerve rootlet, sponginess, infiltration, and thickening of the epidural fiber are manifestations of postoperative reactive changes in the area of resection of a herniated intervertebral disc. The stage of aseptic inflammation is replaced by the fibroblastic stage by the end of the third week. Soft or dense adhesions emerge between the rootlet and the underlying disc [1, 2]. Fibrosis development is the cause of up to 60% unfavorable outcomes in surgical resection of herniated intervertebral discs [5, 8, 9]. Fibrosis occurs in 100% of reoperations [3]. Many authors report an association between the severity of epidural cicatricial adhesion and pain in rootlets. R. Pawl [12] performed a literature analysis to conclude that epidural fibrosis has clinical manifestation in the case of severe cicatricial adhesion process. J. Ross et al. [10–14] performed a multicenter, randomized, blind study and showed that patients with severe peridural fibrosis suffer from relapsing pain in rootlets 3.2 times more often than patients with mild adhesion process.

The role of autoimmunity in the formation of secondary pain syndrome has been proved in the studies devoted to cicatricial adhesion [7, 9]. A number of methods for prevention and minimization of the sequelae of epidural fibrosis are known. Most of the materials used (both synthetic and natural ones) showed low efficiency for preventing cicatricial adhesion. Hence, it seems rather relevant to study this aspect of the problem.

Materials and Methods

Treatment results were analyzed in 90 patients operated on in 2007–2011 at the Department of Neurosurgery of the Russian Medical Academy of Postgraduate Education at the S.P. Botkin Municipal Hospital. Inclusion criteria were as follows: spinal disc herniation at the same level as the level of syndrome of lumboischialgia or radiculopathy. There were 58 men (64.4%) and 32 women (35.6%). The median age was 48.4±3.6 years (range: 23 to 60 years). All patients had monoradicular symptoms.

In test group 1 (30 patients), biodegradable membrane was used to isolate a nerve rootlet from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In group 2 (30 patients), autologous fat tissue harvested during the approach was used to isolate a nerve rootlet from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In the group 3 (control group) consisting of 30 patients, no prevention of cicatricial adhesions was performed after decompression surgery.

In the test group patients, the L5–S1 level was affected most frequently (18 patients (60.0%)); the L4–L5 was affected less frequently (12 patients (40.0%)). In group 2, the most frequent cases (56.1%) of discoradicular conflict were revealed at the L5–S1 level with compression of the S1 rootlet; the L4–L5 level was involved rarely (42.9%). In group 3, discoradicular conflict was most frequently found at the L5–S1 level (72.6%) with compression of the S1 rootlet. The patients were divided according to the side of affected nerve rootlet as follows: 45 (50%) patients had left-sided compression radiculopathy, while 42 (41%) patients had right-sided compres-
sion radiculopathy. Three (3.3%) patients had central compression with right accent. The differences in age, gender, clinical symptoms, disease duration, and damage severity were negligible between the patient groups. Before hospitalization all patients underwent conservative treatment, which turned out to be inefficient.

Routine examination was performed in all patients, including functional radiograms of the lumbosacral spine, MRI in dynamics before and after the intervention (usually 3 months after the surgery). All intervertebral disc herniations were conventionally classified as median, paramedian, posterolateral, and foraminal. Pain syndrome intensity was estimated according to the Visual Analogue Scale (VAS). The Oswestry Disability Index was used to estimate the quality of life.

Statistical analysis of the data was performed using Windows Statistica 6 software. The relative values, mean and standard deviations of the mean were calculated; the significance level was determined using Student’s tests.

ElastoPOB biodegradable membrane was used to prevent cicatricial adhesions in the test group. This membrane is manufactured from bacterial biopolymer having very low antigenic properties (technical specifications TU 9398–002–54969743–2006). In human body, collagen having this structure is relatively quickly resorbed and degraded to simpler compounds, which are subsequently excreted or used in cellular biosynthesis processes. This material also possesses hemostatic properties.

In order to improve visualization of the installed biodegradable membrane, T2-weighted MRI images (TR2500, TE 118) were supplemented with proton density-weighted images with reduction of the MR signal from fat tissue in addition to the conventional T1- and T2-weighted imaging. The scan mode is based on the inversion–recovery pulse sequence in TR1940, TE 31.3. The selected values of FOV 20/20 of 4 mm slice thickness with 1 mm scan step were the same in both scanning modes. Supplementation of the conventional T2-weighted images with PDFS-mode images allowed us to obtain additional information on interaction between the membrane and the surrounding structures by reducing the MR signal from fat tissue; thus, the membrane position could be determined more precisely (Fig. 1).

Results and Discussion

ElastoPOB biodegradable membrane was used to isolate the following structures in the test group after decompression of neural structures: neural rootlet and dura mater from the adjacent bone and ligament structures both at the anterior and posterior sides to completely isolate the neurovascular bundle from involvement in secondary fibrosis.

The ElastoPOB biopolymer has already been proved to be efficient in cardiac and abdominal surgery, where it reduced the severity of cicatricial adhesion changes in the area of membrane grafting [4, 6, 9]. In neurosurgery this material is being widely used in surgery of the peripheral nervous system [7]. The present study is based on assumptions of possible efficiency of using the membrane in prevention of post-discectomy cicatricial adhesions. Efficiency of using this material has been proved by animal experimental studies, as well as in clinical studies for the interventions for peripheral nerves [7].

The commonly used method for prevention of cicatricial adhesions—isoulation of neural structures by autologous fat tissue—was implemented in group 2. Fat tissue was harvested at the approach stage, soaked in prednisolone solution (30 mg), and arranged around the neural structures. In group 3 (control), standard microdiscectomy was performed without any prevention of epidural fibrosis.

The mean period of the catamnesis was 1.8 years (from 6 months to 4 years). The Oswestry Disability Index was used to estimate the quality of life; the Visual Analogue Scale (VAS) was used to estimate the intensity of pain syndrome in postoperative period. Clinical manifestations of radiculopathy and dynamics of MRI data of the lumbosacral spine before and after the surgery were also assessed (Fig. 2).

MRI was performed after 10 days. T2-weighted images in the PDFS-mode allowed one to obtain additional information on interaction between the membrane and the adjacent structures by decreasing an MR signal from the fat tissue and to more precisely determine the membrane position. The S1 rootlet was isolated from the adjacent structures (anterior ones, including posterior longitudinal ligament; the entry site of hernia compression; posterior surfaces of the vertebral bodies; lateral structures, including facet joints and processes; posterior ones, including the muscles and ligament apparatus) by the membrane. Six months after microdiscectomy, post-
operative changes (isolation of the neurovascular bundle from the adjacent structures and cicatricial tissues) were visualized.

No unwanted sequelae of using the biodegradable membrane were found.

All patients had positive results of surgical treatment at the moment of hospital discharge. Postoperative catamnestic follow-up was performed. Patients’ condition was examined at the moment of discharge, 6 and 12 months after surgery, and then annually.

Regression of rootlet pain symptoms was found in 30 (100%) patients of the test group. Out of 15 patients with sensitivity disorders, complete regression was found in 11 (36.3%) patients; partial regression — in 3 (9.9%). The disorders remained at the same level as before the surgery in 2 (6.6%) patients after 6 months. Movement disorders detected in 5 (16.5%) patients had completely regressed by the moment when the long-term outcomes were assessed.

Regression of rootlet pain symptoms was found in 30 (100%) group 2 patients treated with autologous fat tissue. Out of 18 patients with sensitivity disorders, complete regression was found in 12 (39.6%) patients; partial regression — in 6 (19.8%). The disorders remained at the same level as before the surgery in 2 (6.6%) patients after 6 months. Movement disorders found in 7 (23.1%) patients had completely regressed in all patients by the when the long-term outcomes were assessed.

Regression of rootlet pain symptoms was found in 30 (100%) group 3 patients without any prevention of cicatricial adhesions. Out of 18 patients with sensitivity disorders, complete regression was found in 12 (39.6%) patients; partial regression – in 6 (19.8%). The disorders remained at the same level as before the surgery in 2 (6.6%) patients after 6 months. Movement disorders found in 7 (23.1%) patients had completely regressed in all patients by the when the long-term outcomes were assessed.

Significant differences in the VAS score before the surgery and after discharge ($p<0.00001$) were detected in all three groups. A significant improvement was subsequently revealed between values of the test group and both control groups at the discharge and 6 or 12 months later ($p=0.02$). The mean values of pain syndrome intensity (for the rootlet pain syndrome in a leg) as judged by VAS decreased from $7.07\pm1.62$ to $1.53\pm0.68$; after 6 months to $1.42\pm0.5$, and after 1 year — to $1.3\pm0.5$. The Oswestry Index values were $55.8\pm19.9$ before the surgery and $15.8\pm6.4$ 6 months after the surgery. The VAS data suggest a more significant decrease in the pain syndrome at the long-term period in the test group when compared to the control groups (test group — $1.23–0.9–0.8$; group 2 — $1.23–1.2–1.1$; group 3 — $1.53–1.4–1.3$ (Fig. 3).

In the test group, the Oswestry Index values before the surgery were $51.7\pm18.2$ ($m=3.3$), in group 2 — $51.3\pm16.6$ ($m=3.0$), in group 3 — $55.8\pm19.2$ ($m=3.5$) with significance $p<0.00001$. In the dynamic observation 6 or 12 months after the surgery, the Oswestry Index values were as follows: in the test group — $12.7\pm7.3$ ($m=1.3$), in group 2 — $15.1\pm10.0$ ($m=1.8$), in group 3 — $15.8\pm6.4$ ($m=1.2$). Therefore, significant differences in the Oswestry Index values were found before and after the surgery in the groups studied ($p<0.00001$). However, there were no significant differences 6 or 12 months after the surgery ($p>0.05$) (Fig. 4). A better tendency was observed in the test group; however, it was statistically insignificant (Fig. 4).

In 2 (2.2%) cases, a relapse of the rootlet pain syndrome was observed after 1.8–2.2 years after the primary surgery and was accompanied by recurrence of disc herniation (detected by MRI); reoperation was needed. One of these patients was from the test group, the other
one was from the control group. In both cases, fibrosis tissue samples from the peridural area were histologically studied.

A noteworthy feature of reoperation was that a patient who had undergone prevention of cicatricial adhesions using biodegradable membrane had a clear dissection plane when the dura mater and neural rootlets were detached from the fibrosis tissue despite the typical cicatricial process in interlaminar and intermuscular areas. This fibrosis tissue was thin, soft, and easily dissectible. No fragments or traces of the biodegradable membrane were found during the intervention 1.5 years after the primary surgery. Meanwhile, typical cicatricial adhesions with rigid fusion of the fibrosis tissue with dura mater and neural rootlet were found in a patient from the control group. Peridural fibrosis tissue samples were taken for histological studies (Fig. 5).

The results of in vivo histological studies of fibrosis tissue samples taken during the reoperation (secondary microdiscectomy) when biodegradable membrane was used were as follows: thin loose-fibrous hyalinized cicatricial connective tissue at the contacts with neural structures and traces of the adjacent fiber, in the periphery transition to the typical coarse-fibrous fibrosis tissue. The results of in vivo histological studies of fibrosis tissue samples taken during reoperation without epidural fibrosis prophylaxis were as follows: epidural fibrosis tissue and coarse-fibrous connective tissue with sclerosis and hyalinosis, degenerative changes in connective tissue.

Taken together, the results of the study and reoperation data suggest that severity of fibrotic changes in the area of discoradicular conflict after surgery decreases when neural rootlet and dura mater are isolated with the biodegradable membrane ElastoPOB, which creates favorable conditions for functioning of neural structures.
Conclusions

1. Our study and literature analysis indicate that cicatricial adhesions are found after microdiscectomy in all patients. In several patients, this problem becomes the first-priority one in worsening the quality of life and long-term results. The dynamics of the VAS data in short- and long-term results in the control group of patients without prevention was 0.13–0.23.

2. The catamnestic data collected over the period from 6 months to 4 years suggest the following: the Oswestry Index values were almost equal in all three groups; the VAS data suggest a more significant decrease in the pain syndrome at the long-term period in the test group compared to the control groups (test group – 1.23–0.9–0.8; group 2 – 1.23–1.2–1.1; group 3 – 1.53–1.4–1.3).

3. A method suggested for prevention of epidural fibrosis after lumbar microdiscectomy provided barrier function without complications in the area of discoradiculic conflict. The most significant changes were observed during the first 6 months after the surgery (VAS dynamics 0.33 compared to 0.03–0.13 in other groups). Therefore, the test group shows a trend to improvement of the results, which can be result from a decrease in periradicular cicatricial adhesions due to the use of biodegradable material.

4. MRI, VAS, and the data of reoperations prove efficiency of using the biodegradable material to manage periradicular cicatricial adhesions.

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Commentary

The relevance of the present study is beyond any doubt. Prevention of cicatricial adhesions in postoperative period could significantly improve the results of surgical treatment in patients with disc hernias in the lumbar spine by reducing the rootlet pain syndromes. Without any doubt, the key factor in preventing cicatricial adhesions is minimization of interventions: careful planning of the surgical approach, resection of only those structures (bones and ligaments) that are essential for hernia removal and complete decompression of neural structures. Magnifying equipment (such as an endoscope or a microscope) is required for such purposes. The second important factor is thorough hemostasis. Many authors have demonstrated that the presence of even clinically insignificant hematoma in the postoperative wound leads to the formation of cicatrices between the dural sac, the rootlet, and the adjacent tissues. In almost all reoperations, cicatricial adhesions are found between the dura mater, rootlets, and the adjacent tissues. However, the presence of cicatricial adhesions does not necessarily have corresponding manifestations.

The authors have analyzed the results of treatment of lumbar microdiscectomy in 90 patients operated on in 2007–2011 at the Department of Neurosurgery of the Russian Medical Academy of Postgraduate Education within S.P. Botkin Municipal Hospital. In the test group (30 patients), biodegradable membrane was used to isolate a nerve rootlet from the adjacent tissues preventing cicatricial adhesions after decompression surgery. In group 2 consisting of 30 patients, autologous fat tissue harvested during approach was used to isolate the nerve rootlet
from the adjacent tissues to prevent cicatricial adhesions after decompression surgery. In group 3 (control) consisting of 30 patients, no prevention of cicatricial adhesions was performed after decompression surgery.

Having analyzed all three groups, the authors obtained the data strongly suggesting that the use of autologous fat tissue or (which is more effective) biodegradable membrane is reasonable for prevention of cicatricial adhesions. However, the leading Russian hospitals of spine surgery lack experience with using this biodegradable membrane. Final conclusions can only be made after multicenter research involving large groups of patients is conducted.

N.A. Konovalov (Moscow)
Intraarterial Administration of Verapamil to Treat Cerebral Vasospasm in a Patient with Acute Subarachnoid Hemorrhage from an Aneurysm: Case Report

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Cerebral vasospasm is one of the major causes of cerebral ischemia and neurological deficits in patients after subarachnoid hemorrhage (SAH) from an aneurysm. According to angiography data, the vasospasm in the acute stage of the cerebral aneurysm rupture is detected in 50–70% of cases, and the risk of developing vasospasm-related delayed ischemia is 19–46%. One of the new trends in treating cerebral vasospasm is intraarterial administration of calcium channel blockers. The article presents a clinical case of selective intraarterial administration of verapamil for the treatment of cerebral vasospasm in a female patient after severe subarachnoid parenchymal hemorrhage from the internal carotid artery bifurcation aneurysm with a good clinical outcome. The prospects of endovascular treatment of cerebral vasospasm are discussed.

Keywords: cerebral vasospasm, intraarterial administration of verapamil.

Clinical case

A 66-year-old patient Kh. was admitted to the N.N. Burdenko Neurosurgical Institute on the third day after intracranial hemorrhage from an aneurysm (Hunt and Hess grade V). Upon admission, the consciousness level corresponded to coma II, body temperature was 38.0°C. The patient received mechanical ventilation (IPPV). The hemodynamics was instable with a tendency to arterial hypotension. Arterial pressure was maintained 120–140/79–85 mmHg by intravenous administration of vasopressors. Computed tomography of the brain revealed an intracerebral hematoma in the right temporal lobe with subarachnoid hemorrhage and brain edema (Fig. 1). According to cerebral angiography, an arterial saccular aneurysm 4.2×3.7 mm in size was detected in the area of ICA bifurcation. Given the severity of the condition, a ventricular drainage system with an intracranial pressure (ICP) sensor (ICP at that time was 30–32 mmHg) was installed.

The next day (day 5 after SAH) after patient’s condition stabilized, she underwent surgery: endovascular occlusion of the right ICA bifurcation aneurysm with microcoils (Fig. 2). Patient’s postoperative condition was satisfactory; angiography showed moderate arterial stenosis. The patient received intensive therapy in the intensive care unit. Predominant involvement of the left limbs caused by surface sedation was observed in the neuro-
logical status. ICP was 12–18 mmHg, with brief episodes of rising up to 30 mmHg, which were cured by administration of osmodiuretics. On day 2 after surgery (day 6 after SAH), transcranial Doppler ultrasound (TCD) examination revealed an increase in blood flow velocity (BFV) (Table 1).

Taking into account the progression of cerebral vasospasm and a high risk of ischemia in the right ICA system, a decision was made to perform a selective intraarterial administration of verapamil to the patient. During the procedure by the standard Seldinger technique, the ICA was catheterized distally from the ICA bifurcation on the spasm side (right) and verapamil was slowly administered during 30 min at a total dose of 25 mg. As the drug was injected, a transient increase in ICP to 30 mmHg was observed; ICP decreased to 12 mmHg by the end of the procedure (along with open ventricular drainage). No complications were observed. According to the control TCD, BFV in the middle cerebral artery decreased 60 min after the procedure (Table 2).

Table 1. TCD data (BFV, cm/s) on day 2 after surgery (day 6 after SAH).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Right</th>
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<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>MCA</td>
<td>223</td>
<td>72</td>
</tr>
<tr>
<td>ACA</td>
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<tr>
<td>VA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA</td>
<td>61</td>
<td>22</td>
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<tr>
<td>MCA (average)</td>
<td>122,33</td>
<td></td>
</tr>
<tr>
<td>ICA (average)</td>
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<td></td>
</tr>
<tr>
<td>Lindegaard index</td>
<td>3,5</td>
<td></td>
</tr>
</tbody>
</table>

Sedation was gradually discontinued as stable ICP parameters and hemodynamics were attained on day 3 after surgery (day 4 after SAH); the patient became available for contacts. Symptomatic and restorative therapies were performed; the patient was gradually switched to spontaneous breathing. Regression of left-sided hemiparesis was observed in the patient’s neurological status. Postoperative increase in BFV was no longer observed by TCD (Table 3).

At the time of discharge, the patient’s general condition was relatively satisfactory. Neurological condition: the patient was in clear consciousness, answered questions, executed commands, could orient well in time, space, and her own identity. Pupils D=S, photoreaction was alive, face was symmetrical, swallowing and phonation were not disturbed. No focal motor or sensory loss was observed. The patient was discharged in a relatively satisfactory condition. The total length of hospital stay was 30 days.

**Discussion**

Verapamil has been used long enough in patients with coronary vessel spasm. According to many authors, it is a relatively safe and effective treatment for refractory vasospasm of coronary vessels. Availability and low price are also the advantages of this drug [1–3, 12].

The data that intraarterial administration of verapamil improves the angiographic presentation of vasospasm were published earlier [3, 8, 12]. Verapamil has the most favorable profile among all the drugs used, although there have been reports on using other drugs from the group of calcium channel blockers (nicardipine, diltiazem) and papaverine [8] for the same purpose [3, 6, 11]. According to the literature, papaverine is characterized by a fairly high rate of complications.

The technique employed in our report was similar to one described in the study by P. Jun et al. [3]. The authors analyzed the results of endovascular treatment in 189 patients with refractory vasospasm in the acute phase after aneurysm rupture. 286 intraarterial injections of verapamil and 59 combined treatment procedures (administration of verapamil in combination with angioplasty) were performed in this series of patients. Verapamil dosage depended on vasospasm severity and was 2–30 mg per vessel and 3–55 mg per procedure. Repeated administration was conducted in 102 (54%) patients in cases of refractory vasospasm. Complications directly caused by endovascular procedure developed in 6 patients and led to neurological deterioration in two of them. Favorable and adverse treatment outcomes were observed in 115 (61%) and 55 (29%) patients, respectively; 16 patients died due to cerebral causes, 3 patients died of associated complications.

Our report provides the first in Russian scientific literature description of the clinical case of successful endovascular treatment of cerebral vasospasm (developed after a severe SAH in a patient with a right ICA bifurcation aneurysm) using intraarterial verapamil administration.

**Table 2. TCD data (BFV, cm/s) 60 min after selective intraarterial verapamil administration in the right internal carotid artery**

<table>
<thead>
<tr>
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<td>ACA</td>
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<td>72</td>
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<td>VA</td>
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<td>ICA</td>
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<td>MCA (average)</td>
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<td>ICA (average)</td>
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<td>Lindegaard index</td>
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<td>2.67</td>
</tr>
</tbody>
</table>

**Table 3. TCD data (BFV, cm/s) on day 6 after the surgery (day 10 after SAH)**

<table>
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<td>Resistance index</td>
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<tr>
<td>Lindegaard index</td>
<td>3.33</td>
<td>1.54</td>
</tr>
</tbody>
</table>
Conclusion

Endovascular treatment methods play an important, sometimes unique, role in modern vascular neurosurgery, especially in surgery of giant aneurysms and aneurysms of the posterior parts of the circle of Willis. Experience accumulated in the literature demonstrates that endovascular treatment of vasospasm is a relatively safe method with a low rate of complications both using angioplasty and intraarterial verapamil infusion. The publications of the leading foreign endovascular surgeons focused on this issue need further research and need to be adapted to Russian clinical practice. Preliminary results give grounds for concluding that the endovascular technique, in contrast to other methods for treating vasospasm, can be an effective means of reducing the lethality and disability in patients who underwent hemorrhage from an aneurysm.

REFERENCES


Commentary

Vasospasm caused by subarachnoid hemorrhage (SAH) develops in 70—100% of patients with cerebral aneurysm rupture. Symptomatic spasm occurs in 20—30% of patients and is accompanied by a 2—3-fold increase in lethality. In this connection, the subject matter of the article is extremely topical.

The authors presented a very interesting observation of vasospasm treatment by selective intraarterial verapamil administration. The treatment allowed the surgeons to bring the patient admitted to the hospital in a deep coma to her normal life. The clinical case is described in the traditional manner and is well illustrated with tables and figures. The study is very interesting, relevant, and essential to improve the quality of intensive care in patients with vasospasm due to the cerebral aneurysm rupture and can be published.

S.S. Petrikov (Moscow)
Radical Removal of a Malignant Mediastinal Hemangioendothelioma with Restoration of the Main Blood Supply to the Brain


1N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow; 2Blokhin Russian Cancer Research Center, Moscow, Russia

A 46-year-old man with unverified anterior superior mediastinal tumor, which was diagnosed in 2010, sought medical care at the Cancer Research Center of the Russian Academy of Medical Sciences in October 2012. Progressive compartment syndrome of the superior vena cava was observed. CT, MRI, angiography, histological and cytological examination of biopsy material failed to confirm the morphological structure of the tumor. Removal of the tumor with bifurcation of the brachiocephalic trunk prosthetics was performed. Immunohistochemical (IHC) study verified malignant hemangioendothelioma.

Keywords: tumors of the mediastinum, hemangioendothelioma, neurophysiological monitoring.

Mesenchymal tumors may have various histological forms. Vascular tumors (32.6%), adipose tissue tumors (28.8%), fibroblastic and fibrohistiocytic neoplasms (15.3%) comprise a relatively large group, while only sporadic cases have been reported for the other types of tumors [3]. Hemangioendothelioma is a tumor originating from the vascular tissue with different degrees of differentiation: from benign (hemangiomas) [17, 19] to malignant ones (angiosarcomas). Hemangioendothelioma develops in various organs: lungs, liver, spleen, bones; mediastinal hemangioendotheliomas are rather rare.

Clinical manifestations of the tumor are accompanied by non-specific symptoms or the absence of symptoms. Mediastinal hemangioendothelioma is rarely discussed in light of differential diagnosis of mediastinal tumors.

The international experience in treatment of these tumors is rather scant and mostly represented by sporadic clinical cases. Retrospective reviews describe small patient groups [17–19, 22, 23, 25].

Clinical case

A 46-year-old patient received outpatient care at the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences, over the period from October 22, 2012 until January 10, 2013.

The patient was admitted to the hospital with preliminary diagnosis of malignant schwannoma of the anterosuperior mediastinum. His condition was assessed after biopsy of the tumor performed on November 3, 2013. The patient underwent 10 courses of polychemotherapy, beam therapy (TBD 50 Gy; December 8, 2012) at place of residence. Compartment syndrome of the superior vena cava (SVC), right-sided thrombosis of the internal jugular vein, and subcompensation of cerebral blood flow were observed.

When admitted, the patient complained of bursting sensation in his head under insignificant physical activity, hoarse voice, dysphagia, vision impairment, headache, and dizziness.

Past medical history. In November 2010, the patient started to have a bursting sensation in head and eyes when bending his body. He was examined at the place of residence. CT revealed an anterior mediastinal tumor. In February 2011, the patient underwent left-side thoracotomy and tumor biopsy. After re-examination of histological specimens at the Regional Oncology Clinics, the patient was diagnosed with malignant schwannoma. He was given two courses of polychemotherapy with vincristine, doxorubicin, cyclophospham, and dacarbazine, which showed no effect. The chemotherapy regimen was changed. Over the period from July 2011 till April 2012, the patient received 8 courses of polychemotherapy with doxorubicin, mesna, and dacarbazine phosphamide, which also showed no effect. Since June 2012, the patient noted the symptoms of dysphagia, hoarse voice, and vision impairment. Over the period between July 13, 2012 and August 17, 2012 he received a course of gamma therapy (TBD of 50 Gy; SBD of 2 Gy) for the mediastinal tumor at the Republican Oncology Clinics; the CT data showed the minimal clinical effect. The patient was referred to the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences, to receive consultation and determine the further treatment strategy.

Patient’s condition upon admission was relatively satisfactory. Height 170 cm; body weight 67 kg.
Examination revealed swelling of the face and neck (Fig. 1a) and pronounced neck vein swelling (Fig. 1b), which became stronger under physical activity; reddening of the face and neck areas under physical activity and when bending forward (compartment syndrome of the SVC), occasional pulse deficit of the right radial artery. The veins of the anterior thoracic wall both on the left and right sides were dilated.

CT scan obtained on October 15, 2012 (Fig. 2) showed a 3×4.5 cm tumor node visualized in the superior mediastinum along the right common carotid artery (CCA) and the right subclavian artery, as well as in the starting portions of the brachiocephalic trunk. The arterial vessels ran along the posterior surface of the node; only the CCA ran in the bulk for 2 cm; the SVC was stenosed (affected) and ran along the anterolateral surface. The subcutaneous veins and the thoracic vein were dilated. The left brachiocephalic vein was stenosed; no blood circulation was detected in it. Sporadic foci-like nodularities up to 0.3 cm in size (fibrosis?) were detected in the parenchyma of both lungs. Bronchial lumina were unchanged. Conclusion: a tumor node along the mediastinal vessels (a primary tumor? a metastasis?).

Histological conclusion made on October 11, 2012: small fragments of fibrous connective tissue with myxomatosis foci containing cells with oblong nuclei and thin collagen fibers, hemorrhage spots, and hemosiderophages were detected in the specimens. Such regions may occur in case of secondary (degenerative) changes in peripheral nerve sheath tumor (e.g., schwannoma). However, the data were rather scant, making the judgments of the tumor nature hypothetical. The immunohistochemical test did not refine the diagnosis (providing a positive response only to anti-vimentin antibodies).

Endoscopic examination included fibrobronchoscopy (October 29, 2012); the right side of the larynx was immobilized during the phonation. The mucous membrane

Fig. 1. Patient’s appearance before the surgery. 
Fig. 2. SCT of the thoracic organ of the patient before the surgery.
a – swollen face and neck; b – swollen neck veins.
of the larynx was hyperemic. The tracheal lumen was wide; the tracheal rings were well-differentiated. The vascular pattern was enhanced. The carina was straight; its base was non-dilated. Examination of the both halves of the bronchial tree revealed no tumor pathologies. The bronchial lumina accessible for examination were unobstructed. The mucous membrane was pink, smooth, and shiny. There was a small amount of mucous contents in the bronchial lumen. Conclusion: paresis of the right half of the larynx. No tumor pathology was revealed in the tracheobronchial tree.

Fibroesophagogastroduodenoscopy was performed on October 29, 2012. No changes were detected in the esophagus lumen; the walls were flexible; the mucous membrane in the upper and medium thirds of the esophagus was paste-like. The mucosal rosette at the cardiac orifice was flexible and closed completely. The stomach contained a moderate amount of mucus. The lumen was unchanged; the walls were flexible; the mucous membrane was pale pink. The strongly curved folds were soft and mobile. The bulb and postbulbar portions of the duodenum were unchanged. No biopsy was performed. Conclusion: visual signs of venous stasis at the levels of the upper and medium thirds of the esophagus. No pathological changes were observed in the stomach and duodenum.

MRI was performed on October 24, 2012: no accumulation of a contrast agent in the brain was reported. No reliable data on disturbance of the architecture of cerebral arteries were obtained. The ventricular system was neither dilated nor displaced. During the examination of the neck vessels, the right jugular vein was not detected; however, the wide collateral emissarium was determined paravertebally. The left jugular vein was unchanged. The right vertebral artery was considerably narrower than the left one. The other arteries of the neck were almost unchanged. A large tumor node was detected upwards and in the medial direction from the SVC. Unstenosed brachiocephalic arteries ran in its bulk and in the medial direction from the node (blood circulation in these arteries was unchanged). The left brachiocephalic vein was found to originate from the tumor; its walls were thickened; the lumen was narrowed. This vein approximately at the level of the lower third of the neck was not visualized.

Ultrasonographic examination performed on October 9, 2012: no signs of distant metastases were revealed.

Ultrasonographic examination performed on October 26, 2012: the common carotid arteries were linear. The intima–media complex thickness was 0.5 mm. No signs of stenosis or occlusion were revealed. The blood stream was symmetrical. The vertebral arteries were passable, without any signs of stenosis or occlusion. Thrombotic masses (0.4×0.4 in size; up to 3.0 cm long) were visualized on the right side of the lumen of the internal jugular vein; the blood flow was mapped above. The superficial and deep veins of the lower extremities were passable on both sides over the entire length and compressible; their lumen was unobstructed; the blood flow was mapped. Conclusion: local right-sided thrombosis of the internal jugular vein. No data on thrombosis of the veins of the lower extremities were obtained.

Magnetic resonance angiography of cerebral vessels in the reformation mode revealed signs of anterior communicating artery and right-side posterior communicating artery. Tentative clamping of the right CCA under control of duplex scanning and simultaneous monitoring of the linear velocity of blood flow (LVBF) in the middle cerebral artery (MCA) at the right side resulted in a decrease in LVBF in the right MCA from 75 to 40 cm/s followed by an increase in LVBF to 45–50 cm/s in 1 min after the clamping. No focal symptoms emerged during the 2–3 min of clamping. Thus, signs of subcompensation of the cerebral blood flow were caused by clamping the right CCA according to the data of clinical and instrumental examination. Decision regarding temporary shunt placement when performing reconstruction of the CCA should be made intraoperatively according to the data of neurophysiologic ultrasound monitoring. Patient’s condition was discussed at the clinical conference at the N.N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences. Surgical treatment was recommended. During the preoperative preparation, the patient received several consultations from Academician M.I. Davydov and vascular neurosurgeons working at the N.N. Burdenko Neurosurgical Institute.

The surgical treatment was carried out on November 8, 2012 by surgeons M.I. Davydov, V.A. Sobolevsky, L.A. Nikulichev, D.Yu. Usachev, S.S. Gerasimov, V.A. Lukshin, and anesthesiologist V.E. Gruzdev.

Radicality of surgical intervention: resection of the anterior mediastinal tumor and prosthetics of the brachiocephalic arterial trunk, CCA, and the subclavian artery was performed. Resection of SVC and the right clavicle was carried out through a combined transternal approach.

Surgery course: partial manubrio–sternotomy along the 3rd right intercostal space in combination with the “collar” approach. The sternocleidomastoid muscle was isolated and transected. Resection of two thirds of the right clavicle was performed followed by pericardiectomy.

A 5×6 cm tumor node infiltrating in the mediastinal pleura was visualized during the revision in the upper mediastinum along the right CCA and right subclavian artery, as well as in the initial portions of the brachiocephalic trunk. Arterial vessels ran in the nodular bulk, while the SVC was stenosed (affected) and ran along the anterolateral surface. The subcutaneous veins and the thoracic vein were dilated. The left brachiocephalic vein was narrowed; no blood flow was detected in it. Mediastinal adipose tissue was dense. The left brachiocephalic vein was isolated and ligated.

The SVC was mobilized by being resected in its distal portion and at the level of the jugular vein in the proximal portion using an US30 surgical stapling instrument.

The tumor with the great vessels (the brachiocephalic trunk, the right CCA, and the right vagus nerve) was
mobilized. The vessels were isolated and a tourniquet was applied (Figs. 3, 4).

The right vertebral artery was visualized and a tourniquet was applied.

The tumor was resected together with the mobilized vessels.

Arterial vessels were reconstructed using a Gore-Tex bifurcation graft (Figs. 5a, b).

Radical surgery was performed. The total duration of the surgery was 5 h 30 min. The vascular grafting stage included multimodal neurophysiological monitoring (transcranial ultrasound dopplerography with detection of the MCA on the right side and cerebral oxymetry (CO) [6, 14]. Taking into account the pattern of compensation for cerebral circulation under conditions of moderate arterial hypertension (reduction of LVBF from 80 to 60 cm/s after the CCA was clamped, while the CO indicators remained unchanged), a decision was made to perform the main stage of reconstruction without using a temporary intraluminal shunt. The stage of clamping the right CCA took 26 min. The stage of clamping the right subclavian artery took 40 min. The total blood loss was 2500 ml; 1000 ml of autologous blood was replaced using a Cell Saver system. The patient was awakened and extubated while lying on the operating room table; no signs of neurological deficit were revealed.

Features of the anesthetic support

The main task of an anesthetist during the surgeries involving interventions for the great cerebral vessels is to maintain adequate cerebral perfusion pressure. It is extremely important to prevent increased levels of brain metabolism and increased myocardial load [9].

The procedure of combined multimodal anesthesia, which is commonly used in most European clinics and in the Russian Cancer Research Center, was selected. This procedure allows one to perform well-controlled anesthetic support of various trauma surgeries of different duration and localization [1, 8].

To ensure perioperative anesthesia, an epidural catheter was placed at the Th2–Th3 level [24]. A ropivacaine (Naropin), fentanyl, and adrenaline mixture was infused through the catheter.

After anesthetic induction with barbiturates, the anesthesia was maintained by sevoflurane inhalation. This inhaled anesthetic agent allows easy, prompt, and safe control of anesthetic depth within a wide range at any stage of the surgery [5].
There are special requirements to vital function monitoring when performing such complex surgeries. The standard set of parameters (12-lead ECG, SpO₂, HBR, and complete blood gas analysis) was supplemented with invasive monitoring of blood pressure (BP) and controlling the EEG parameters according to the entropy values. Neurophysiological monitoring prevented the development of cerebral ischemia at the stages of clamping and replacing the right CCA. With allowance for the international recommendations, the normal or slightly elevated level of BP was maintained [15, 16, 20].

The adequate and continuous venous approach was ensured by a femoral vein catheter. Blood from the surgical wound was collected by a reinfusion device. The combination of these measures ensured the smooth intraoperative course and possibility of early extubation of the patient on the operating room table without any signs of neurological disorders.

Fig. 6 shows the indicators of cerebral oximetry measured separately for each hemisphere.

Fig. 7 shows the stability of the main (“non-specific”) indicators of monitoring.

**Morphological examination of the surgical material (November 19, 2012)**

The neoplasm mostly consists of dense fibrous tissue with thin collagen fibers, fibroblast- and histiocyte-like cells spreading to the arterial walls (mainly near the outer tunic — the adventitial tunic) (Fig. 8) and propagating to the venous wall and obliterating its lumen. Cell aggregates with round-shaped and oblong nuclei localize in some spots of the fibrous tissue; the periphery of these aggregates is characterized by hematomas of various prescription, lymphohistiocytic infiltration, and deposition of calcium salts. A fragment of adipose tissue contained lymphatic nodules without tumor growth signs. Conclusion: tumor histogenesis could not be verified based on the light microscopy data only. An immunohistochemical examination was required to determine the tumor type.

An immunohistochemical examination was performed on November 27, 2012 to refine the diagnosis (blocks...
39014/12 — paraffin blocks obtained before radiosurgery) using a broad panel of antibodies against vimentin, desmin, Ki-67, S100, CD34, CD31, β-catenin, CD57, GFAP, CD68, CD117, CD99, bcl2, α-antitrypsin, FAP, type IV collagen, chromogranin, synaptophysin, HMB-45, SMA, and caldesmon. Expression of CD34, CD31, type IV collagen was detected in the tumor cells. No expression of vimentin, desmin, S100, β-catenin, CD57, GFAP, CD68, CD117, CD99, bcl2, α-antitrypsin, FAP, chromogranin, synaptophysin, HMB-45, SMA, and caldesmon was detected. Conclusion: with allowance for the morphological and immunohistochemical patterns (extended sclerotic fields in the tumor, which are associated with the previous treatment), the clinical examination data, and features of the disease course, this tumor should be regarded as a transitional epithelioid hemangioendothelioma (Ki-67 labeling index was 5%).

Postoperative period

The patient stayed at the intensive care unit for 4 days and was subsequently transferred to the thoracic department. Abundant serous discharge (up to 600 ml per day) via the mediastinal drainage was observed up to December 1, 2012, when the amount of the discharge started to decrease. The drainage was removed on December 4, 2012. Hyperthermia developed on December 6, 2012; the mediastinal cavity was redrained. The material obtained was referred to bacteriological examination; antibiotic treatment was prescribed. Despite the therapy, the hyperthermia persisted and the patient’s condition deteriorated. On December 11, 2012, significant amount of fluid in the pericardial cavity was detected during echocardiography. The patient underwent pericardiocentesis in the operating room; 500 ml of turbid yellow/pink fluid was isolated. On December 12, 2012, ultrasonographic examination revealed a significant amount of fluid in the right pleural cavity; the patient was subjected to pleurocentesis; up to 100 ml of chylous fluid (chylothorax); a drain was placed. On December 18, 2012, the patient complained of dyspnea and sensation as if the sternum was compressed. CT scanning and ultrasonography showed a significant amount of liquid in the pericardial cavity. The patient underwent pericardiocentesis in the operating room; 670 ml of turbid yellow/pink fluid was isolated; the drain was placed into the pericardial cavity. On December 19, 2012, additional 520 ml of chylous fluid was evacuated from the pericardial cavity (the chylous nature of the fluid was verified by biochemical examination).

According to the data of cytological examination performed on December 19, 2012, the fluid obtained by draining the pleural and the pericardial cavities contained mesothelial, plasma, and lymphoid cells. No tumor cells were detected.

A bacteriological examination of the fluids isolated on December 17, 2012 from the pleural and pericardial

Fig. 8. Macrospecimen of the tumor.

a — infiltration of tumor vessels; b — lumen of the brachiocephalic trunk in the tumor; c — lumina of the common carotid and subclavian arteries in the tumor.
cavities, of venous blood and wound discharge provided a negative result (no growth on culture media).

Patient’s condition considerably improved after massive antibacterial therapy, infusion therapy with parenteral nutrition, and fat-free diet. The drains were removed on January 1, 2013 after the X-ray control. With allowance for the histological subtype and low mitotic activity, the adjuvant therapy was not indicated. Dynamic follow-up every three months was recommended.

The recovered patient was discharged from the hospital. Patient’s condition at discharge was satisfactory.

Discussion

Hemangioendotheliomas are attributed to the group of soft-tissue sarcomas, subgroup of vascular tumors, and subtype of endotheliocytic tumors. The total incidence rate of soft-tissue sarcomas is 1.4 per 100,000 population (in individuals older than 80 years, 8.0 per 100,000 population). The WHO classification of soft-tissue and bone tumors is commonly used [10].

When determining the biological potential of a tumor, WHO recommends subdividing the soft-tissue tumors into the four categories as follows: benign, locally aggressive, rarely metastasizing, and malignant ones [3]. These categories should not be confused with the degree of malignancy. The degree of malignancy of soft-tissue sarcomas is currently evaluated using three indicators (the FNCLCC grading system): tumor differentiation, proliferative activity of tumor cells, presence and intensity of tumor tissue necrosis [4, 11, 12].

I. Tumor differentiation: score 1 – sarcomas closely resembling normal, adult soft tissue; score 2 – sarcomas with signs of slight resemblance with the normal adult soft tissue; score 3 – embryonal sarcomas, undifferentiated sarcomas, and sarcomas of doubtful tumor type.

II. Mitotic activity (mytosis count per high-power field under x400 magnification): score 1 – 0 to 9 mitoses; score 2 – 10 to 19 mitoses; score 3 – 20 or more mitoses.

III. Tumor necrosis: score 0 – no tumor necrosis; score 1 – less than or equal to 50% tumor necrosis; score 2 – more than 50% tumor necrosis.

The total score of all three micromorphological indicators determines three degrees of malignancy of soft-tissue sarcomas: grade I – score 2–3, grade II – score 4–5, and grade III – score 6–8.

Hemangioendotheliomas are tumors originating from the vascular tissue and can be subdivided into three types: epithelioid hemangioendothelioma [25], endovascular papillary angioendothelioma (or Dabska tumor) [21], and spindle cell hemangioendothelioma [18]. Hemangioendotheliomas may affect any organ (lungs, liver, spleen, bones). It is a rare type of tumor and can be accompanied by clinical symptoms induced by other oncological processes occurring in the mediastinum (dyspnea, glottic spasm, cough, thoracic pain, dysphagia, etc.) or can be asymptomatic (in this case, it is radiologists who detect them). Hemangioendotheliomas occur equally often in adult males and females and almost do not occur in children [13].

S. Weiss et al. were the first to describe hemangioendotheliomas as a separate subtype of vascular tumors [25]. The authors performed a follow-up of 46 patients after surgical treatment for epithelioid hemangioendotheliomas for 48 months. Local relapses were detected in 13% of cases; metastases were observed in 31% of cases; the lethality rate was 13% in patients with soft-tissue epithelioid hemangioendotheliomas and 40 and 65% in patients with epithelioid hemangioendotheliomas of the lungs and liver, respectively.

Mytosis count per high-power field, the presence of necrosis and metaplasia of bone, as well as increased cellular pleomorphism are the key histological prognostic parameters.

Epithelioid hemangioendotheliomas are tumors with boundary malignancy and are regarded as low-malignancy angiosarcomas. Most cases are characterized by low lethality; however, in some cases fatal metastases were revealed. A. Deyrup et al. [7] in their observation of 51 patients with hemangioendotheliomas in 1989–2005 reported a 81% five-year survival rate. Among 11 (21%) patients, metastases to the lungs were detected in 6 patients; to the lymph nodes (in 4 patients); to the liver (in 2 patients); and to bones, soft tissues, and the retroperitoneal space (in 1 patient in each case). When performing a univariate analysis, the mitotic activity and tumor size were associated with high lethality ($p=0.007$ and $p=0.004$, respectively). Tumor localization, degree of cellular atypia, presence of necrosis is not statistically significant. Patients with the verified high risk of metastasis survive more than 5 years in 59% of cases; the patients with the low risk of metastasis survive more than 5 years in 100% of cases.

Biopsy is not recommended because of the risk of massive hemorrhage. The objective of the treatment is to perform radical excision of the tumor masses. With allowance for the possible infiltration of the brachiocephalic arteries (as it was reported in this clinical case), the possibility of radical surgery followed by reconstruction of branchiocephalic arteries depends on patient’s tolerance to temporary occlusion of the CCA. The choice of the tactics for brain protection in these cases is determined according to the results of multimodal neurophysiological monitoring when planning the surgical intervention and intraoperatively.

Surgical intervention is the only radical therapy. Radiation therapy does not ensure satisfactory results; nevertheless, many authors recommend irradiating to reduce tumor growth and the risk of metastasis in case of inoperable vascular tumor [2].

If a tumor with high degree of malignancy was verified, radiation or chemotherapy can be proposed as an adjuvant treatment [22].
REFERENCES


Commentary

There are two aspects why the aforesaid described clinical case is of interest. On one hand, a rare tumor (malignant mediastinal hemangioendothelioma) has been resected. On the other hand, an up-to-date vascular procedure has been used, which made it possible to radically remove the tumor together with the brachiocephalic trunk involved in the oncological process and to recover blood flow along the vital arteries.

The favorable outcome of this surgery was possible only provided that oncologists and vascular surgeons worked together. At the current stage of development of surgery it is only cooperation, close collaboration, and mutual understanding between surgeons of various specializations, anesthetists, and resuscitation specialists that can allow them to achieve good results of treatment in patients with combined polyfactor pathologies.

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Topics to be covered in our next issue:

- Diagnosis and principles of surgical treatment for tumors of the skull base
- fMRI studies of the dominant hemisphere
- Anesthesiological management in transnasal surgery