Burdenko Neurosurgical Institute, Moscow, Russia
Official journal of the Association of Neurosurgeons of Russia

«Zhurnal voprosy neirokhirurgii imeni N N Burdenko» (Burdenko's Journal of Neurosurgery) is a bimonthly peer-reviewed medical journal published by MEDIA SPHERA Publishing Group. Founded in 1937.

Sponsored by fund «Neuro»

Journal is indexed in RSCI (Russian Science Citation Index), Web of Science (Russian Science Citation Index — RSCI), Scopus, PubMed/Medline, Index Medicus, Chemical Abstracts, Ulrich’s Periodicals Directory, Google Scholar.

EDITORIAL BOARD

Editor-in-Chief A.N. Kononov
Deputy Editor-in-Chief O.N. Drevau
Executive Editor A.V. Kozlov

Science Editors B.A. Kadashev, O.B. Belousova

FUNDAMENTAL AND PRACTICAL JOURNAL

Vol. 81 4’2017

EDITORIAL COUNCIL

S.K. Akhulakov (Astana, Kazakhstan), S.R. Arustamyan (Moscow, Russia), A.Kh. Bekuashev (Moscow, Russia), A.Yu. Belyaev (Moscow, Russia), V.P. Bersnev (St. Petersburg, Russia), O.A. Gadzhieva (Moscow, Russia), Yu.A. Grigoryan (Moscow, Russia), G.A. Koshunov (Moscow, Russia), Yu.V. Kusal (Moscow, Russia), V.V. Krylov (Moscow, Russia), I.N. Pronin (Moscow, Russia), A.S. Saribekyan (Moscow, Russia), S.V. Tanyashin (Moscow, Russia), T.P. Tissen (Moscow, Russia), Yu.A. Tomyk (Moscow, Russia), V.A. Vecherak (Moscow, Russia), V.A. Shabalov (Moscow, Russia), A.R. Shakhnovich (Moscow, Russia), V.N. Shimansky (Moscow, Russia), L.V. Shishkina (Moscow, Russia), Sh.Sh. Eliava (Moscow, Russia),...
## CONTENTS

### ORIGINAL ARTICLES

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shekhtman O.D., Eltsova Sh.Sh., Pilenko Yu.V., Konовал An.N. On the Classification of Large and Giant Paraclinoid Internal Carotid Artery Aneurysms</td>
<td>15</td>
</tr>
<tr>
<td>Galaktionov D.M., Dubovoy A.V., Kiselev V.S., Sosnov K.S., Perfilyev A.M., Cherepanov A.V. Combination Treatment of Cerebral Arteriovenous Malformations Using Endovascular and Microsurgical Techniques</td>
<td>23</td>
</tr>
<tr>
<td>Kim S.A., Letyagin G.V., Danilin V.E., Synoeeva A.A. Shunt-Induced Craniosynostosis: Topicality of the Problem, Choice of the Approach, and Features of Surgical Treatment</td>
<td>37</td>
</tr>
<tr>
<td>Kushel’ Yu.V., Belova Yu.D., Tekoev A.R. Intramedullary Spinal Cord Tumors and Hydrocephalus: an Analysis of the Results of Surgical Treatment in 541 Patients</td>
<td>47</td>
</tr>
<tr>
<td>Astaf’eva I.I. The Efficacy of Desmopressin in the Treatment of Central Diabetes Insipidus After Resection of Chiasm-Sellar Region Tumors</td>
<td>51</td>
</tr>
</tbody>
</table>

### CASE REPORTS

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korshunov A.E., Kushel’ Yu.V. Expansive Suboccipital Cranioplasty in Chiari-1 Malformation (a Case Report and Technical Notes)</td>
<td>92</td>
</tr>
</tbody>
</table>

### REVIEW

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abramov I.T., Pitskhelauri D.I., Serova N.K. Pineal Cyst</td>
<td>97</td>
</tr>
</tbody>
</table>
In accordance with the resolution of the Higher Attestation Commission of the Ministry of Education and Science of the Russian Federation, the Problems of Neurosurgery named after N.N. Burdenko 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.

---

**Topics to be covered in our next issue**

- Frameless electromagnetic navigation in neurosurgery
- Indications for surgical management of prolactin-secreting pituitary adenomas
- Relevant respiratory strategies in neuroresuscitation

A.N. SHKARUBO1, K.V. KOVAL’1, G.F. DOBROVOL’SKII1, M.A. SHKARUBO1, V.V. KARNAUKHOV1, B.A. KADASHEV1, D.N. ANDREEV1, I.V. CHERNOV1, O.A. GADZHIEVA1, O.YU. ALESHKINA2, E.A. ANISIMOVA2, P.I. KALININ1, M.A. KUTIN1, D.V. FOMICHEV1, O.I. SHARIPOV1, D.B. ISMAILOV1, E.S. SELIVANOV3

1Burdenko Neurosurgical Institute, Moscow, Russia; 2Razumovskiy Saratov State Medical University, Saratov, Russia; 3Regional Clinical Hospital, Saratov, Russia

**Objective** — to describe the main topographic and anatomical features of the clival region and its adjacent structures for improvement and optimization of the extended endoscopic endonasal posterior (transclival) approach for resection of tumors of the clival region and ventral posterior cranial fossa.

**Material and methods.** We performed a craniometric study of 125 human skulls and a topographic anatomical study of heads of 25 cadavers, the arterial and venous bed of which was stained with colored silicone (the staining technique was developed by the authors) to visualize bed features and individual variability. Currently, we have clinical material from more than 120 surgical patients with various skull base tumors of the clival region and ventral posterior cranial fossa (chordomas, pituitary adenomas, meningiomas, cholesteatomas, etc.) who were operated on using the endoscopic transclival approach.

**Results.** We present the main anatomical landmarks and parameters of some anatomical structures that are required for performing the endoscopic endonasal posterior approach. The anatomical landmarks, such as the intradural openings of the abducens and glossopharyngeal nerves, may be used to arbitrarily divide the clival region into the superior, middle, and inferior thirds. The anatomical landmarks important for the surgeon, which are detected during a topographic anatomical study of the skull base, facilitate identification of the boundaries between the different clival portions and the C1 segments of the internal carotid arteries. The superior, middle, and inferior transclival approaches provide an access to the ventral surface of the upper, middle, and lower neurovascular complexes in the posterior cranial fossa.

**Conclusion.** The endoscopic transclival approach may be used to access midline tumors of the posterior cranial fossa. The approach is an alternative to transcranial approaches in surgical treatment of clival region lesions. This approach provides results comparable (and sometimes better) to those of the transcra nial and transfacial approaches.

**Keywords:** endoscopic transclival approach, clivus, skull base anatomy, cranial nerves, posterior cranial fossa.

---

**Abbreviations:**

FM — foramen magnum  
ICA — internal carotid artery  
OC — occipital condyle  
HC — hypoglossal canal  
DM — dura mater  
ETA — endoscopic transclival approach  
EEA — endoscopic endonasal approach

The posterior cranial fossa region, including the clivus and ventral surface of the brainstem, is the hardest-to-reach area in skull base surgery.

Despite the active development of various surgical techniques in recent decades, treatment of tumors of the clivus region and surrounding anatomical structures still remains a challenge for the surgeon.

The topographoanatomical clivus may be conditionally divided into superior, middle, and inferior parts. This classification of the clival parts is based on the use of external landmarks identified by neurosurgeons during the transnasal approach [1, 2].

Our study is focused on the relationships between the bone structures of the outer and inner surface of the clivus as well as on endoscopic anatomy of the brainstem, vascular structures, and cranial nerves.

The study purpose (Part 1) is to perform a topographic and anatomical study of the clival region and its surrounding structures for identification of the main anatomical landmarks of the superior, middle, and inferior parts of the clivus and to use the results of the craniometric study for optimization of the transclival approach.
Material and methods

The craniometric study of 125 human skulls was performed in the Craniometric Laboratory of the Anatomical Museum of the Human Anatomy Department of the Razumovskiy Saratov State Medical University. We performed statistical processing of the obtained data and calculated mean values and mean errors. We obtained data on the area of safe resection of the clival region structures and an additional area of occipital condyle resection as well as identified relatively common bone structures and their relationships, which may be used as the main anatomical landmarks for safe resection of the clivus and occipital condyles during removal of midline skull base tumors extending into the posterior cranial fossa.

Our experience in the surgical treatment of different skull base tumors located in the clival region and ventral posterior cranial fossa (chordomas, pituitary adenomas, meningiomas, cholesteatomas, etc.) using the endoscopic transclival approach (ETA) includes more than 120 patients. According to the international literature, the

Filling of the arterial and venous vessels of the skull base and brain for their subsequent study was carried out in 25 cadaveric heads using the authors' technique (priority of Russian Federation invention No. 2016135280 of August 30, 2016 was established). Then, an endoscopic dissection of the midline skull base structures and craniovertebral junction was performed.

Results

The clivus that is formed by the sphenoid and occipital bones is a wide shallow depression inclined anteriorly and upward from the foramen magnum. The sphenoid bone forms the superior third of the clivus, which corresponds to the region located posterior and inferior to the dorsum sellae. The main part of the clivus is represented by the basilar part of the occipital bone. The occipital and sphenoid bones are joined together by the sphenoe-occipital synchondrosis just below the dorsum sellae, which completely ossifies and becomes inconspicuous in adults by about 23 years of age. Anteriorly, the clivus is inclined approximately 45° relative to the horizontal plane of the foramen magnum (FM) [8, 9].

When explored through the nasal cavity, the outer surface of the clivus appears convex and inclined downwards. The inferior surface of the sphenoid bone body is located anterior to the basilar portion of the occipital bone. The base of the vomer is represented by two wings that are connected to the inferior surface of the sphenoid bone. When viewed anteriorly along the hard palate axis, the lateral part of the skull base is largely shielded by the upper jaw body. The basilar part of the occipital bone can be visualized through the lower part of the nasal cavity and through the posterior nasal aperture (choana), through which the nasal cavity communicates with the nasopharynx [10].

The posterior end of the pterygoid (Vidian) canal that contains the pterygoid artery and pterygoid nerve opens to the upper part of the anterolateral margin of the foramen lacerum. In the foramen, the deep petrosal nerve from the sympathetic plexus of the internal carotid artery merges with the greater petrosal nerve into the Vidian nerve. An extended approach used in some pathological processes in the clival region requires in-depth knowledge of the topographic anatomical relationships of structures throughout the nasal corridor to the clivus [11, 12].

Frontal viewing of the external surface of the basilar part of the occipital bone reveals a small prominence (pharyngeal tubercle) located along the median line (Fig. 1b, d). The pharyngeal tubercle is the attachment site of the superior pharyngeal constrictor (Fig. 1b). It is located at an average distance of 17.4 mm posteriorly to the posterior edge of the vomer and 10.8 mm anteriorly and superiorly to the anterior edge of the foramen magnum. The longus capitis muscle is attached to the clavus lateral to the pharyngeal tubercle. The rectus capitis anterior muscle (a small muscle located in the deep layers of the longus capitis muscle) is attached superiorly in a small depression, the so-called supracondylar groove, situated immediately above the occipital condyle (Fig. 1a).

This groove serving for attachment of the rectus capitis anterior muscle that is located 9.0 mm above the anterior...
margin of the FM can also be represented as a small prominence called the precondylar tubercle. The supracondylar groove is an important anatomical landmark for identification of the hypoglossal canal and its external opening. The hypoglossal canal lies deeper than the groove (Fig. 1b). The extracranial opening of the hypoglossal canal and the jugular foramen occur lateral to the groove. The anterior margin of the foramen magnum is the attachment point of the anterior atlanto-occipital membrane. The paired lateral parts of the occipital bone are located on each side of the FM (Fig. 1)[8, 9]. The occipital condyles whose articular surfaces articulate with the atlas are located lateral to the anterior half of the FM, oval in shape, and convex downwards; the articular sur-

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>Side</th>
<th>Min, mm</th>
<th>Mean, mm</th>
<th>Max, mm</th>
<th>σ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsum sellae height</td>
<td>—</td>
<td>5.0</td>
<td>8.2</td>
<td>14.0</td>
<td>1.88</td>
</tr>
<tr>
<td>Dorsum sellae width at base</td>
<td>—</td>
<td>11.0</td>
<td>16.3</td>
<td>22.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Clivus length, from base to FM</td>
<td>—</td>
<td>29.0</td>
<td>35.6</td>
<td>42.0</td>
<td>2.6</td>
</tr>
<tr>
<td>From HC to basion</td>
<td>Left</td>
<td>12.0</td>
<td>15.2</td>
<td>20.0</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>12.0</td>
<td>14.9</td>
<td>19.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Distance between HCs</td>
<td>—</td>
<td>19.8</td>
<td>26.5</td>
<td>32.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Internal diameter of HC</td>
<td>Left</td>
<td>3.5</td>
<td>5.5</td>
<td>7.5</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>3.5</td>
<td>5.2</td>
<td>7.0</td>
<td>0.97</td>
</tr>
<tr>
<td>From HC to inferior margin of OC</td>
<td>Left</td>
<td>7.5</td>
<td>11.3</td>
<td>17.0</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>8.0</td>
<td>11.6</td>
<td>18.2</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Footnote. Here and in Table 2: OC — occipital condyle, PC — hypoglossal canal, FM — foramen magnum, σ — mean sampling error.
Fig. 3. Venous emissaries (canals) of the clivus.

a — skull base, an inside view, median clival canal. 1 — a probe in the median clival canal, 2 — petroclival fissure, 3 — internal openings of the hypoglossal canal; b — skull base, an outside view, median clival canal. 1 — a probe was introduced into the median clival canal from the inner surface of the skull base, 2 — the probe emerging from the median clival canal to the outer surface of the clivus, 3 — pharyngeal tubercle, 4 — condyle occipital, 5 — vomer, 6 — left foramen lacerum, right foramen lacerum, 8 — medial and lateral pterygoid processes, 9 — left pterygoid process of the sphenoid bone; c — skull base, an inside view, a view from the inside, paired opening of the median clival canal. 1, 2 — pori of the median clival canal on the inner surface of the skull base, 3 — internal opening of the hypoglossal canal, 4 — internal opening of the auditory canal, 5 — jugular foramen, 6 — petroclival groove; d — skull base, an outside view, disseminated venous emissaries of the clivus. 1 — disseminated venous emissaries on the outer surface of the skull base, 2 — pharyngeal tubercle, 3 — jugular tubercle, 4 — right jugular foramen, 5 — external opening of the right hypoglossal canal, 6 — left occipital condyle, 7 — left foramen lacerum, 8 — lateral pharyngeal tubercle, 9 — right occipital condyle.
The face is directed downwards and lateral; their long axes are directed anteriorly and medially. The hypoglossal canal is located above the middle third of the antero-posterior axis of the condyle and is directed anteriorly and laterally relative to the intracranial opening of the canal (Fig. 1c, d) [8, 9].

The following parameters were examined on the outer skull base (Tables 1 and 2): the length and width of the clivus in its superior, middle, and inferior parts; the length, width, and thickness of the occipital condyles; the distance between different parts of the occipital condyles and the external opening of the hypoglossal canal; the distance between apex of the pharyngeal tubercle and the basion. The following parameters were measured on the inner surface of the skull base (Fig. 1c, d) (Table 2): the width and height of the dorsum sellae; the diameter of the internal openings of the hypoglossal canals and the distance between them; the position of the hypoglossal canals relative to the basion.

When planning surgery and defining the limits of safe resection of the clival bone structures, it is necessary to know the area of maximum possible resection of the clivus (Fig. 2). In our craniometric study, the area of external resection of the clivus was 8.1 cm² on average; in the case of additional resection of the dorsum sellae (necessary in some cases), the approach area increases by 1.34 cm² on average, and, as a result, can amount to 9.44 cm² on average. The anterosuperior border of an irregular quadrilateral is the entire dorsum sellae; the inferior border is the anterior part of the FM; laterally, the border extends along the petroclival fissure from the posterior clinoid process to the anterior edge of the hypoglossal canal.

Yu.A. Gladilin and V.N. Nikolenko [13] first provided morphometric characterization of the “unsafe area of the outer skull base” limited by the openings through which the main arteries enter the brain — internal carotid and vertebral arteries; also the authors described the forms of “unsafe area” variability depending on the skull base shapes.

In a study performed by J. Sanmillan and co-workers on 12 skulls [14], the access area of ETA was compared to that of the subtemporal anterior transpetrosal approach. The study revealed that the surgical window area of ETA was much larger compared to that of the subtemporal anterior transpetrosal approach: 10.46±1.85 cm² vs. 2.00±0.80 cm², respectively. This indicates the obvious advantages of ETA. However, the results of this study can not be considered statistically significant because of a small sample size.

In our topographic anatomical study, we observed rare anatomical bone structures of the clival region; only single reports of these structures are available in the international literature [15, 16]. One of these structures was the so-called median clival canal (Fig. 3a). It should be noted that the openings at the anterior margin of the FM on the inner surface of the skull base have been described in the literature as the median clival canal. According to A.I. Osna [17] and E.A. Anisimova [16], the median clival canal may be referred to the category of venous emissaries. The canal can be opened to different sites (Fig. 3b). The occurrence rate of the median clival canal is 5.7% [16]. We found a variant of the canal structure with two openings on the inner surface of the clivus (Fig. 3c). A.I. Osna [17] and O.Yu. Aleshkina and E.A. Anisimova [16] have noted that the median clival canal contains venous emissaries that are connected with...
the basilar venous plexus of the clival region or with the marginal sinuses of the FM region.

In addition, we also found variants of disseminated bone canals containing venous vessels with multiple openings on the outer skull base (Fig. 3d). Therefore, we present specimens of rare cases of venous canals in the clival bone structures.

Their presence can complicate implementation of the transclival approach during the drilling stage due to potential development of hard-to-control diffuse venous bleeding from these canals and also due to air embolism, especially with the patient operated in the semi-sitting or sitting position.

Superior, middle, and inferior parts of the clivus

The superior part of the clivus is located between the dorsum sellae and the dural porus of the abducens nerve; the inferior part of the clivus is located between the level of the internal porus of the glossopharyngeal nerve and the anterior margin of the FM; the middle part of the clivus is situated between the superior and inferior parts (Fig. 4) [1, 2, 9]. According to T. Funaki et al. [1], the distance between the posterior clinoid process and the dural porus of the abducens nerve amounts to 13.2 mm (12—17 mm), on average; the distance between the opening of the abducens nerve canal and the glossopharyngeal nerve canal is 21.4 mm (19—24 mm); and the

---

**Fig. 5. Occipital condyle resection limits.**

a — skull base, an outside view. The area of maximum possible resection of the clivus (indicated by black hatching) and the area of maximum possible resection of the occipital condyle (indicated by blue hatching); b — skull base, an outside view. Black hatching indicates the maximum possible area of the endoscopic transclival approach (with resection of bone structures of the clivus, both occipital condyles, and anterior FM). In this situation, instability of the craniovertebral junction may develop, which will require stabilization surgery; c — skull base, a posterior view, an oblique projection. The area of maximum possible resection of the occipital condyle (46%) is shown: from the basion to the anterior hypoglossal canal.
distance between the glosopharyngeal nerve and the dental porus of the hypoglossal canal is 25.4 mm (23—30 mm).

According to T. Funaki et al. [1] and G. Iaconetta [18], relative to bone structures, the border between the superior and middle clivus is located 3.4 mm (1.5—6.0 mm) below the superior margin of the petrous apex, and the border between the middle and inferior clivus is located at the level of the infrajugular process on the medial part of the jugular foramen (Fig. 4).

**Borders of the superior and middle clivus**

In most cases, the border between the superior and middle clivus occurs at the level of the dural pori of the abducens nerves, approximately in the sphenoid sinus floor region. The relationships between the pori of the abducens nerves and the sphenoid sinus floor are variable and depend on the degree of sinus pneumatization. The lower border of the cavernous segment of the internal carotid artery (ICA) occurs at the join between the foramen lacerum segment and the paracaval segment and is a landmark for the dural pori [18]. The abducens nerve enters the pontomedullary groove and rises to the pontine cistern, reaching the dural porus. The abducens nerve is a stable and permanent bony prominence located on the medial part of the jugular foramen (Fig. 4)

**Borders of the middle and inferior clivus**

The border between the middle and inferior clivus is demarcated by a horizontal line passing through the glosopharyngeal nerve canals that correspond to the upper medial border of the jugular foramina. Frontal visualization of the extracranial portion of the jugular foramen reveals the glosopharyngeal nerve emerging from an opening in the sigmoid region. The pharyngeal tubercle is a stable and permanent bony prominence located on the middle line, which is a reliable landmark for identification of the border between the middle and inferior clivus. When visualized anteriorly and parallel to the hard palate line, the border between the middle and inferior clivus is located approximately at the level of the anterior margin of the pharyngeal tubercle, about 3.9 mm (2—8 mm) above the tubercle tip. The border is located 7.0 mm (4—10 mm) above the supracondylar groove where the rectus capitis anterior muscle is attached. Opening the clivus immediately below the anterior end of the pharyngeal tubercle exposes a cisternal portion of the glosopharyngeal nerve immediately after its exit from the DM [2, 21, 22].

A variant of additional extension of ETA to tumors of the inferior third of the clivus (with resection of the occipital condyle)

In the case of the extended endoscopic endonasal approach (EEA) to the inferior third of the clivus, the resection area can be extended outwards by means of the so-called mono- or bilateral transcondylar approach (with condyle resection) [2].

The standard EEA to the inferior third of the clivus has a trapezoidal shape formed due to resection of a narrow area between the condyles (Fig. 5a). Inferolateral borders of this approach are formed by anterior portions of the occipital condyles that confine the transverse dimension of lower resection to 19 mm (59% of the transverse size of the FM). In the EEA, unilateral anteromedial removal of the condyle can increase the approach window downwards up to 22.5 mm (70%), while bilateral resection of the condyles increases the access area to 26 mm (81%) without damaging the hypoglossal canals (Fig. 5b). In addition, anteromedial resection of the condyle in the standard transclival approach provides additional extension of the surgical corridor to 10 mm in the inferolateral direction [15, 19].

The external surface of the condylar part of the occipital bone has a distinctive feature — the supracondylar groove that is an excellent landmark for identification of the superior margin of the hypoglossal canal. The supracondylar groove as an intraoperative landmark was first described by V. Morera et al. [2]. This term is absent in the international anatomical nomenclature (2003) (Fig. 1a). The safe approach zone through the occipital condyle is the lower part of the hypoglossal canal. The hypoglossal canal is located posterior to the supracondylar groove. The distance between the supracondylar groove and the articular surface of the occipital condyle amounts approximately to 10 mm. Therefore, anteromedial resection can be performed by drilling downwards from this groove, without damaging the 12th pair of cranial nerves. This surgical approach provides an additional 10 mm of height of the surgical corridor [2].

Bilateral resection of more than 50% of the occipital condyles may cause craniocervical instability, which will require stabilization surgery. Unilateral resection of 50% of the occipital condyle is also unsafe because craniovertebral junction instability may develop. Unilateral resection of one-third of the occipital condyle is safe [2, 23, 24]. In this study, the mean anterior-posterior size of the occipital condyle was 25.1 mm on the left and 24.8 mm on the right, while the mean distance between the intracranial portion of the hypoglossal canal and the anterior margin of the occipital condyle was 11.3 mm, thereby demonstrating the topographically important location of the hypoglossal canal: almost in the middle of the condyle along the anterior-posterior axis. Therefore, the anterior cortical bone layer, up to the hypoglossal canal, should be used as an indicator of maximum anterior-posterior resection when 50% of the condyle is planned to
nerves in the lower neurovascular complex - glossopharyngeal, vagus, accessory, and hypoglossal. The dura oblongata, posterior inferior cerebellar artery, and anterior inferior cerebellar artery, and abducens, facial, and vestibulocochlear nerves are a landmark of the inferior third of the clivus (Fig. 4) [2, 25].

The division of the clivus into the superior, middle, and inferior parts by drawing transverse lines at levels of the dural pori of the abducens and glossopharyngeal nerves is based on the concept of three neurovascular complexes in the posterior cranial fossa [1]. Approaches to the superior, middle, and inferior clivus provide an access to the anterior–medial parts of the three neurovascular complexes [1, 2, 26]. An access to the superior clivus with its extension provides an approach to the middle brain, upper half of the pons, superior cerebellar artery, and also oculomotor and trigeminal nerves in the upper neurovascular complex. An access to the middle clivus provides an approach to the lower half of the pons, anterior inferior cerebellar artery, and abducens, facial, and vestibulocochlear nerves in the middle neurovascular complex. An access to the inferior clivus exposes the medulla oblongata, posterior inferior cerebellar artery, and glossopharyngeal, vagus, accessory, and hypoglossal nerves in the lower neurovascular complex (Fig. 4).

V. Morera et al. [2] suggested using the transcondylar approach to access the lateral portion of the inferior third of the clivus. To ensure safety of this approach, the following factors should be considered: the anatomical relationship between the occipital condyle and the parapharyngeal segment of the ICA; location of the hypoglossal canal; amount of condyle resection, as well as involvement of the alar ligament in the process.

A variant of the extended approach with resection of the occipital condyle increases the surgical corridor to 59—70%. This also provides an access to the vertebral artery to enable its greater proximal control. An additional vertical extension of this corridor can be achieved through the transjugular transtubercular approach, which provides visualization of the distal cisternal segments of the causal group of nerves. These modifications enable lateral extension of the surgical corridor up to 26 mm [2]. If the condyle is unilaterally resected less than 50%, the joint surface is spared, and attachment points of the alar ligaments are preserved, then further stabilization of the craniovertebral junction can be avoided [2].

Understanding the relationship between structures of the external and internal clivus is important in performing the EEA to the clivus and anatomical structures of the ventral posterior cranial fossa [20, 27].

In our next publications (Parts 2 and 3), we will present the results of a topographic anatomical study of the clivus projections on structures of the brainstem and main vessels, operative technique features, and analysis of surgical treatment outcomes in patients with different skull base tumors who were operated on using the extended (transclival) EEA.

Authors declare no conflict of interest.

REFERENCES


Commentary

Surgery of tumors of the clival region and ventral posterior cranial fossa is the most challenging field in surgical neuro-oncology. The progress in this field of neurosurgery is associated with basic research in clinical neuro-anatomy exploring the nervous system structure in health and disease, as well as in surgical neuro-anatomy, the main objective of which is to describe the position of an organ of the nervous system in general as an object of surgical intervention.

Regarding this article, it should be noted that operative endoscopic neurosurgery, based on the current achievements of neuro-anatomy and neurophysiology, has developed optimal procedures for exposing organs of the nervous system using the most rational operative endoscopic approaches and performing a certain type of minimally invasive surgical treatment in accordance with the classical principles by N.N. Burdenko: anatomical accessibility, technical capability, and physiological permissiveness.

The paper presents the main topographic anatomical features and endoscopic landmarks of the clival region and its adjacent structures, which enable improving and optimizing the extended endoscopic endonasal posterior (transclival) approach for removing tumors of the clival region and ventral posterior cranial fossa as well as describes the results of a craniometric examination of 125 human skulls and a topographic and anatomical study of 25 cadaveric heads, the arterial and venous beds of which were stained with colored silicone using the technique proposed by the authors to visualize anatomical features and individual variability.

The study provided the description of the main anatomical landmarks and parameters of the neuroanatomical structures necessary to perform the extended endoscopic endonasal posterior (transclival) approach, which enable conditional division of the clival region into the superior, middle, and inferior thirds. The intradural porti of the abducens and glossopharyngeal nerves are considered as the most important anatomical landmarks. The topographic anatomical landmarks revealed by the authors facilitate identification of the borders between different parts of the clivus and the C1 segments of the internal carotid arteries, and the described superior, middle, and inferior transclival approaches provide an access to the ventral surface of the upper, middle, and lower neurovascular complexes of the posterior cranial fossa. The authors proved that the endoscopic transclival approach is an alternative to transcranial approaches in surgical treatment of clival region lesions and can be used for approaching medial tumors of the posterior cranial fossa region.

At the same time, the article concluded that “the results of using endoscopic transclival approaches are comparable with those of transcranial and transfacial approaches, and in some cases exceed them”. However, there are no clinical data on comparison of the results of endoscopic transclival, transcranial, and transfacial approaches in removal of tumors in the clival region and ventral posterior cranial fossa. We suppose that these data will be substantiated and presented in the second clinical part of the study.

The article lacks data on various forms of the cerebral cranium, typical and individual features of the Blumenbach clivus and ventral posterior cranial fossa in brachy-, dolicho-, and mesocranic skulls. In this regard, there is a question of the authors’ attitude to the clinical significance of these anatomical factors.
The article lacks the authors’ attitude to the qualitative and quantitative criteria for evaluation of the extended endoscopic endonasal posterior (transclival) approach, which include the operative action axis as well as inclination angle and direction of the axis with respect to the frontal, sagittal, and horizontal planes; angle at which the surgeon views the surgical scene; angle of operative action; depth and index of the wound; zone of surgical accessibility, corresponding to the surgical wound floor area; upper aperture and wound floor ratio that underlies the rationality and minimal invasiveness of the approach.

It seems to be reasonable for the authors to evaluate the influence of different forms of the cerebral cranium, the typical and individual structural features of the Blumenbach clivus and ventral posterior cranial fossa in brachy-, dolicho-, and meso-cranic skulls on the qualitative and quantitative parameters of the extended endoscopic endonasal posterior (transclival) approach used for removal of tumors of the clival region and ventral posterior cranial fossa. In the case of the extended endoscopic endonasal posterior (transclival) approach, a narrow and deep wound requires combination of qualitative analysis of the operative action axis direction (anterior-posterior, superior-inferior, lateral-medial) and quantitative analysis in terms of degrees relative to the wound aperture plane.

This article demonstrates the considerable effort and modern methodological level of conducted research, high significance of its results that are of great interest for neurosurgeons and anatomists, teachers, students of postgraduate and additional education faculties, graduate students, and clinical residents of medical universities.

Yu.A. Shcherbuk (St. Petersburg, Russia)

The study topic is indisputably important. Optimal solutions to the existing issues of surgical treatment for tumors of the clival region and ventral posterior cranial fossa are based on interdisciplinary and complex studies. A similar approach is present in this paper. The authors successfully combined topographic anatomical studies and anatomical material. Both domestic and foreign scientists work in this direction of clinical and anatomical research, as shown in the cited references; it also indicates that the authors have correctly chosen the vector of new technology development in neurosurgery. The authors have the world’s largest clinical experience of surgery using the endoscopic transnasal transclival approach to various hard-to-reach tumors of the clival region and ventral posterior cranial fossa. The article presents unique anatomical specimens demonstrating the most important anatomical structures for surgery in this area: the median clival canal and disseminated venous canals of the clivus. The obtained cranio-metric data are reliable and statistically significant. The presented anatomical photographs and authors’ drawings illustrate the study concept and make the presented material clear, meaningful, and complete.

V.N. Nikolenko (Moscow, Russia)
Large and giant intradural ICA aneurysms or the so-called paraclinoid aneurysms are a surgical challenge requiring high qualification of the neurosurgeon. Despite numerous publications on this topic, there is still no generally accepted classification of paraclinoid aneurysms. In this paper, we analyzed the definitions and classifications of paraclinoid aneurysms, which were available in the medical literature. The paper presents our own surgical classification of paraclinoid ICA aneurysms, which has been developed by Prof. Sh.Sh. Eliava and co-authors at the Burdenko Neurosurgical Institute. The classification is based on the aneurysm neck position relative to the ICA wall, aneurysm dome direction, and type of aneurysm clipping.

Keywords: aneurysm, internal carotid artery, clipping, classification.

Abbreviations:
ICA — internal carotid artery
IBA — intravascular blood aspiration
PCA — posterior connective artery
CT — computed tomography
AVA — anterior villous artery
ACA — anterior cerebral artery
ACP — anterior clinoid process
SCT-AG — spiral computed tomography angiography
MCA — middle cerebral artery
CAG — cerebral angiography

According to the literature, the incidence of large and giant aneurysms of cerebral vessels amounts to 3—13.5% of all intracranial aneurysms. The natural course of the disease is unfavorable. For example, according to S. Peerless et al. [1], out of 31 patients with giant aneurysms under observation 68% died within 2 years of the follow-up, and 85% died within 5 years.

The treatment of large and giant intradural ICA aneurysms is a complex surgical task that requires a highly professional neurosurgeon and a clear understanding of anatomical and topographic features of these aneurysms. Despite numerous publications on this topic, there is still no generally accepted classification of such aneurysms.

The aim of this work is to analyze the definitions and classifications of ICA aneurysms available in the medical literature and to present our own surgical classification of paraclinoid ICA aneurysms.

Material and Methods

The proposed classification is based on the analysis of surgical treatment of 260 patients with large and gigantic ICA aneurysms admitted to the Burdenko Neurosurgical Institute in the period from 2001 to 2015. These aneurysms amount to ca. 50% of all large and giant aneurysms in the cohort of patients admitted to the Burdenko Neurosurgical Institute, i.e. 30—45 patients per year. The typical age of onset for such aneurysms is 30 to 50 years, and they more often found in women, with a gender ratio of 2.5:1. Clinically, ICA aneurysms manifest as intracranial hemorrhages (63%), pseudotumoric course (27%), and, less often, as single or repeated thromboembolism, epileptic attacks, have mixed course of disease or represent incidental findings [2]. The analysis of anatomical and topographic features of the aneurysms was performed based on the data of comprehensive instrumental examination, including CAG, SCT-AG, MRI and intraoperative data. In each case, the localization of the aneurysm was juxtaposed with options for its clipping.

Results

Analysis of the literature revealed that various definitions and classifications are used to describe ICA aneurysms, especially those that are large and giant in size. In the scientific literature, large (1.5—2.5 cm) and giant (>2.5 cm) intradural ICA aneurysms are united by the concept of “paraclinoid aneurysms”, since their surgical treatment is rather similar. The term “paraclinoid aneurysm” is believed to be pioneered by S. Nutik [3], who
first used it in his article back in 1978. The name is derived from the term for the anterior clinoid process (ACP), a bony landmark that is well differentiated in the lateral projection of cerebral angiograms and had been previously used by neurosurgeons to define a putative boundary between intra- and extradural sections of the ICA. Aneurysms, whose neck lay distally to the apex of the ACP, were referred to as supraclinoid, while those that lay proximally were called infra- or subclinoid. The first type is a fairly convenient object for clipping, since the surgeon had reliable proximal control of the blood flow to the ICA during isolation of the aneurysm as well as the ability to turn it off above the aneurysm, if necessary. There is no direct control of blood flow during intervention on an infraclinoid aneurysm. Such aneurysms were previously clipped by direct bandaging of the ICA at the neck or by progredient occlusion with a Selverstone clamp [4]. If the aneurysm is large or giant in size, it is impossible to establish its localization relative to a rather small ACP, which was the reason for appearance of the term “paraclinoid”.

In the Department of Vascular Surgery of the Burdenko Neurosurgical Institute the term “paraclinoid aneurysm” has been used since 1990s for all intracranial aneurysms of the proximal sections of the ICA, exceeding the average size (>1.5 cm). The data of surgical interventions demonstrate that the relationships between anatomical structures in the parasellar region can change significantly in the process of development of a paraclinoid aneurysm: the chiasmus, optic nerves, the trunk of the ICA and its branches are deformed and shifted. The traditional assignment of an aneurysm name based on the artery mouth is no longer justified in this case. For example, many specialists, relying on the proposal of A. Day et al. [5], continue to call medial giant aneurysms “aneurysms of the superior pituitary artery”. It should be noted, however, that according to H. Gibo et al. [6] the pituitary artery has an average caliber of 0.25 mm and, as a rule, has 2—3 trunks (an average of 2.2 per hemisphere), and is virtually indistinguishable on angiograms. In foreign literature, these aneurysms are often combined into one group, and referred to as “ophthalmic”, without specifying their anatomical and topographic features, which, in our opinion, are important for planning of microsurgical treatment.

The anatomical classification of ICA aneurysms into segments, which was first proposed by H. Gibo et al., [6], A. Bouthillier [7], is generally accepted in modern vascular neurosurgery. It divides the ICA into 5 segments (Fig. 1): C1 — cervical, C2 — petrous, C3 — cavernous, C4 — clinoid, and C5 — supraclinoid.

The intracranial segment of the ICA (C5 segment), is, in turn, divided into the ophthalmic, connective (communicative) and villous (choroidal) segments in accordance with the permanent branches of the ICA. Each segment gives rise to small perforating arteries, the anatomy of which is unique. The small branches of the ophthalmic segment supply the optic nerve and the chiasm, the funnel and trunk of the pituitary gland, as well as the bottom of the third ventricle. The perforating arteries of the communicative segment are involved in the blood supply of the visual tracts and the hypothalamus. The branches of the choroid segment are involved in the blood supply of the subcortical structures through the anterior perforated space [8, 9].

Large and giant aneurysms of the ICA are distinguished by a wide neck, which extends over 2 segments or more, which makes the classification described above not
entirely applicable. In our work, we use the following classification of large and giant ICA aneurysms (Fig. 2):

1) cavernous-intradural (transitional): aneurysm neck originates in the cavernous segment and extends to the supraclinoid section of the ICA (proximal blood flow control is possible only at the cervical level);

2) paraclinoid: aneurysm neck originates at the level of the outer dural ring (proximal control of blood flow is possible only at the cervical level);

3) supraclinoid: aneurysm neck originates in the region of the mouth of the posterior connective artery (direct proximal control of blood flow in the ICA is possible);

4) fusiform (pansegmentary): aneurysm neck is not differentiated; the aneurysm extends to the entire ICA;

5) bifurcational (distal part of the ICA): aneurysm neck in the area of the ICA fork.

We use the topographic anatomical classification proposed by Sh. Eliava for evaluation of angiography data and planning surgical intervention in patients with large and giant ICA aneurysms. The classification is based both on the analysis of the point of origin of the aneurysm neck, and on the location of the aneurysm sac relative to the supraclinoid segment, as well as on the nature of the dislocation of the optic nerve, which in turn defines the approach to clipping.

**Medial aneurysms** are the most numerous group, accounting for 41.5% of all aneurysms included in the study. The neck of such aneurysms is localized in the medial wall of the ICA. By spreading into the suprasellar region, they can mimic tumors of this localization (adenoma of...
the pituitary gland, meningioma of the tubercle of the Turkish saddle). In rare cases, such aneurysms can cause hormonal disorders associated with compression of the pituitary stalk (diabetes insipidus). A distinctive surgical feature of such aneurysms is that the dome is always located under the optic nerve, roughly deforming it and the chiasm, and therefore they most commonly manifest clinically as visual disturbances. To turn off the aneurysm, it is necessary to dissect it from the optic nerve, decompress the optic nerve canal roof and resect the ACP. Clipping of such aneurysms is more often performed by standard clips (straight, curved), which are superimposed along the medial wall of the ICA (Fig. 3).

**Anterior (superior) aneurysms.** Anterior aneurysms accounted for 21% of all large and giant paraclinoid aneurysms [2]. These aneurysms are formed from the anterior (superior) wall of the ICA with the dome directed upwards. A distinctive surgical feature of an aneurysm of this localization is the location of the dome above the optic nerve, so visual disturbances are rare in such patients. At the same time, the anterior aneurysm neck can be associated with the ACP and the ipsilateral optic nerve, causing its tension and compression. It is important to take into account that anterior aneurysms can be welded to the basal parts of the frontal lobe, which can provoke an intraoperative rupture during traction. Therefore, in order to reduce the impact of the traction on the frontal lobe, the preparation of the sylvian gap and the exit to the M1-segment of the MCA are recommended as initial steps, followed by a retrograde release of the ICA. Clipping of such aneurysms rarely require ACP resection. The standard clipping of the aneurysm neck with straight or curved clips along the upper wall of the ICA is used (Fig. 4).

---

**Fig. 4. Paraclinoid aneurysm of the anterior (superior) localization.**

a — CAG, direct projection; b — CAG, lateral projection; c — surgical view (ACP — anterior clinoid process; A1 — segment ACA; M1 — segment of MCA; arrow denotes the body of aneurysm); d — diagram of the surgical view: the dome of the aneurysm is directed upwards, the ICA, ACA and MCA are under the aneurysm.
Posterior (inferior) aneurysms. Posterior aneurysms accounted for 18% of all large and giant aneurysms of the ICA [2]. The fundus of the aneurysm of this localization is directed posteriorly, toward the cavernous sinus and the base of the middle cranial fossa. Posterior aneurysms may often have mixed direction of the dome: in the posteromedial or posterolateral direction. The PCA and, more rarely, AVA commonly lay closely to the body of large ICA aneurysms of posterior localization, which makes their dissection laborious. Posterior aneurysms, as a rule, are switched off by tunneling clips of various configurations with the formation of the ICA lumen in the areas of fenestration of the clips (Fig. 5).

Lateral aneurysms. Lateral paraclinoid aneurysms accounts for 16% of all major and giant aneurysms of the ICA [2]. Such aneurysms move the ICA anteriorly and its dome is adjacent to the ACP. Since the ACP is a rather rigid structure, as the body of the lateral paraclinoid aneurysms grows, it shifts to the supraclinoid space and can reach the oculomotor nerve and the basal parts of the temporal lobe. The branches of the ICA (AVA and PCA) can be displaced and pressed upwards. In a number of cases, intracranial proximal (relative to aneurysm) control of the ICA can be achieved for large lateral paraclinoid aneurysms after the resection of the ACP. Such aneurysms must be clipped with standard clips along the posterolateral wall of the ICA with the preservation of the PCA and AVA mouths (Fig. 6).

Cavernous-intradural (transitional) aneurysms. This group accounts for 4% of all major and giant aneurysms of the ICA [2] and includes paraclinoid aneurysms that extend from the cavernous sinus to the supraclinoid segment through the dilated dural ring. Complete clipping of such aneurysms is impossible without opening the
cavernous sinus, even in IBA conditions. At present, patients with such aneurysms undergo endovascular installation of flow-guiding stents or microsurgical trapping after the creation of a wide arterial anastomosis. It is possible to partially clip an aneurysm when the part of an aneurysm that remains extradural in the cavernous sinus remains unconnected (Fig. 7).

**Discussion**

The first classification of paraclinoid (ophthalmic) aneurysms was proposed in 1971 by P. Kothandaram et al. [10]. The authors identified three types of aneurysms, based on relative position of the aneurysm and the chiasma: subchial, suprachiasmal and parachiasmal. The authors described the results of treatment of 19 patients with aneurysms of paraclinoid localization, schematically depicting angiographic and intraoperative data. Later, G. Almeida et al. [11] and C. Thurel et al. [12] described variants of similar classifications that did not introduce any major changes. All authors built their conclusions on small series of observations, without considering the entire range of possible aneurysm in this area.

A. Day et al. [5] published the results of surgical treatment of 80 patients with paraclinoid aneurysms and proposed their own classification, dividing aneurysms into ophthalmic, upper-pituitary paraclinoid and upper-pituitary suprasellar. The two latter types referred to the medial aneurysms and differed in the direction of the dome: the upper pituitary paraclinoid were directed back, while the suprasellar ones were directed medially. The paper provided the detailed description of clinical manifestations of ophthalmic aneurysms in general and variants of visual defects in particular. Aneurysms of all sizes, including giant ones (their incidence was not indicated), were analyzed together, which makes the comparison...
difficult. The classification did not take into account such types of aneurysms, as the lateral and anterior.

The classification proposed by H. Batjer et al. became relatively widespread [13] and is based on the relationship between the aneurysm and branches of the ICA. The authors identified ophthalmic aneurysms, upper pituitary aneurysms and proximal posterior wall aneurysms. Later G. Fries et al. [14] suggested adding the fourth type of aneurysms, partially-intracavernous, which correspond to the transient ones in our classification. The modified version of this classification was described in 1999 by O. De Jesus [15]. The authors identified 4 groups of aneurysms: clinoid, ophthalmic, upper pituitary and posterior paraclinoid. According to this classification, each type of aneurysm was divided into subtypes, based on the direction of development of the aneurysm body: anterior, posterior, medial, lateral. The classification was complex, which limited its use.

Another variant of classification was proposed in 2005 by the American neurosurgeon F. Beretta et al. [16] based on surgical anatomy and neuroimaging data. It included 4 variants of aneurysms localization: ophthalmic anterior, ophthalmic medial, upper pituitary suprasellar and upper pituitary paraclinoid. In our opinion, in case of giant aneurysms the last two groups are hardly distinguishable and, therefore, from a practical point of view, this classification is inconvenient.

**Conclusion**

The nomenclature and classification of large and giant ICA aneurysms remain a controversial issue, the ap-

---

**Fig. 7.** Paraclinoid aneurysm of the transitional type.

a — CAG, direct projection; b — CAG, lateral projection; c — surgical view (ON — optic nerve, ACP — anterior clinoid process, ICA — internal carotid artery, A1 — segment of ACA, M1 — segment of MCA, arrows indicate body of the aneurysm); d — diagram of the surgical view: the aneurysm begins extradurally and spreads to the entire intradural part of the ICA.
In the article the authors present their classification of the so-called paraclinoid aneurysms of large and giant size, based on the experience of surgical treatment of more than 260 similar aneurysms of the brain. The classification proposed by the authors takes into account such parameters as the localization of the aneurysm neck relative to the ICA wall and the direction of the aneurysm dome, which in turn determines the type of aneurysm clipping. The authors described each type of such aneurysms in detail and provide detailed analysis of the clinical manifestations, most commonly used types of clipping using clips of different configurations, and possible complications depending on localization of such aneurysms.

It should be noted that the term “paraclinoid” aneurysm is not adopted in the Russian-language literature, where the definition of aneurysms are based on their location in this or that section or segment of the ICA, and not in their relation to the anterior clinoid process.

V.V. Krylov, N.A. Polunina (Moscow, Russia)
Combination Treatment of Cerebral Arteriovenous Malformations Using Endovascular and Microsurgical Techniques


Federal Center of Neurosurgery, Novosibirsk, Russia

Material and Methods. The study included 40 patients with cerebral AVMs. In the study group, 14 (35%) patients underwent microsurgical resection without preliminary embolization (1st group), and 26 (65%) patients underwent combined treatment (endovascular embolization and microsurgical intervention, 2nd group). The first group included patients with S&M grade I—III AVMs, and the second group included patients with S&M grade II—V AVMs. Treatment outcomes were evaluated with allowance for completeness of AVM resection, operative blood loss, duration of surgery, changes in clinical and neurological impairments according to the modified Rankin scale, and rate of neurological and surgical complications.

Results. According to postoperative findings, AVMs were totally resected in all patients. Persistent focal neurological symptoms developed in 2 (7.7%) cases in the second group; neurological complications occurred in 1 (7.1%) patient in the first group. The mean blood loss during resection of AVMs without preliminary embolization and embolized AVMs in patients with S&M grade I—III AVMs was 271.4 mL and 149.1 mL, respectively. The duration of surgery and blood loss did not differ significantly in microsurgery and combination treatment groups.

Conclusion. Combination treatment, including microsurgical intervention after endovascular embolization, is an effective treatment for AVMs, in particular for high grade (S&M grade III—V) AVMs. Teamwork and coordination among the surgeon, endovascular surgeon, and radiologist in treatment of AVMs is a prerequisite for a good outcome.

Keywords: arteriovenous malformation, combination treatment, surgical treatment of AVM, preoperative embolization.

Material and Methods

The study included 40 patients (20 males, 20 females, aged 18 to 69 years (mean age 40.5±14.2 years)) with cerebral AVM operated on at Novosibirsk Federal Center of Neurosurgery in the period from February, 2013 to October, 2015.

All patients underwent a comprehensive examination including clinical and neurological examination, recording of complaints and medical history, consultations with related specialists: ophthalmologist, otoneurologist, and therapist. Furthermore, all patients underwent instrumental examination: computed tomography (CT) of the brain, multidetector CT angiography (SCT), magnetic resonance imaging (MRI) of the brain, cerebral angiography (CA).

Clinical manifestation of the disease was associated with hemorrhage in 13 (32.5%) patients and with epileptic syndrome in 14 (35%) patients. One (2.5%) patient developed ischemic symptoms of acute impairment of cerebral circulation on the vascular territory adjacent to the AVM. A total of 12 (30%) patients were diagnosed with AVM due to the complaints of headache, dizziness and other manifestations of chronic cerebral circulatory insufficiency.

Headache prevailed among the study patients (16 (40%) cases). Pyramidal insufficiency due to a previous hemorrhage in the region of motor tracts was detected in 3 (7.5%) patients, visual impairments and aphasic disorders were noted in 2 (5%) and 2 (5%) patients, respectively. One (2.5%) patient had ataxia due to a previous...
hemorrhagic stroke in the cerebellar hemisphere; dizziness and visual hallucinations were observed in 2 (5%) and 1 (2.5%) patients, respectively.

The degree of disability was assessed in all patients using the modified Rankin’s scale (mRS, 1988) (Fig. 1). The majority (42.5%) of the patients had no functional disorders prior to surgery (0 mRS points). AVM was localized in the right hemisphere in 20 (50%) cases and in the left hemisphere in 18 (45%) cases. AVM was most frequently observed in the temporal lobe (complete or partial localization): 18 (45%) patients in total. Two (5%) patients were diagnosed with cerebellar AVM. The localization of AVM in the studied patients is presented in Table 1.

Preoperative evaluation of AVM was carried out using the Spetzler and Martin (S&M) scale [8]. S&M grade II and III AVM patients (17 (42.5%) and 15 (37.5%) patients, respectively) prevailed in the study (Fig. 2).

Microsurgical resection of AVM without preliminary embolization was performed in 14 (35%) patients (group 1), combination treatment (endovascular embolization and microsurgical resection) was performed in 26 (65%) patients (group 2).

Group 1 consisted of patients with S&M grade I—III AVM, group 2 included patients with S&M grade II AVM (see Fig. 2).

Endovascular embolization of AVM was performed using transfemoral arterial access under combined endotracheal anesthesia and controlled hypotension. As an embolic agent, cyanoacrylates were used in 6 (23.1%) cases, non-adhesive Onyx polymer was applied in 13 (50%) cases, and combination of adhesive sealant and non-adhesive agents was used in 7 (26.9%) patients.

The degree of AVM embolization was evaluated using CT angiography images in two planes based on the volume of the contrast medium as a percentage of the initial figures. The amount of AVM embolization before surgery had an average value of 84.5%, median value of 90%, interquartile range of 75; 96.5 (minimum volume, 50%; maximum volume, 100%).

All of the patients underwent control CT of the brain immediately after endovascular surgery in order to exclude possible hemorrhage, ischemia and vasogenic edema.

One-stage embolization was performed in 12 (46.2%) cases, 2-stage, 3-stage and 4-stage embolization was conducted in 8 (30.8%), 2 (7.7%) and 1 (3.8%) patients, respectively, prior to AVM resection. Three (11.5%) patients underwent ≥5 embolizations.

All surgeries were scheduled. The terms between the last embolization and microsurgical intervention varied from a few hours to 10 months depending on the results of control CA and the patient’s consent to the next stage of surgical treatment. The period between the last embolization and surgical intervention averaged 45.2 days; median, 7 days; interquartile range, 4; 75.2 days.

In the combined treatment group, 10 (38.5%) patients were changed to open surgical intervention due to the technical impossibility of further embolization, which was established based on the results of control CA performed in the period of 3—6 months from the last embolization. The impossibility of embolization was associated with the lack of available afferents for catheterization and putative high risk of complications during embolization due to the functional significance of afferents. Microsurgical intervention was the original method of choice in 16 (61.5%) patients.

Osteoplastic trepanation of the skull was performed with AVM node resection in all cases at the stage of open surgical treatment. In all patients, intervention was carried out under endotracheal anesthesia combined with controlled hypotension. The position on the operating table was determined by AVM localization and the selected type of access. Head was firmly fixed in the Mayfield clamp. Preoperative planning was carried out using a frameless navigation system. The size of the trepanation window, as a rule, exceeded the size of malformation, the dura mater was opened along the edge of the bone defect. The main stage was performed using a surgical microscope and intraoperative contact Doppler sonography.

The following parameters were taken into account in evaluation of the results of surgical treatment: completeness of AVM resection, operative blood loss, duration of surgery, changes in disability according to the modified Rankin scale, and the rate of neurological and surgical complications.

Statistical processing of the obtained data was carried out using R ver. 3.2.4 software (R Foundation). The methods of descriptive statistics were used for analysis of the study results: calculation of the arithmetic mean (M), standard deviation (m), median (Me), lower and upper quartiles. Normality of distribution was verified using the Shapiro–Wilk test. The Welch’s t-test (normally distributed values), the Mann–Whitney’s U test, and the exact Fisher’s test with modification for contingency tables larger than 2×2 were used for comparison of the groups. The correlation was determined using the Spearman

### Table 1. Distribution of patients by AVM localization

<table>
<thead>
<tr>
<th>Localization</th>
<th>Number of patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal lobe</td>
<td>13 (32.5)</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Frontal and temporal lobes</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Temporal and occipital lobes</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>Parietal and occipital lobes</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>Frontal, parietal and temporal lobes</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>Parietal and temporal lobes</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>Cerebellar hemisphere</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (100)</td>
</tr>
</tbody>
</table>
method. Differences were considered statistically significant at $p<0.05$.

**Results**

Groups 1 and 2 were comparable in gender ($p=1.0$), age ($p=0.42$) and the degree of functional disorders and disability according to the Rankin scale ($p=0.11$) but statistically significantly differed in patient distribution according to the S&M scale ($p=0.04$).

Subtraction CA was performed in 8 (20%) patients in the postoperative period, the remaining patients underwent SCT. According to the examination data, AVM was completely resected in all patients.

There were no deaths. One patient with S&M grade II AVM localized in the occipital lobe developed stable quadrant homonymous hemianopsia after endovascular embolization, which persisted after microsurgery. One patient with S&M grade V AVM localized in the right temporal lobe developed left-sided hemiparesis of up to 3 points associated with ischemia in the capsula interna due to the occlusion of perforating arteries after the third stage of embolization.

Thus, persistent focal neurological symptoms developed in 2 (7.7%) cases in group 2.

Neurological complications were noted in 1 (7.1%) cases after microsurgical interventions: a patient with S&M grade II AVM of the left frontal lobe developed mild paresis of the facial nerve and motor aphasia symptoms, which partially regressed during therapy.

Surgical complication in the form of hematoma of 30 mL in the bed of the resected AVM occurred in 1 (7.1%) patient from the first group. This complication was clinically manifested in the form of hemiparesis, which developed on the first day after surgery. The patient underwent revision of the operative wound and hematoma resection. No signs of residual AVM were observed during revision. Neurological symptoms regressed completely after repeated surgery. In 2 (7.7%) patients of the second group, ligature fistulas were formed after 1.5—2 months, which required revision of the postoperative scar and fistula excision.

Analysis of neurological disorders and the degree of disability after surgery according to the modified Rankin scale showed that 1 (7.1%) patient of the first group experienced negative changes (1-point deterioration). Among the second group patients, 1 (3.8%) patient showed deterioration by 1 point and another (3.8%) patient experienced 3-point deterioration (Fig. 3). There were no statistically significant differences.

Comparison of the volume of blood loss and surgery duration between the groups was conducted only among patients with S&M grades I—III AVM (14 patients of the group 1, 22 patients of the group 2), which was caused by the absence of S&M grades IV—V patients in the group 1.

Mean blood loss in the group 1 was 271.4 mL (median, 100 mL; interquartile range, 50 to 250 mL). Mean blood loss in the group 2 was 149.1 mL (median, 100 mL; interquartile range, 50 to 200 mL). There were no statistically significant differences in blood loss between the groups (Mann—Whitney test, $p=0.664$).

Mean duration of surgery was 290.4±104.3 min in group 1 and 280.7±97.1 min in group 2. There were no
statistically significant differences in surgery duration between the groups (Student’s test $p=0.78$).

Mean blood loss was 50, 50, 700 and 1000 mL, respectively, in 4 patients of the group 2 with S&M grade IV—V AVM, the duration of surgery was 205, 330, 600 and 365 min, respectively.

No correlation was revealed during analysis of the effect of amount of embolization on blood loss in group 2 patients.

**Discussion**

Microsurgical resection, which provides early improvement and subsequently reduces the risk of hemorrhage to practically zero, is the most radical method of AVM treatment [9]. It can be solely performed only in patients with a low risk of surgery. The risk is associated with hard-to-reach sources of AVM blood supply, intranidal aneurysms, large fistulas, large linear dimensions and volume of AVM, localization in functionally important areas.

Total occlusion of AVM can be achieved by endovascular intervention in 16—32.8% of cases [10—12]. Some authors [13] present higher rates of AVM embolization: 51%, with a 2—8.7% risk of complications and a mortality rate of 0.8—3%. According to A. Nataraj et al. [2], residual AVMs are found after treatment in patients with high-grade AVM after embolization as the only method of treatment in 41% of cases, while microsurgical resection results in only 2% of residual AVMs. Moreover, incomplete occlusion does not prevent re-hemorrhage, and, according to some data [2, 14, 15], increases the risk of hemorrhage compared to patients who have not received any treatment at all. According to our observations, as well as according to some authors, even after complete AVM obliteration according to angiographic criteria, the residual filling of the AVM center through the feeding vessels is determined during the subsequent microsurgical surgery [6].

Taking into account low completeness, intravascular interventions for AVM are currently being considered primarily as a preliminary stage for more radical methods: microsurgical resection or radiation. Endovascular embolization allows reducing the AVM volume and the amount of arteriovenous shunting, shutting off the feeding arteries that are difficult to access in direct intervention and areas of malformation that are potentially dangerous with respect to rupture.

In our study, 26 patients were treated using combination approach (endovascular + microsurgical methods). There were no deaths; the incidence of persistent neurological disorders was 7.7%.

According to the article by R. Crowley et al. [16], which demonstrates the results of treatment of 342 patients with AVM, the relationship between the number of the stages of endovascular intervention and neurological complications was revealed (the average number of embolization stages with complications was $1.57 \pm 0.75$, the average number of embolization stages without complications was $1.26 \pm 0.53, p=0.01$). Postoperative neurological complications and deaths accounted for 11.4%. L. Kim et al. [17] revealed a direct relationship between the S&M grade of AVM and the rate of complications. In 2009, R. Starke et al. [18] published results of the treatment of 202 patients who underwent embolization prior to microsurgical resection or radiosurgery: postoperative neurological deficit developed in 14% of cases. It has been established that the risk factors for postoperative neurological disorders are the need for more than one embolization, AVM diameter is less than 3 cm or more than 6 cm, deep venous drainage, and localization in the functionally significant region.

According to the literature data [6], the complication rates of combined treatment vary widely and reach 28.6%, severe complications of combined treatment and lethality are found in 4.6—7% and 2.3% of cases, respectively.

In our study, the mean blood loss during combined treatment of the patients with S&M grade II—III AVMs was 149.1 mL (median 100 mL), the duration of surgery was 280.7 min. These results are comparable to the blood loss values for the group with microsurgical intervention. Similar results were obtained in the study by O.D. Shekhtman et al. [12] presenting a comparative analysis conducted between the two groups (40 patients with AVM underwent preliminary embolization and 40 patients were subjected to microsurgical resection of AVM only). There were no significant difference in the mean duration of surgery and blood loss, which exceeded the standard value (more than 500 mL), between the study and control groups. In the work by S. Natarajan et al. [6], the mean blood loss in the group of 28 patients with an average S&M grade of 2.75, who underwent combined treatment, with an average embolization rate of 74.1%, was 348 mL. In our study, we managed to minimize the blood loss values for the group with microsurgical intervention.

![Fig. 3. Distribution of group 1 and 2 patients according to the Rankin scale after surgery.](image-url)
loss and decrease the duration of surgery in a series of cases with S&M grade IV—V AVM. These results are comparable with the results obtained for the group of patients with S&M grade I—III AVM, which is due to the positive effect of preliminary embolization on the technical aspects of microsurgical intervention. Moreover, subjectively speaking, preliminary embolization technically simplifies the microsurgical resection of the AVM center, allows performing dissection as close as possible to the site and avoiding damage to the surrounding brain tissue. Embolization allows one to switch off the deeply located affereents that limit the excision of the S&M grade IV—V AVM [2].

We have not revealed any correlation between the blood loss and the degree of embolization. In addition, we have not found any indications of a “golden mean” between the degree of AVM embolization and the rate of ruptures and neurological complications that require open surgical intervention in the literature. According to F. Vinuela et al. [5], no effect of embolization was observed in resection of AVM embolized by less than 50%. Embolization of more than 75% of the AVM volume facilitated the dissection, while providing the control over bleeding from the feeding arteries during the intervention.

The decision on the choice of treatment method, number of stages, and the amount of surgical intervention should be made by a multidisciplinary team with participation of a neurosurgeon, an endovascular surgeon, and a radiologist. Microsurgical intervention is preferred in small, S&M grade I—II AVMs that are located superficially and beyond functionally important areas. Taking into account high variability of the grade III AVM, the decision is to be made individually in each particular case; the combined treatment is preferred. Combined treatment is also recommended in grade IV—V AVM.

When choosing a combined treatment strategy (endovascular embolization + microsurgery), it is necessary to strive to reduce the number of endovascular interventions and, maybe, not achieve complete occlusion of AVM (the recommended amount of embolization before microsurgery is more than 75%) [5]. Particular attention should be paid to switching off the deep feeding arteries from the bloodstream. In addition, it is necessary to decrease the time between the last embolization and the microsurgical stage as much as possible to minimize the risk of hemorrhage and AVM recanalization [11].

**Conclusion**

The treatment of cerebral arteriovenous malformations remains to be one of the most complex and contradictory issues in vascular neurosurgery. As the literature data and the results of our study show, a multidisciplinary approach involving neurosurgeons and endovascular surgeons is required in order to reduce the risk of neurological and surgical complications as well as to increase the completeness of surgical intervention and improve the quality of the patients’ life at the modern stage of medical development. Preoperative embolization in patients with high S&M grade AVM allows technical facilitation of AVM resection and reduction in the risks of surgical intervention.

**Authors declare no conflict of interest.**

**REFERENCES**


The article by D.M. Galaktionov et al. is devoted to an important problem: evaluation of the role of preoperative embolization in increasing the effectiveness of the treatment of cerebral arteriovenous malformations (AVMs).

Cerebral AVM is one of the most complicated cerebrovascular medical condition, which often requires a multidisciplinary approach in the treatment. There are few papers devoted to the issues of combined treatment of AVM. Therefore, the studies in this area are of particular interest.

The study presents analysis of the results of treating patients with cerebral AVM using microsurgical and combined approaches (microsurgical resection after endovascular embolization). I think that the groups to be compared have not been formed quite correctly. A group of patients who initially had to undergo preoperative embolization with subsequent AVM resection was combined with a group who failed to achieve complete endovascular AVM thrombosing (including multistage embolization). Therefore, microsurgical excision of the AVM was performed. In addition, it was often performed in a long period after embolization. This combined group is compared with the group that underwent only microsurgical interventions of AVM removal. Thus, the principle of selecting patients for combined interventions has been violated. Furthermore, when determining the complexity of surgical interventions, one should take into account not only the angioarchitectonics of malformation (the number of afferent arteries and drainage veins, their location and accessibility) but AVM localization as well. For example, AVM of the right frontal lobe with complicated angioarchitectonics is technically easier to resect than the less complex malformations of the mediobasal regions of the temporal lobe. Determination of indications for preliminary endovascular shutdown of the deep afferents of the AVM and the associated malformation sector prior to its microsurgical removal much depends on localization.

Nevertheless, such publications are important, since they reflect the current understanding of the need to coordinate the possibilities of endovascular technique with direct microsurgical interventions to alleviate technical problems that arise during AVM resection, increase the percentage of radical interventions and reduce the number of intraoperative complications.

Sh.Sh. Eliava (Moscow, Russia)
Spinal Dural Arteriovenous Fistulas. A Series of Clinical Cases and an Analysis of the Literature Data

K.N. BABICHEV, V.P. ORLOV, A.V. STANISHEVSKIY, A.V. SAVELLO, D.V. SVISTOV
Military Medical Academy named after S. M. Kirov, St. Petersburg, Russia

Spinal dural arteriovenous fistulas (SDAVFs) are the most common vascular malformation of the spinal cord, causing segmental lesions of the spinal cord due to venous ischemia. Functional outcomes of treatment in SDAVF patients are favorable, but the rate of improvement varies from 25 to 100%, which complicates prediction of the treatment outcome.

**Aim** — the study aim was to identify a relationship between fistula localization and clinical manifestations and evaluate the effect of disease duration and severity of neurological impairments on immediate and long-term treatment outcomes, based on analysis of the literature and own data.

**Material and methods.** In September 2016, we performed a PubMed search for publications using keywords «spinal arteriovenous fistula», «treatment», and «outcome». We selected publications containing information on the patient’s age, fistula location, disease duration, and evaluation of symptom severity (Aminoff-Logue scale) preoperatively, postoperatively, and at least 3 months after surgery. The analysis also included data on patients operated on at the clinic. A total of 187 patients were included in the analysis.

**Results.** The fistula was most often located at the T6, T7, and T9 level, with motor disorders being more severe for fistulas located at or below the T9 vertebra. Surgical isolation of the fistula improved the functional state of patients, with patients under the age of 60 years having a better prognosis for recovery of impaired functions. Motor disorders significantly regressed in the early postoperative period in all patients, but in the long-term period, there was worsening of motor disorders in patients with a better baseline functional state.

**Keywords:** spinal dural fistula, treatment, outcomes.

Spinal dural arteriovenous fistulas (SDAVFs) are vascular malformations of the spinal cord and its surrounding dura mater that consist of a low-flow vascular shunt between a dural branch of radicular artery and a vein on the dura mater of the spinal nerve root sleeve [1]. SDAVFs are rare; however, they accounts for 80% of spinal arteriovenous malformations [2—5].

The clinical signs and symptoms of disease are non-specific, so the final diagnosis is established relatively late after the initiation of diagnostic evaluation, commonly, when marked neurological deficit is developed. Nevertheless, functional outcomes of treatment in patients with SDAVFs are favorable, but the rate of improvement varies from 25 to 100%, which complicates prediction of the treatment outcome [6—12]. Patient’s age, fistula location, disease duration, intensity of neurological disorders, and nature of venous outflow have been postulated to influence treatment outcome, but contribution of each of these factors to outcome has not been assessed.

To date, the related literature includes a significant number of publications that contain relatively small series of patients [4, 7—12] and a small number of papers where the number of patients exceeds 100 [2, 13]. However, the literature lacks summarized data on the relationship between fistula anatomy and clinical manifestations, as well as their influence on treatment outcome.

The aim of this study was to reveal a relationship between fistula location and clinical manifestations, to assess influence of disease duration and intensity of neurological disorders on the immediate and long-term treatment outcomes, based on the analysis of published and own data.

**Material and methods**

In September 2016 we explored a PubMed database (https://www.ncbi.nlm.nih.gov/pubmed) for key words “spinal arteriovenous fistula”, “treatment”, “outcome” and found 218 publications. At first we planned to select papers describing at least 5 clinical cases of spinal dural arteriovenous fistulas (SDAVFs) that indicated the following data for each of the patients:

— age;
— location of fistula;
— the time elapsed between onset of symptoms and diagnosis/surgery;
— ALS score of symptom intensity (Aminoff—Logue scale) [3] preoperatively, postoperatively, and in at least 3 months after surgery.

However, most publications do not contain complete data on clinical manifestations and fistula anatomy. Hence, we reviewed papers with incomplete information on the above criteria, but those that indicated fistula location and neurological symptoms on the ALS scale.

The selected papers included data on 179 SDAVFs cases. Only 2 papers contained the required data in full. In other cases, there were some variations in selection
criteria. Table 1 presents a brief description of the selected papers.

The analysis also includes data on 8 patients operated on at our neurosurgical clinic, whose medical information met the above criteria. Table 2 shows summarized data on these patients.

Surgical isolation of fistulas via endovascular and microsurgical procedures was performed in 33.7% (n=63) and 66.3% (n=124) cases, respectively. Combined treatment was required in 10.7% (n=20) of cases.

Methods of statistical analysis

Statistical data analysis was performed using the Microsoft Excel spreadsheet program (Microsoft) and Statistica for Windows software (Stat Soft Inc., USA.). The differences were estimated using nonparametric tests: Kruskal—Wallis, Mann—Whitney or Friedman. Contingency tables were constructed for frequency data. Difference significance between several groups was revealed by a posteriori comparisons with adjustments of significance level based on the number of comparisons. A p<0.05 (95% confidence) was significant. Association between variables was analyzed using the Spearman rank correlation coefficient.

Characteristics of patients

A total of 187 patients (157 (84%) — men) were analyzed. The mean age was 60.5 years (95% CI 58.7—62.4). Age of disease onset was similar in men and women (Mann—Whitney UZ=−1.267; p=0.205).

There were approximately equal numbers of patients above 60 years (n=95, 53.1%) and 40—60 years (n=72, 40.2%); a smaller number of cases (n=12, 6.7%) were under the age of 40 years. In 8 cases, the age of patients is unknown.

Results

Fistula location. In most cases, SDAVFs were localized at the thoracic (n=133, 71.1%) or lumbar (n=42, 22.5%) spine. Much less frequently and in approximately equal numbers of cases, SDAVFs were located at the cervical and sacral spine level — 7 (3.7%) and 5 (2.7%) cases, respectively.

A deeper analysis of SDAVFs location revealed a roughly equal number of fistulas at the mid-thoracic (T5—T8) and lower-thoracic (T9—T12) spine — 69 (36.9%) and 59 (31.6%) of cases, respectively. In the thoracic spine, three levels carried the most frequent location of SDAVFs: T6 (n=21, 15.7%), T7 (n=20, 14.9%), and T9 (n=23, 17.2%). In the lumbar spine, SDAVFs were more often located at the L1 vertebral level — 18 (42.9% of fistulas at the lumbar spine). Fig. 1 shows the distribution of SDAVFs according to location.

Clinical presentation

Preoperatively, the average ALS score (ALS scores have a range of 0 to 11) was 4.9 (95% CI 4.5—5.2), while it was 4.6 (95% CI 4.0—5.17) and 3.9 (95% CI 3.45—4.4) — at discharge and in the long-term period, respectively. Fig. 2 shows the distribution of patients according to the functional status at the time of surgery. The patients of different age groups did not differ by the intensity of neurological symptoms in the preoperative period: Kruskal—Wallis test Z=−0.580; p=0.748.

Intensity and duration of symptoms

In our selected papers, precise information on the time between symptom occurrence and diagnosis was available for 105 (56.2%) cases. The time between symptom occurrence and diagnosis of SDAVFs was less than 1 month only in one case. In other cases, the time between onset of symptoms and diagnosis was at least several months. The maximum time was 240 months [16]. Median time between symptom occurrence and diagnosis was 13 months (Me=13 months, Q1=7 and Q3=36). It is noteworthy that disease duration less than or more than 13 months did not affect the intensity of neurological deficit at the time of surgery — χ²(2)=0.731; p=0.694. Fig. 3 shows the distribution of patients according to disease duration before diagnosis of SDAVFs.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Number of cases</th>
<th>Data on symptom duration</th>
<th>Location of SDAVFs</th>
<th>ALS score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>preoperative</td>
<td>at discharge</td>
</tr>
<tr>
<td>L. Tacconi [14], 1997</td>
<td>25</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>M. Kohno [10], 1998</td>
<td>10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>M. Steinmetz [15], 2004</td>
<td>18</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sh. Nagata [11], 2006</td>
<td>13</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>F. Ruiz-Juretschke [16], 2011</td>
<td>19</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>S. Inagawa [7], 2013</td>
<td>14</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Y. Ofran [8], 2013</td>
<td>8</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>M. Rashad [17], 2014</td>
<td>12</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>R. Andres [18], 2008</td>
<td>21</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>S. Gokhale [9], 2014</td>
<td>27</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>P. Yen [19], 2014</td>
<td>12</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
The patient’s age did not affect the time of diagnosis and surgery: Kruskal–Wallis test $\chi^2(2)=1.359; p=0.507$.

The information on symptom duration and intensity of neurological deficit at the time of surgery was available for 97 (51.9%) patients. Statistical analysis did not reveal any differences in the intensity of neurological symptoms ($\chi^2(4)=2.680; p=0.613$), including motor disorders ($\chi^2(4)=1.766; p=0.779$) among patients with different times of symptom occurrence. In contrast to motor disorders, the intensity of impairments in the pelvic organs depended on disease duration. The patients with mild pelvic disorders (0—1 scores on ALS) had a shorter disease history in contrast to patients with more significant disorders (3 scores on ALS): Mann–Whitney $U=2.390; p=0.017$. In addition, there were no differences in the length of anamnesis in patients with marked (2 scores on ALS) and more significant pelvic disorders (3 scores on ALS): Mann–Whitney $U=2.143; p=0.032$, as well as between patients with mild and severe pelvic disorders: Mann–Whitney $U=2.143; p=0.032$.

Next, a relationship between SDAVF location and the nature of motor disorders is presented:
1) above T8, T9—T12 and below T12 vertebrae;  
2) at the C1—T2 level (cervical spine and cervical thickening), T3—T8, T9—L2 (thickening of the lumbar-sacral spine), L3 and below;  
3) above, below or at the T9 vertebral level.

Only in the case of fistula location above, below or at the T9 vertebral level, differences in intensity of motor disorders were revealed: $\chi^2(2)=5.24; p=0.014$. The differences were only observed between groups of patients with mild (ASL 0—2) and moderate (4—5 ALS) motor disorders: $\chi^2(1)=8.319; p=0.004$. Pelvic organ impairments did not depend on fistula location: $\chi^2(2)=4.675; p=0.097$. Fig. 4 shows patient distribution according to intensity of motor function loss and location of SDAVFs relative to the T9 vertebra.

**Surgical outcomes**

Isolation of SDAVFs led to a complete or partial regression of neurological symptoms: Friedman test $\chi^2(2)=8.827; p=0.012$. The dynamics of neurological status in the early postoperative period was studied in 82 patients; both in the early and in the long-term postoperative periods — in 33 patients; in the long-term postoperative period — in 129.

A significant improvement was revealed when preoperative intensity of neurological disorders was compared to intensity of neurological disorders in the early postoperative period on the ALS scale (Wilcoxon test $Z=-4.605; p<0.001$) as well as when preoperative intensity of neurological disorders was compared to that in the long-term follow-up (Wilcoxon test $Z=-4.894; p<0.001$). Improved functions included increased muscle strength in the limbs (Wilcoxon test $Z=-5.534; p<0.001$) and better control over the function of pelvic organs (Wilcoxon test $Z=-3.594; p<0.001$).

In the early postoperative period, neurological symptoms regressed in patients with mild or moderate symptoms (ALS 0—5): Wilcoxon test $Z=-3.339; p=0.001$, and

![Fig. 1. Location of spinal dural arteriovenous fistulas in the analyzed cases.](image1)

![Fig. 2. The distribution of patients according to the intensity of clinical symptoms on the ALS scale at the time of surgery.](image2)
with severe clinical symptoms at the time of surgery (ALS 6—11): Wilcoxon test Z=−2.959; p=0.003.

Meanwhile, the neurological symptoms in the long-term period in patients with mild (0—2 ALS) or moderate (3—5 ALS) symptoms did not differ from the baseline preoperative level: Wilcoxon test Z=−0.714; p=0.475 and Wilcoxon test Z=−1.852; p=0.64, respectively. A better dynamics of functional outcomes in the long-term period was noted only in patients with initially more severe symptoms (6 scores and more on ALS) — Wilcoxon test Z=−5.409; p<0.0001. Tables 3—5 show the dynamics of neurological status according to the length of postoperative period.

As seen from the Tables, surgery decreased the intensity of neurological symptoms. A positive dynamics was particularly evident in the early postoperative period, regardless of the baseline intensity of disorders. Meanwhile, the proportion of patients with deterioration, regardless of the initial functional status, increased in the long-term period. The share of patients with neurological improvement in the long-term postoperative period was maximal in the group with the most severe baseline disorders (ALS 6—11), reached 72.7% and increased compared to the early postoperative period. Nevertheless, even in this group symptoms deteriorated compared to the early postoperative period. The worst dynamics of neurological disorders in the long-term postoperative period was observed in the group with initially better functional state (ALS 0—2): the proportion of patients with improvement reduced (from 66.7 to 41.7%), while the proportion of patients with deterioration increased (from 0 to 29.9%).

Control angiography was not performed in all cases in the long-term follow-up and thus deterioration of neurological symptoms in the long-term period could be because of the progression of neurological disorders during recanalization or SDAVFs formation at another level.

However, according to statistical analysis, patients with moderate intensity of symptoms (ALS 3—5) experienced better treatment outcome than patients with severe neurological deficit, despite differences in the dynamics of neurological status. Despite significant improvement in functional status in patients with severe neurological deficit (ALS 6—11), these patients did not reach the same functional level as in groups with minor symptoms (ALS 0—2).

We revealed a correlation between baseline intensity of neurological disorders and the likelihood of improvement in the early and long-term periods. The correlation was stronger when preoperative functional status was compared with functional status in early postoperative periods (r=0.6; p<0.001; n=82) than when preoperative functional status was compared with that in the long-term postoperative outcome (r=0.34; p<0.001; n=129) (Fig. 5).

The treatment outcomes in patients of different age groups did not differ in the early postoperative period: χ2(6)=2.779; p=0.836. In the long-term period, the best functional outcomes were observed in patients younger than 60 years (Fisher’s Exact Test=0.016), in the absence of differences in patients aged under 40 and from 40 to 60 years: Fisher’s Exact Test=0.649. However, this is true only for alterations in motor function. The intensity of pelvic disorders in the long-term period did not differ in different age groups: χ2(4)=4.430; p=0.434.

Disease duration did not affect functional outcomes in the long-term postoperative period: χ2(4)=5.473; p=0.242.

Discussion

Spinal dural arteriovenous fistulas are the most common type (up to 80%) of spinal cord vascular malformation [15, 16]. The disorder can be a challenge to diagnose and the presenting clinical symptoms and signs are non-specific at onset leading to late diagnosis and underestimation of the number of patients with this pathology [8, 17—19].

SDAVFs represent a low-flow shunt between a dural branch of radicular artery and a radicular vein within the dural root sleeve. Venous hypertension in the veins draining the spinal cord venous flow diminishes the arteriove-
nous pressure gradient and leads to a decreased drainage of normal spinal veins resulting in clinical symptoms [1]. A draining vein is commonly enlarged, twisted and ascends to reach the perimedullary venous plexus. Histological examination of the draining fistula veins reveals thickening of the inner and middle layers, thrombosis of various grades — from occlusion to complete recanalization [1, 20, 21].

SDAVFs occur more frequently in men, the disease is typical for patients older than 40 years; fistulas are usually located in the lower thoracic spine [14—17, 19]. The cause for the formation of fistulas is unclear. However, intraspinal fistulas embrace some features of intracranial arteriosinus anastomoses that are preceded by sinuses thrombosis [22].

According to morphological studies [21, 23], spinal cord veins are devoid of valves, but venous pressure remains constant independent of the intra-abdominal or intra-thoracic pressure, which is associated with the peculiarities of structure of these veins: the veins have no middle layer in the area of passage through spinal dura mater and vein wall is represented by the arachnoid and dura mater; the veins have a Z-shape passage and a narrowing. These features form a system that impedes retrograde venous outflow from the epidural venous plexus into spinal cord veins [20]. Increased pressure in the epidural venous system leads to closure of veins through a valve-like mechanism [20, 21]. Blood flow through a radicular vein can be disturbed in patients with thrombosis of epidural veins [24] or in case of impaired system of a “functional valve”, which triggers a pathological cascade resulting a fistula.

Our analysis has shown that fistulas most often located at the lower thoracic and lumbar spine levels, with more severe clinical symptoms when fistula was located at the T9 vertebra level or below the T9 vertebra. The higher occurrence of SDAVF at the lumbar and lower thoracic spine can be explained by the anatomical features of veins: (1) a smaller diameter of the spinal cord draining veins at this level, which makes them more sensitive to hemodynamic changes; (2) because the lower thoracic and lumbar regions have relatively fewer venous outflow channels compared with the cervical region [21].

It is believed that clinical outcome worsens over time [5, 25], but our analysis did not confirm this, similar to other publications [10, 13]. The possibility of SDAVF’s existence without clinical manifestations is still to be proven, when only acute aggravation of venous outflow disorders leads to decompensation and clinical manifestations. This possibility is confirmed by the presence of arteriovenous anastomosis in dura mater occurring in the norm [26].

Some authors note the worst outcomes in patients with longer disease history [8, 10—12], though not supported by all citations [5, 11, 15, 16]. In our study, we also revealed no significant effect of disease duration on treatment outcomes.

### Table 3. Changes in neurological status in the early postoperative period compared to preoperative symptoms

<table>
<thead>
<tr>
<th>Preoperative ALS scores</th>
<th>Dynamics of neurological status, abs.;%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>worsening</td>
<td>stable</td>
</tr>
<tr>
<td>0—2</td>
<td>—</td>
<td>2; 33.3</td>
</tr>
<tr>
<td>3—5</td>
<td>3; 7.1</td>
<td>11; 26.2</td>
</tr>
<tr>
<td>6—11</td>
<td>3; 8.8</td>
<td>9; 26.5</td>
</tr>
<tr>
<td>Total</td>
<td>6; 7.3</td>
<td>22; 26.8</td>
</tr>
</tbody>
</table>

**Footnote.** Here and in Tables 4, 5: percentage was estimated for a line.

### Table 4. Changes in neurological status in the long-term postoperative period compared to preoperative clinical symptoms

<table>
<thead>
<tr>
<th>Preoperative ALS scores</th>
<th>Dynamics of neurological status, abs.;%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>worsening</td>
<td>stable</td>
</tr>
<tr>
<td>0—2</td>
<td>7; 29.2</td>
<td>7; 29.2</td>
</tr>
<tr>
<td>3—5</td>
<td>11; 22</td>
<td>6; 12</td>
</tr>
<tr>
<td>6—11</td>
<td>2; 3.6</td>
<td>13; 23.6</td>
</tr>
<tr>
<td>Total</td>
<td>20; 15.5</td>
<td>26; 20.2</td>
</tr>
</tbody>
</table>

### Table 5. Changes in neurological status in the long-term period compared to the early postoperative period

<table>
<thead>
<tr>
<th>ALS scores in the early postoperative period</th>
<th>Dynamics of neurological status, abs.;%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>worsening</td>
<td>stable</td>
</tr>
<tr>
<td>0—2</td>
<td>—</td>
<td>3; 75</td>
</tr>
<tr>
<td>3—5</td>
<td>—</td>
<td>4; 36.4</td>
</tr>
<tr>
<td>6—11</td>
<td>4; 22.2</td>
<td>7; 38.9</td>
</tr>
<tr>
<td>Total</td>
<td>4; 12.1</td>
<td>14; 42.4</td>
</tr>
</tbody>
</table>

Similar to the authors of many publications [8, 10—12], we noted the effect of age and intensity of neurological symptoms on treatment outcomes. The best outcomes were observed in patients younger than 60 years who had mild clinical symptoms. In addition, L. Tacconi et al. [14] reported that in operated patients, the long-term functional status decreased in the form of slow but steady decline in functions after improvement at the early period. A possible cause of this deterioration can be recanalization or fistula formation at a different level [13, 14, 27].

According to our data, the long-term symptom deterioration is typical for patients with milder baseline neurological symptoms, while patients with severe neurological deficit retain improvement in the long-term follow-up compared to the baseline status.

Significant variations in clinical presentation demand assessing the grade of arteriovenous shunt as a predictor of the natural course of disease and possibility for postoperative improvement. According to P. Yen et al. [19], patients with contrast agent filling of fistula draining veins at ≥7 vertebral levels reported greater neurological dysfunction. S. Hetts et al. also reported similar data [6]. Arteriovenous fistulas draining into the anterior
and posterior spinal veins are a factor of rapid disease progression [20].

Conclusions

1. Spinal dural arteriovenous fistulas have a slow progression of clinical symptoms and cause segmental lesions of the spinal cord due to venous ischemia resulting from abnormal arteriovenous shunt located on the dura mater of a spinal nerve root.

2. The thoracic spine, mainly at the T6, T7 and T9 vertebral levels, is the most frequent location of SDAVFs, which should be taken into account when diagnostic spinal angiography is performed.

Fig. 5. The dynamics of symptom regression depending on the baseline status.

a — dynamics of regression of neurological symptoms in the early postoperative period; b — dynamics of regression of neurological symptoms in the long-term postoperative period.
3. The intensity of motor disorders occurring in SDAVsFs is not associated with disease duration; the intensity of motor disorders is more severe when fistula is located at or below the T9 vertebra.

4. Dysfunction of pelvic organs is more severe in patients with a long disease history, but does not depend on the level where the lesion occurs.

5. Surgery for SDAVsFs improves functional status of patients; subjects under 60 years have the best chance to recover impaired functions.

6. Motor disorders significantly regress in the early postoperative period in all patients, but motor disorders aggravate in the long-term follow-up in patients with initially better functional state on the ALS scale.

Authors declare no conflict of interest.

REFERENCES


Received: 20.01.17
The authors performed a search for publications related to diagnosis and treatment of SDAVFs up to including 2016 and found 218 papers. Equal data on clinical symptoms and fistula anatomy were not contained in all of these papers and the authors analyzed papers containing the most complete information on fistula location and neurological symptoms assessed on the ALS scale.

The selected papers included data on 179 SDAVFs (Table 1). The analysis also includes data on 8 patients who met the inclusion criteria and were operated at the Neurosurgical Clinic of the Military Medical Academy, Saint-Petersburg.

Isolation of fistulas was performed using endovascular and microsurgical interventions: 33.7% (n=63) and 66.3% (n=124) patients, respectively. A total of 187 patients were analyzed; most of them were men — 157 (84%). The mean age of patients was 60.5 years. Age of disease onset did not differ between men and women.

The authors propose evaluation of neurological disorders pre/postoperatively and in the long-term follow-up using the ASL scale for objective clinical data. It is unknown whether the patients before surgery for SDAVFs received any other treatment, for example, whether intervertebral discs were resected? Whether the patients underwent hormone therapy, which enhances spinal cord edema and can lead to paraplegia?

In contrast to arteries, spinal cord veins can penetrate through the dura mater for a considerable distance from the nerve root. This causes биметамерного строения of dural arteriovenous fistulas. One dilated draining vein extends from an extradural “leg” that is the beginning of a microscopic shunt located within the dura mater. This vein pierces the dura mater near the nerve trunk to reach the perimedullary region. Subsequently, hypertrophy and hypertension in spinal venous system develop. Alterations in the spinal cord due to hypertension can be imaged on MRI. T2-weighted images of the spinal cord at the thoracic level reveal a signal enhancement characteristic of the spinal cord lesion and axial slices visualize lesions in spinal cord pathways in the anterior and posterior horns. Venous hypertension decreases arteriovenous pressure gradient and reduces perfusion, leading to progressive spinal cord hypoxia, impaired autoregulation and a progressive dysfunction in spinal cord conduction.

Endovascular embolization of SDAVFs with adhesive agents with preservation of hypertrophied veins eliminates the above pathological effects on the spinal cord. The next day, patients note improvement in neurological status, indicating a positive effect of endovascular surgery. The absence of changes on MRI six months or a year postoperatively indicates the correct choice of an intervention and disease elimination.

Numerous papers that assess treatment outcomes of endovascular surgery and microsurgery showed that treatment outcome does not depend on the chosen method if complete occlusion of a fistula is achieved. The authors believe that by completeness of fistula isolation, microsurgical fistula disconnection has significant advantages over endovascular embolization. In addition, I would like to mention the analysis of surgical treatment performed by N. Bakker et al. who analyzed 35 publications (1,112 patients) for association of recanalization rate and a chosen treatment method.

Despite the large number of papers focused on this issue, the factors influencing functional outcomes of treatment have not been identified.

The authors have made a considerable amount of work and established a relationship between clinical symptoms and location of fistula, which is important for establishing angiographic diagnosis. The authors note that clinical symptom deterioration in the long-term follow-up is typical for patients with milder neurological symptoms, while patients with severe neurological symptoms report improvement in the long-term follow-up after surgery compared to baseline. Pelvic disorders are more significant in patients with a long disease history, but do not depend on the level of spinal cord injury. Impaired functions improved more often in patients under the age of 60. Motor disorders regress in the early postoperative period in all patients.

For clear evaluation of treatment outcomes in dural fistulas, a prospective study involving a large number of patients in different clinics treated with endovascular and microsurgical approaches are necessary. The authors developed the criteria for such a study. The results presented in the paper are of practical importance and facilitate prediction of treatment outcomes.

T.P. Tissen (Moscow, Russia)
Shunt-Induced Craniosynostosis: Topicality of the Problem, Choice of the Approach, and Features of Surgical Treatment

S.A. KIM, G.V. LETYAGIN, V.E. DANILIN, A.A. SYSOEVA

Federal Neurosurgical Center, Novosibirsk, Russia

Shunt-induced craniosynostosis is one of the late complications of CSF shunting surgery, which affects the patient’s condition, clinical picture, and treatment approach.

**Objective** — to evaluate the prevalence rate and clinical significance of this disease, define the indications for surgery, and choose the optimal surgical approach.

**Material and methods.** The study included 59 children with shunt system dysfunction, aged 1 to 14 years, who were treated at the Department in the period from 2014 to 2016. The inclusion criteria were as follows: 1) age at the time of examination is older than 1 year; 2) implantation of a shunt system in the first 12 months of life. The state of cranial sutures was assessed using three-dimensional reconstruction of patient’s computerized tomography images. Images obtained before or in the first months after primary implantation of a shunt system were used to exclude cases of primary craniosynostosis.

**Results.** Premature synostosis of the cranial sutures was detected in 27 (46%) cases. Of these, 3 (11%) patients with clinical symptoms of increased intracranial pressure and radiographic signs of craniocerebral disproportion underwent cranial vault remodeling surgery: two biparietal craniotomies and one fronto-parieto-occipital reconstruction. In two cases, simultaneous replacement of a valve with a programmable one was performed. There were no complications after reconstructive surgery.

**Conclusion.** Shunt-associated craniosynostosis is one of the late complications of CSF shunting surgery. However, its presence is not an indication for surgery and should not be a reason for surgical aggression. Surgery for increasing the intracranial volume is indicated only for secondary craniosynostosis combined with signs of craniocerebral disproportion. In these cases, reconstructive surgery is an effective treatment option for improving the patient’s condition.

**Keywords:** secondary craniosynostosis, craniocerebral disproportion, slit ventricle syndrome, ventriculoperitoneal shunt complications, hydrocephalus, cranial vault remodeling.

**Abbreviations**

CSFSS — cerebral spinal fluid shunt surgery
ICP — intracranial pressure
CCD — craniocerebral disproportion
SVS — slit ventricle syndrome
SRC — shunt-related or induced craniosynostosis

To date, CSF shunt surgeries (CSFSS) are the most common method of surgical correction of various types of hydrocephalus. Up to 300,000 of such surgeries are carried out in the world annually [1]. Introduction into routine practice and the subsequent improvement of shunting systems allowed significant reduction in mortality rate while increasing life expectancy of patients with hydrocephalus. However, shunt surgeries, which are not devoid of shortcomings, have a quite significant percentage of complications [1]. The cumulative incidence of complications over a 5-year follow-up period reaches 32% and more, with the largest part of them occurring in the first year after implantation [2]. The origin of such complications can be obstruction, mechanical damage or disconnection of system components, infection, hypo or hyper drainage, and etc. Due to the growth in the number of patients with implanted CSF shunt systems and increase in their life expectancy, later types of complications have also become more common, part of which have a chronic course, which makes them unobvious in several cases and, therefore, often undetectable. One of such complications of chronic extrathecal drainage of CSF is shunt-related or induced craniosynostosis (SRC).

**Material and Methods**

The single-center retrospective study included 59 children with shunt system dysfunction, aged 1 to 14 years, who were treated at the Department in the period from 2014 to 2016. The inclusion criteria were as follows: 1) age at the time of examination is older than 1 year; 2) shunt system was implanted in the first 12 months of life. Medical history data, pre- and postoperative bone window CT of the brain with three-dimensional reconstruction were analyzed for assessment of the state of cranial sutures. Of 60 children meeting the inclusion criteria, 1 patient was excluded due to the lack of CT images and the resulting failure to assess bone structures. Medical history data, pre- and postoperative bone window CT of the brain with three-dimensional reconstruction were analyzed for assessment of the state of cranial sutures. Of 60 children meeting the inclusion criteria, 1 patient was excluded due to the lack of CT images and the resulting failure to assess bone structures. Medical history data, pre- and postoperative bone window CT of the brain with three-dimensional reconstruction were analyzed for assessment of the state of cranial sutures. Of 60 children meeting the inclusion criteria, 1 patient was excluded due to the lack of CT images and the resulting failure to assess bone structures.
Constriction of pre- or postoperative computerized tomography images of the patient using Jemys software: RIS+PACS. Images obtained before or in the first months after primary implantation of a shunt system were used to exclude cases of primary craniosynostosis.

When determining indications for surgical intervention, the most significant one was a combination of clinical manifestations of intracranial hypertension, radiologically confirmed synostosis of the cranial sutures, narrowed subarachnoid spaces and brain ventricles. Additional diagnostic criteria can be thickening of the bones of the cranial vault, profound “convolutional markings”, acquired Chiari malformation, as well as the results of invasive monitoring of intracranial pressure (ICP).

Results

Of 59 patients, 27 (46%) cases were diagnosed with premature synostosis of the cranial sutures (Table 1). Synostosis of sagittal and both coronal sutures was observed most frequently (41%). Isolated fusion of sagittal sutures occupied the second place in incidence (37%). Next, the descending order is as follows: bicornoral synostosis (11%), pancraniosynostosis (7%), and unilateral coronal synostosis (4%). There were no cases of focal lesions of lambdoid sutures (Table 2).

Hydrocephalus was congenital in 12 (44%) cases, post-inflammatory in 6 (22%) cases, posthemorrhagic in 3 (11%) cases, while 3 (11%) patients had a combination of intraventricular hemorrhage and ventriculitis. In 1 child, hydrocephalus was associated with tumor. The etiology of hydrocephalus remained unexplained in 2 cases. Most children (52%) had medium-pressure valve implanted during primary surgery both with and without installation of an anti-siphon device. One low- and one high-pressure valves have been identified. Shunt system parameters could not be established in the remaining 11 children due to the lack of indication on the type of valve in the discharge documents on the primary surgery and in the protocols of revision interventions (Fig. 1).

A total of 24 patients with shunt system dysfunction underwent replacement of the whole shunt or its individual components, after which an improvement in their condition was noted. One of these patients was diagnosed with apparent signs of dysfunction of the distal catheter of the shunt system associated with secondary craniosynostosis and slit-like ventricles but preserved subarachnoid spaces, apparent signs of dysfunction of the distal catheter of the shunting system were diagnosed. Improvement in the child’s condition was achieved after shunt revision. A decision was made to perform a reconstructive surgery in 3 (11%) cases, considering the presence of clinical symptoms of elevated ICP and radiographic signs of craniocebral disproportion (CCD). Two patients underwent biparietal craniotomy, one patient was subjected to fronto-parieto-occipital reconstruction. In addition, simultaneous replacement of a valve with a programmable one was performed in two cases. There were no complications after reconstructive surgery. Patients were discharged with improvement and in satisfactory condition.

Clinical case №1

Patient A., 7 years of age. Shunt was installed at the age of 3 months in association with hydrocephalus, which developed after tumor removal. She was admitted with slit ventricle syndrome manifestations. The patient’s condition was improved after the surgery we performed. The patient was discharged on day 9 in satisfactory condition. Follow-up duration was 11 months. Improvement in the patient’s development was noted, she learned to read and walks with support. The patient has no complaints of headache (Fig. 2).

Clinical case №2

Patient B., 8 years of age. The patient underwent medium-pressure shunt installation in association with congenital hydrocephalus (Dandy—Walker syndrome) at the age of 4 months. The condition remained stable for 7 years. Intense headache appeared 6 months prior to the hospitalization, which was accompanied by nausea and vomiting. The frequency rate and severity of pain progressed for 2 months and significantly limited daily activity of the child. Examination revealed slit-like lateral ventricles. In this connection, shunt revision with replacement of the valve with a programmable one was performed. The patient’s condition was improved after surgery. However, 3 months later, complaints of headache, nausea and vomiting resumed, double vision appeared. The patient was hospitalized for the second time. In addition to general cerebral symptoms, convergent strabismus due to the paresis of the right abducens nerve was revealed in the neurological status. Sagittal craniosynostosis with narrowing of the convexity subarachnoid spaces and slit-like lateral ventricles were diagnosed based on the results of examination and careful analysis of CT scan data, including three-dimensional reconstruction of the images (Fig. 3a, b). Based on the absence of shunt system dysfunction signs and the presence of evident CCD, a decision was made to perform cranial vault remodeling surgery in order to increase its volume. The patient underwent biparietal craniotomy with formation of two parietal flaps and a bone bridge over the superior sagittal sinus. Clinical improvement of the child’s condition was noted after surgery: headache and evacuation disorders were stopped; fundus congestions were regressed. Postoperative CT examination also demonstrates positive dynamics in the form of ventricular size normalization, formation of subarachnoid spaces (see Fig. 3c, d). The patient was discharged on day 10 after remodeling surgery. To date, the medical history accounts for 12 months. The patient’s condition remains stable and satisfactory. There were no repeated interventions. There are no complaints of headache and nausea, oculomotor apraxia regressed. The child attends school.
Introduction of a wide range of CSF shunt systems significantly reduced the mortality rate and increased the effectiveness of the treatment of patients with hydrocephalus. Among those patients who underwent shunt system implantation for hydrocephalus at the early age, there is a subgroup with premature synostosis of the sutures, which is a characteristic of secondary SRC (Fig. 4). During its growth, the brain gradually overfills the available internal space of a closed, rigid skull, which signifies transition of the disease to the stage of craniosynostosis. These changes further lead to a discrepancy between the volume of the skull and the volume of the rapidly growing brain re-

<table>
<thead>
<tr>
<th>N</th>
<th>Patient, years</th>
<th>Age of primary VPS</th>
<th>Etiology of hydrocephalus</th>
<th>Valve type</th>
<th>Synostosed sutures</th>
<th>Age at which craniosynostosis was diagnosed</th>
<th>Slit ventricle syn-drome</th>
<th>CCD</th>
<th>Reconstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A., 7 years</td>
<td>3 months</td>
<td>After tumor removal</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>7 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes+valve replacement</td>
</tr>
<tr>
<td>2</td>
<td>B., 10 years</td>
<td>3 months</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Sagittal</td>
<td>10 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>B., 12 months</td>
<td>2 months</td>
<td>Post-inflammatory</td>
<td>Medium pressure</td>
<td>Bicoronal</td>
<td>1 year</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>B., 8 years</td>
<td>4 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>8 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>V., 26 months</td>
<td>4 months</td>
<td>IVH, meningitis</td>
<td>Low pressure</td>
<td>Bicoronal + sagittal</td>
<td>21 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>V., 18 months</td>
<td>6 months</td>
<td>IVH, meningitis</td>
<td>Medium pressure</td>
<td>Bicoronal + sagittal</td>
<td>18 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>G., 13 years</td>
<td>3 months</td>
<td>IVH</td>
<td>Medium pressure</td>
<td>Pancreanosynostosis</td>
<td>13 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>G., 14 years</td>
<td>3 months</td>
<td>Congenital</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>14 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>D., 7 years</td>
<td>3 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>7 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>D., 6 years</td>
<td>6 months</td>
<td>Congenital</td>
<td>Unknown</td>
<td>Sagittal</td>
<td>6 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>D., 23 months</td>
<td>6 months</td>
<td>Congenital</td>
<td>Unknown</td>
<td>Bicoronal</td>
<td>23 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>Zh., 30 months</td>
<td>5 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Coronal on the left side</td>
<td>30 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>K., 12 months</td>
<td>7 months</td>
<td>Post-inflammatory</td>
<td>Medium pressure</td>
<td>Bicoronal</td>
<td>13 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>K., 4 years</td>
<td>6 months</td>
<td>IVH</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>4 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>K., 22 months</td>
<td>3 months</td>
<td>IVH</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>22 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>L., 18 months</td>
<td>3 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>18 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>M., 3 years</td>
<td>5 months</td>
<td>Post-inflammatory</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>19 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>18</td>
<td>M., 7 years</td>
<td>3 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Bicoronal + sagittal</td>
<td>7 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>19</td>
<td>M., 4 years</td>
<td>4 months</td>
<td>Post-inflammatory</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>4 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes+valve replacement</td>
</tr>
<tr>
<td>20</td>
<td>P., 4 years</td>
<td>9 months</td>
<td>Unknown</td>
<td>Medium pressure</td>
<td>Bicoronal + sagittal</td>
<td>4 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes+valve replacement</td>
</tr>
<tr>
<td>21</td>
<td>C., 3 years</td>
<td>5 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Bicoronal + sagittal</td>
<td>3 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>22</td>
<td>C., 11 years</td>
<td>5 months</td>
<td>IVH, meningitis</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>11 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>23</td>
<td>F., 5 years</td>
<td>2 months</td>
<td>Post-inflammatory</td>
<td>Unknown</td>
<td>Pancreanosynostosis</td>
<td>5 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>24</td>
<td>H., 3 years</td>
<td>9 months</td>
<td>Post-inflammatory</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>3 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>25</td>
<td>Ch., 2 years</td>
<td>9 months</td>
<td>Congenital</td>
<td>Medium pressure</td>
<td>Sagittal</td>
<td>24 months</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>26</td>
<td>Sh., 4 years</td>
<td>1 months</td>
<td>Congenital</td>
<td>Unknown</td>
<td>Bicoronal + sagittal</td>
<td>4 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>27</td>
<td>E., 10 years</td>
<td>2 months</td>
<td>Congenital</td>
<td>Unknown</td>
<td>Sagittal</td>
<td>10 years</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
sulting in refractory intracranial hypertension. R. Pudenz and E. Foltz [3] suggested that the development of secondary craniosynostosis requires 2—3 years after shunt implantation. J. Weinzweig et al. [4] wrote about the average interval of 26 months. At the same time, a number of authors [5—7] describe cases of the development of secondary craniosynostosis in infants in a few months after shunt surgery. We also have patients in our group with synostosis of the cranial sutures observed during the period from 6 to 18 months after shunt implantation.

Clinical case №3

Child L. Was operated on at the age of 3 months for congenital hydrocephalus associated with meningomyelocele. A medium-pressure shunt was installed.

Discussion

The concept of SRC is directly related to such pathological conditions as CCD and the slit ventricle syndrome (SVS). Understanding the nature of these disorders is the key to choosing an adequate treatment for this group of patients.

It is necessary to distinguish between anatomical reduction in ventricular size, which does not require treatment, and SVS, which has specific clinical manifestations. Small, or slit-like, ventricles are observed by neuroimaging in 20—53% of children with shunts, while clinical manifestations of SVS are found in 1—37% of cases [4, 8—15]. The syndrome develops mainly in children operated on during the first year of life [16]. The mean age of SVS manifestation is 6—7 years [9, 13]. However, an earlier development of this condition is also possible [6]. Explanation of the origin of the pathology causes a lot of disagreement, while selection of tactics in SVS is still the subject of discussion [1, 17—22]. However, it is quite obvious that all attempts to elucidate the mechanism of SVS development associated with SRC inevitably lead us to the problem of CCD.

CCD is a condition where the volume of the growing brain exceeds the available intracranial space. Meanwhile, normal physiological fluctuations of intracranial contents (volume of intracranial blood and cerebrospinal fluid) lead to an increase in ICP with typical clinical manifestations. There are different terms in the literature that describe this pathology: cephalocranial disproportion [23—26], postshunt craniosynostosis [4], hyperostosis of the skull [27], secondary craniosynostosis [28, 29], shunt-induced craniosynostosis [17, 30], secondary microcrania [24], and etc.

A. Sandler et al. [31] present two categories of CCD:

1) primary CCD: it is caused by a primary pathological process leading to a diffuse thickening of the bones of the cranial vault or premature ossification and synostosis of the joints. An example of such CCD is primary craniosynostosis;

2) secondary CCD: it is an iatrogenic phenomenon, which is initiated by implantation of a shunt system in early childhood.

The incidence of secondary CCD is unknown, since no such studies have been conducted so far. Severe disabling headache occurs in 42% of adolescents with shunts [32]. A study of 3,100 patients who underwent CSFSS revealed that 1.6% of patients had craniosynostosis [1]. In our group consisting of 59 children, 27 (46%) patients were diagnosed with premature synostosis of the sutures, while CCD signs were observed in only 3 (5%) cases. Apparently, the approximate incidence rate of CCD can be indirectly evaluated based on the incidence of the slit ventricle syndrome. It is quite possible that a significant proportion of patients with this syndrome suffer from CCD, and small, slit-like ventricles can be a manifestation of an overfilled skull.

In CCD, the ability of the brain to compensate for physiological fluctuations in the intracranial volume is compromised by a number of reasons [33]. First, the discrepancy between the normal brain volume and the small volume of the cranium leads to an increase in the extraparenchymal resistance. Secondly, the reduced volume

<table>
<thead>
<tr>
<th>Table 2. Types of affected cranial sutures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected suture</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Number in the group (abs.)</td>
</tr>
</tbody>
</table>

Fig. 1. Patient distribution according to the valve type of the shunt system installed during primary intervention.
of the ventricles and subarachnoid spaces, which normally participate in the compensation of increased ICP, significantly reduces the potential for damping ICP fluctuations [34]. Thirdly, impaired venous outflow in CCD leads to an increase in the pressure in the upper sagittal sinus, which deteriorates absorption of the cerebrospinal fluid [14]. In addition, venous congestion leads to changes in the turgor of the brain tissue while increasing its rigidity and decreasing its compliance [11, 14].

**Clinical manifestations**

These patients are usually operated on for hydrocephalus at an early age (up to 1 year), and, as a rule, they have a medical history of repeated revisions and multiple visits to a doctor for severe chronic headache despite the well-functioning shunt. As for the drug treatment, even if it yields an effect, the effect of such treatment is often insignificant or evanescent. The severity of headache limits daily activity, including schoolwork and professional activity [35, 36]. In contrast to the “low-pressure” headache, which occurs in the hyperdrainage state, prone position does not reduce the pain severity in CCD. Other manifestations of increased ICP can be diplopia, ataxia, dizziness, and impaired consciousness. There are also cases of acute deterioration of the condition leading to death [26].

**Diagnosis**

In a number of patients, the typical skull deformity is revealed during examination: microcephaly, scapho-
cephaly, plagiocephaly. X-ray imaging reveals thickening of the bones of the cranial vault, apparent “convolutional markings”, erosion of the inner table of skull due to the pressure of the adjacent grooves, thickening or calcification of the diploe, imposition of bones in the suture area and their synostosis. Neuroimaging demonstrates normal or slit-like ventricles that are not always expanded, even during a period of exacerbation. This is not only due to a decrease in the brain compliance, but also the lack of intraventricular obstruction [22]. CT and MRI determine narrowed convexity subarachnoid spaces, as well as the overfilled cranial cavity, especially in the posterior cranial fossa. In addition, both ascending and descending dislocations of the cerebellum can develop in that case [24, 37]. Increase in ICP does not always lead to fundus congestions [22]. A. Sandler et al. [31] revealed a correlation between headaches and the appearance of plateau waves of elevated ICP by invasive monitoring of ICP in such patients.

**Treatment**

In case of radiologically confirmed secondary craniosynostosis and the presence of CCD signs (clinical manifestations of intracranial hypertension, narrowed subarachnoid spaces and cerebral ventricles), surgical intervention aimed at decompression of intracranial structures is indicated. Thickening of the bones of the cranial vault, apparent “convolutional markings”, and the ac-

---

Fig. 3. Clinical case 2. a — brain CT reconstruction reveals synostosis of the sagittal suture; b — slit-like lateral ventricles, Convexity subarachnoid spaces are not observed; c — CT after skull reconstruction; d — positive CT dynamics: normalization of ventricular size, appearance of subarachnoid spaces.
Fig. 4. Clinical case 3. a — CT of the child that was performed during shunt system replacement at the age of 10 months; b — synostosis of the sagittal suture was diagnosed by CT during repeated intervention at the age of 18 months; c, d — scans obtained during shunt dysfunction at the age of 2 years. Thickening of the bones of the cranial vault is observed; e, f — the catheter was reinstalled into the occipital horn and resulted in regressed hypertension syndrome manifestations. The presence of wide lateral ventricles provides a reserve intracranial space, in association with which there are currently no indications for skull reconstruction.
quired Chiari malformation can serve as additional criteria.

In 1974, F. Epstein et al. [20] published the results of a subtemporal craniectomy performed on 2 children with small ventricles, who had previously undergone shunt implantation. The method itself involves creation of the artificial surgical fontanel, which provides additional space for the brain and allows palpatory determination of increased pressure. Such decompression can be performed on one and both sides [22]. However, the authors themselves noted low effectiveness of such interventions and unacceptable cosmetic consequences: the skull acquired the shape of a clover leaf due to bulging of the temporal flaps [22]. Another method, which was used by F. Epstein et al. [11] in 2 children with shunts, was skull morcellation: “radical cranial expansion ... by morcellation of the skull from the coronal suture to the transverse sinuses posteriorly and the squamosal sutures laterally”.

Open reconstructive interventions aimed at increasing the skull volume became widely used [1, 4, 6, 17, 38]. Particular attention deserves the fact that in case of secondary dislocation of the cerebellum, supratentorial reconstruction of the skull is pathophysiologically more justified than decompression of the posterior cranial fossa [24]. When performing reconstruction, it is advisable to replace the valve of the shunt system with a higher-pressure valve or a programmable one or add an antisiphon device to the system [1].

Another effective method of correcting secondary craniosynostosis and CCD is the use of distraction devices. Distraction osteogenesis can be defined as the growth of bones that is surgically induced by the application of expanding forces in the area of osteotomy [39]. Simultaneous use of invasive ICP monitoring sensors and gradual distraction of the skull bones allow individualization of the technique in relation to each patient while performing a required amount of distraction to normalize ICP values [31].

Conclusion

Premature synostosis of cranial sutures is one of the complications of CSFSS, which can develop both a few years [3, 4] and several months after the intervention [5—7]. The significance of this problem is indicated by the fact that secondary craniosynostosis was diagnosed in 46% of the 59 children included in our study. Unfortunately, these data can not reflect the true incidence of SRC, since only those patients who were hospitalized with signs of shunt system dysfunction were considered while the proportion of SRC among compensated patients remains unclear.

Risk factors for the development of SRC can be implantation of the shunt system in infancy, early verticalization of patients, pronounced ventriculomegaly and craniomegaly before surgery, and the use of a low- or medium-pressure valve [1]. However, the use of a high-pressure valve also does not exclude the formation of craniosynostosis and, in addition, can lead to inadequate monitoring of hydrocephalus (hypo drainage).

It should be emphasized that the presence of shunt-induced craniosynostosis only is not an indication for surgery and should not be a reason for surgical aggression. This pathology should be considered as part of the pathophysiological process leading to CCD along with such parameters as increased ICP and slit-like ventricles. Intervention aimed at increasing the intracranial volume and ICP normalization is carried out only in association of secondary craniosynostosis with CCD manifestations, i.e. when it reaches the stage of craniosynostosis. Such manifestations include severe headache, thickening of the bones of the cranial vault with a reduction in the available intracranial space, narrowed subarachnoid spaces and cerebral ventricles, apparent “convolutional markings”, erosion of the inner table of skull, ascending or descending dislocation of the cerebellum. In cases when the diagnosis of CCD requires clarification, invasive ICP monitoring can be used [33].

In our group of 27 patients with SRC, only 3 (11%) children had CCD signs, which required reconstructive surgery. As for the remaining 24 patients, development of CCD in association with the existing craniosynostosis cannot be excluded in the future. This is the reason why such patients require close dynamic monitoring. In case if the signs of intracranial hypertension appear, in addition to suspicion of the shunt system dysfunction, a diagnostic search aimed at excluding CCD is required. This will help avoiding unnecessary revisions and choose the most appropriate method of treatment for the patient.

Authors declare no conflict of interest.
REFERENCES


The authors studied the incidence of cranial suture synostosis in 59 patients aged 1 to 14 years based on the CT data; all patients under the age of 1 year underwent implantation of the CSF shunting systems for hydrocephalus, and they had signs of shunt dysfunction at the time of examination. Craniosynostosis was found in 27 (46%) patients; preoperative CT scans demonstrated normal cranial sutures in all of the cases, which confirmed synostosis formation after CSF shunting surgery. Simple revision of the shunt system was performed in 24 (89%) patients, which led to improvement in the condition. Three patients with the signs of intracranial hypertension and cranioencephal disproportion underwent cranial vault remodeling (two cases included additional replacement of the shunt system valve); all patients were discharged in satisfactory condition.

The discussion includes in-depth description of the pathogenesis of shunt-related craniosynostosis (SRC) and craniosynostosis, clinic course, diagnosis and treatment of craniocerebral disproportion caused by CSF drainage.

The obtained data are interesting and instructive; they draw one’s attention to the urgency of the problem of chronic excess drainage, which is the cause of secondary craniosynostosis and craniosynostosis in children with hydrocephalus who underwent shunt surgery in infancy. The condition of the cranial sutures should be taken into account when choosing the method of treating patients with signs of shunt dysfunction and slit-like ventricles. The authors successfully applied remodeling of the cranial vault in 3 patients with cranioencephal disproportion and SRC (these are 11% of patients with SRC). Such approach is noteworthy and deserves consideration in such difficult clinical situations in patients with slit ventricle syndrome. The disadvantages of cranial vault remodeling are long surgery duration, inevitable prolonged exposure of the shunting system, which creates the risk of infection, the possibility of trauma to venous sinuses and blood loss. Subtemporal decompression remains a safe and effective alternative to date [1, 2].

Optimal parameters for CSF drainage through the shunt system are different for infants and older children. As the authors note, transition from prone position to the upright posture sharply increases CSF discharge down the shunt in case if a standard shunt of differential pressure is used; in this regard, I recently prefer shunts with a gravity device in children of the first year of life, which eliminates excess drainage associated with a vertical position. Normal values of intracranial pressure are significantly lower in infants of the first months of life than in adults, especially in premature infants; the use of high-resistance shunts in this situation delays compensation of hydrocephalus and is likely to deteriorate the rehabilitation prognosis. In this case, implantation of the adjustable valve is reasonable, which allows increasing system resistance during the child’s growth. Diameter of the head circumference and the size of the cerebral ventricles are monitored during the first years of the child’s life (at the age of 6 months, in the period from 1 to 3 years); in case if slit-like ventricles appear or the head circumference approaches the 3rd percentile, the question of the planned reduction in the shunt capacity is to be solved in the period of up to 3 years of life, when the cranial bones are still pliable and there is a chance of accelerating the rate of the head circumference growth. At an older age, surgical treatment of the slit ventricle syndrome primarily involves optimization of the ventricular catheter position and simultaneous elimination of excess drainage by implantation of an adjustable shunt with a gravity device and subsequent step-by-step reduction in its capacity. With this approach, there is recently no need for cranial cavity volume-increasing surgeries after CSF shunt interventions in my practice.

In conclusion, it should be noted that the article is devoted to an essential and little-discussed problem, it contains reliable data on the incidence of SRC and craniosynostosis in patients with hydrocephalus. The study was carried out at a high methodical level, it is well-illustrated, complex problems of the pathogenesis of diagnosis and treatment in the discussion section are presented at the modern level of the study of this issue, as well as in detail and concisely. I congratulate the authors and readers of the journal with an excellent publication.

A.E. Korshunov (Moscow, Russia)

REFERENCES
Intramedullary Spinal Cord Tumors and Hydrocephalus: an Analysis of the Results of Surgical Treatment in 541 Patients

YU.V. KUSHEL’, YU.D. BELOVA, A.R. TEKOEV

Burdenko Neurosurgical Institute, Moscow, Russia

The article addresses the problem of intramedullary tumors (IMTs) combined with hydrocephalus (HC).

**Purpose.** The study purpose was to explore, based on large clinical material, the occurrence of hydrocephalus combined with intramedullary tumors, possible pathogenetic mechanisms of its development, effect of tumor resection on the course of hydrocephalus, and need and timing of shunting surgery.

**Material and methods.** We present and analyze the data of the largest individual series of patients of all age groups operated on for IMTs of the spinal cord: 541 patients; 586 operations; age from 2 months to 72 years.

**Results and conclusion.** Our findings confirm a potential pathogenetic relationship between IMT and HC. The overall occurrence rate of HC in IMT patients was 6.3%. In patients with benign tumors (WHO Grade 1—2; 449 patients), HC developed in 25 (5.6%) cases; in patients with malignant tumors (WHO Grade 3—4; 84 patients), HC developed in 7 (8.3%) cases. A statistically significant prevalence of cervico-medullary tumors was found in HC patients: 19 (59.4%) cases. According to our data, dissemination of the tumor process is a potential factor of HC development.

**Keywords:** intramedullary tumors, cervico-medullary tumors, hydrocephalus, benign and malignant tumors, tumor dissemination.

The development of hydrocephalus (HC) in patients with spinal cord tumors is a well-known clinical condition. A spinal cord tumor located at the thoracic spine that was manifested with an increased intracranial pressure was first described in 1931 by Kyrieleis. About 300 individual cases of combination of two diagnoses, “spinal cord tumor” and “hydrocephalus”, in one patient were described over the next 80 years [1]. Most of these cases were described before the use of MRI in clinical practice. Only one large clinical series of 25 patients with intramedullary tumors (IMTs) of spinal cord and HC has been published [2]. An analysis of the published data shows that there is no information on the occurrence rate of HC in combination with IMTs, pathogenetic mechanisms of HC formation, the effect of tumor resection on the course of HC, need and timing of shunt surgery [1—3]. We analyze individual series of operated patients with IMTs and assess IMT relationship with HC based on the largest clinical material available at present.

The aim of this paper is to explore the occurrence rate of hydrocephalus combined with intramedullary tumors, possible pathogenetic mechanisms of its development, the effect of tumor resection on the course of hydrocephalus, need and timing of shunt surgery based on large clinical material.

**Material and methods**

Over the period of 2002—2016, the first author performed 586 operations for IMTs on 541 patients at the age from 2 months to 72 years. Indications for surgery were the same during all these years: any symptomatic IMT confirmed by MRI data or asymptomatic IMT with documented signs of progression on repeated MRI. All clinical data (including data on the presence of HC and intracranial hypertension) were collected prospectively in a formal database of patients with IMTs in the Excel table since 2002. An analysis of the collected data revealed 34 (6.3%) patients with HC symptoms. In this study, HC was defined as ventriculomegaly with clinical manifestations of intracranial hypertension: congestive optic nerve discs, persistent and intractable headache, nausea, vomiting, and state of reduced wakefulness. Ventriculomegaly was defined as Evans’ ratio>0.3 on CT/MR imaging of the brain [4].

**Results**

All 34 (6.3%) patients with concomitant HC had clinically significant manifestations of HC that required distinct addressing and treatment. Only 2 (5.9%) of 34 patients were adults. The first patient was a 21-year-old girl with a long history of neurofibromatosis type 2, with giant bilateral vestibular schwannomas. HC was caused by occlusion at the IV ventricle level. She underwent shunt surgery at the place of residence, prior to surgery for tumors of the cerebellopontine angle and intramedullary piloid astrocytoma at C0—C4. The second patient aged 29 years suffered from posterior fossa medulloblastoma with intramedullary metastasis spreading to C1—C2. No evident signs of meningeal tumor dissemination were revealed, but tumor resection from the posterior cranial fossa and from the spinal cord did not lead to resolution of HC and the patient underwent shunt surgery a week after the primary surgery. We suppose that the nature of HC is not directly related to IMTs and the tumor itself is a part of a wider problem in these patients. Therefore, both patients were excluded from further analysis. Thus, the study group was reduced to 32 patients (the study group). Sum-
The remaining 507 patients without HC were included in the control group.

The study group included 14 (43.8%) men and 18 (56.2%) women. The IMT group without HC included 265 (52.4%) males and 241 (47.6%) females. The differences were not significant (two-tailed Fisher’s exact test, \( p=0.367 \)). All subjects belonged to cohort of pediatric patients aged from 4 months to 15 years (the mean age was \( 7.0\pm5.1 \)). To analyze the possible relationship between tumor biology and the risk of HC development, we divided all operated tumors into benign (WHO 1—2) and malignant (WHO 3—4). In patients with benign tumors (449 patients), HC developed in 25 (5.6%) cases; in patients with malignant tumors (84 patients), HC developed in 7 (8.3%) cases. The differences were not significant (two-tailed Fisher’s exact test, \( p=0.319 \)). All subjects belonged to cohort of pediatric patients aged from 4 months to 15 years (the mean age was \( 7.0\pm5.1 \)). To analyze the possible relationship between tumor biology and the risk of HC development, we divided all operated tumors into benign (WHO 1—2) and malignant (WHO 3—4). In patients with benign tumors (449 patients), HC developed in 25 (5.6%) cases; in patients with malignant tumors (84 patients), HC developed in 7 (8.3%) cases. The differences were not significant (two-tailed Fisher’s exact test, \( p=0.319 \)).

The literature [1, 5, 6] widely discusses the role of tumor dissemination in the development of HC in patients with IMTs. The analysis of our series showed dissemination signs only in 1 (0.2%) patient with anaplastic ependymoma among 507 patients with IMTs without HC, whereas dissemination was observed in 8 (25%) patients among 32 patients with HC (two-tailed Fisher’s exact test, \( p<0.0001 \)). Taking into account the discussed role of the occlusion component in the genesis of HC in patients with IMTs, we analyzed the occurrence rate of cervico-medullary tumors in the study and control groups. Eighteen true cervico-medullary tumors were detected in the study group. A female patient with a solid tumor component at C6—Th5 vertebrae had a large syringomyelia cyst that extended to the medulla oblongata and caused evident occlusion at the level of Magendie foramen. Thus, cervico-medullary tumor location was revealed in 19 (59.4%) patients from the study group and in 67 (13.2%) from the control group. The revealed prevalence of cervico-medullary tumors in the HC patient group was significant (two-tailed Fisher’s exact test, \( p<0.0001 \)).

Characterization of patients with intramedullary tumors and hydrocephalus

<table>
<thead>
<tr>
<th>№</th>
<th>Age, years</th>
<th>Gender</th>
<th>Tumor location</th>
<th>Tumor histology</th>
<th>Manifestation of hydrocephalus</th>
<th>VP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>F</td>
<td>Th3—Th6</td>
<td>A2*</td>
<td>COND*, macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>F</td>
<td>C0—C5</td>
<td>PA**</td>
<td>COND, HA*, nausea, vomiting</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>M</td>
<td>C0—Th2</td>
<td>A2</td>
<td>HA, nausea, vomiting, macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>M</td>
<td>C2—C4</td>
<td>A2</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>M</td>
<td>C0—C3</td>
<td>PA</td>
<td>COND, HA, nausea, vomiting</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>1.7</td>
<td>F</td>
<td>C5—Th8</td>
<td>AE***</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>M</td>
<td>C0—Th3</td>
<td>PA</td>
<td>COND, HA, nausea, vomiting</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>M</td>
<td>C0—L2</td>
<td>PA</td>
<td>COND, HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>7</td>
<td>M</td>
<td>C0—C6</td>
<td>PA</td>
<td>HA, nausea, vomiting</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>11</td>
<td>M</td>
<td>C0—C5</td>
<td>PA</td>
<td>Macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>13</td>
<td>F</td>
<td>C0—Th5</td>
<td>GBM****</td>
<td>COND, HA</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>2.1</td>
<td>M</td>
<td>C0—Th4</td>
<td>AE</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>6</td>
<td>F</td>
<td>C7</td>
<td>A2</td>
<td>HA</td>
<td>+</td>
</tr>
<tr>
<td>14</td>
<td>1.3</td>
<td>F</td>
<td>C2—Th1</td>
<td>PA</td>
<td>Vomiting, macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>15</td>
<td>6</td>
<td>M</td>
<td>C0—C4</td>
<td>PA</td>
<td>Depression of consciousness</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>13</td>
<td>F</td>
<td>C0—C4</td>
<td>E</td>
<td>COND</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>2.3</td>
<td>F</td>
<td>Th8—Th12</td>
<td>AE</td>
<td>COND, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>18</td>
<td>13</td>
<td>F</td>
<td>C7—L1</td>
<td>PA</td>
<td>COND, atrophy, HA</td>
<td>-</td>
</tr>
<tr>
<td>19</td>
<td>15</td>
<td>F</td>
<td>C5—Th2</td>
<td>GBM</td>
<td>Depression of consciousness</td>
<td>+</td>
</tr>
<tr>
<td>20</td>
<td>1.2</td>
<td>F</td>
<td>C2—Th1</td>
<td>PA</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>21</td>
<td>6</td>
<td>M</td>
<td>Th7—L3</td>
<td>PA</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>22</td>
<td>15</td>
<td>M</td>
<td>C0—C6</td>
<td>E</td>
<td>HA, nausea, vomiting</td>
<td>-</td>
</tr>
<tr>
<td>23</td>
<td>11</td>
<td>F</td>
<td>Th4</td>
<td>PA</td>
<td>COND, HA</td>
<td>+</td>
</tr>
<tr>
<td>24</td>
<td>3</td>
<td>M</td>
<td>C3</td>
<td>A2</td>
<td>HA</td>
<td>+</td>
</tr>
<tr>
<td>25</td>
<td>9</td>
<td>M</td>
<td>Th4—Th6</td>
<td>GBM</td>
<td>Depression of consciousness, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>26</td>
<td>15</td>
<td>F</td>
<td>C0—C2</td>
<td>PA</td>
<td>Depression of consciousness</td>
<td>+</td>
</tr>
<tr>
<td>27</td>
<td>11</td>
<td>F</td>
<td>C0—C3</td>
<td>PA</td>
<td>Vomiting</td>
<td>+</td>
</tr>
<tr>
<td>28</td>
<td>2.5</td>
<td>F</td>
<td>C0—C6</td>
<td>PA</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
<tr>
<td>29</td>
<td>0.9</td>
<td>F</td>
<td>C2—Th4</td>
<td>A2</td>
<td>Vomiting</td>
<td>+</td>
</tr>
<tr>
<td>30</td>
<td>0.3</td>
<td>F</td>
<td>C0—C7</td>
<td>AA†</td>
<td>Vomiting, macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>31</td>
<td>0.9</td>
<td>M</td>
<td>C0—C3</td>
<td>PA</td>
<td>Vomiting, macrocrania</td>
<td>+</td>
</tr>
<tr>
<td>32</td>
<td>9</td>
<td>F</td>
<td>C0—C1</td>
<td>PA</td>
<td>HA, nausea, vomiting</td>
<td>+</td>
</tr>
</tbody>
</table>

Footnote. *A2 — fibrillary astrocytoma (WHO-2); **PA — piloid astrocytoma (WHO-1); ***AE — anaplastic ependymoma (WHO-3); ****GBM — glioblastoma multiforme (WHO-4). E — ependymoma, VP — ventriculoperitoneal shunting. AA† — anaplastic astrocytoma (WHO-3); † — this female patient had undergone endoscopic ventriculostomy four years prior to tumor resection; ‘COND — congestive optic nerve disc; ‡ — headache.
Tumor removal resulted to resolution of HC only in 8 (25%) patients. Other 24 (75%) patients needed cerebrospinal fluid (CSF) shunt surgery. All patients in whom tumor removal led to resolution of HC had cervico-medullary tumors (odds ratio OR=0—0.57; 95% CI). The upper pole of the tumor caused the occlusion of Magendie foramen or the caudal part of the IV ventricle. Signs of a subarachnoid tumoral metastasis at the level of spinal cord conus/epiconus region were revealed only in 1 (12.5%) female patient aged 13 years with WHO-2 ependymoma. Among 24 patients with CSF shunt surgery, 7 (29.2%) showed evident signs of subarachnoid metastasis. However, despite the tendency, this difference was insignificant (two-tailed Fisher’s exact test, \( p=0.642 \)). Shunt surgeries were performed in 12 (50%) patients before the diagnosis of “intramedullary tumor” in the period from 0.5 to 84 months after the development of the disease (14.4±27.2). This large variance in the periods is more likely accounted for by some random events that caused untimely diagnosis of IMTs. Four (33.3%) patients had signs of subarachnoid metastasis, clearly indicating that a CSF shunt was necessary in any case. Meanwhile, 5 (22.7%) patients from the total number of all CSF shunt surgeries had cervico-medullary tumors with an evident occlusion component, and it is likely that the primary operation, tumor resection, could solve the problem of HC. Other 12 (50%) patients after resection of IMT needed shunt surgeries at period from 3 days to 1.5 months postoperatively (0.8±1.1). Signs of tumor dissemination were observed in 3 (25%) patients. Comparison of IMT dissemination rates in the group with shunt surgery performed before identification of tumor diagnosis and after resection of IMT did not reveal significant differences (two-tailed Fisher’s exact test, \( p>0.999 \)). We also tested a hypothesis that a larger percentage of patients with more severe postoperative course of the disease will need CSF shunt surgery. We chose the need for tracheostomy and prolonged (more than 2 days) stay in the intensive care unit as the criterion of severe postoperative course. In the early postoperative period, tracheostomy was required in 1 (12.5%) female patient aged 13 years with WHO-2 ependymoma. Among 24 patients with CSF shunt surgery, 7 (29.2%) showed evident signs of subarachnoid metastasis. However, despite the tendency, this difference was insignificant (two-tailed Fisher’s exact test, \( p=0.642 \)). Shunt surgeries were performed in 12 (50%) patients before the diagnosis of “intramedullary tumor” in the period from 0.5 to 84 months after the development of the disease (14.4±27.2). This large variance in the periods is more likely accounted for by some random events that caused untimely diagnosis of IMTs. Four (33.3%) patients had signs of subarachnoid metastasis, clearly indicating that a CSF shunt was necessary in any case. Meanwhile, 5 (22.7%) patients from the total number of all CSF shunt surgeries had cervico-medullary tumors with an evident occlusion component, and it is likely that the primary operation, tumor resection, could solve the problem of HC. Other 12 (50%) patients after resection of IMT needed shunt surgeries at period from 3 days to 1.5 months postoperatively (0.8±1.1). Signs of tumor dissemination were observed in 3 (25%) patients. Comparison of IMT dissemination rates in the group with shunt surgery performed before identification of tumor diagnosis and after resection of IMT did not reveal significant differences (two-tailed Fisher’s exact test, \( p>0.999 \)). We also tested a hypothesis that a larger percentage of patients with more severe postoperative course of the disease will need CSF shunt surgery. We chose the need for tracheostomy and prolonged (more than 2 days) stay in the intensive care unit as the criterion of severe postoperative course. In the early postoperative period, tracheostomy was required to one (12.5%) patient from the group without shunts and to 3 (12.5%) in the group of patients with CSF shunts. According to tumor biology, malignant tumors (WHO 3—4) were revealed in 21 (79.2%) patients and benign tumors were detected in 25 (78.1%). Three (42.9%) patients with malignant tumors had signs of tumor dissemination, whereas dissemination was observed in 5 (20%) patients in the benign tumor group. The revealed differences were insignificant (two-tailed Fisher’s exact test, \( p=0.327 \)). In the group of malignant tumors, all patients (85.7%), except one, needed shunt surgery. Shunt surgery was required in 18 (72%) patients with benign tumors, which was neither significant (two-tailed Fisher’s exact test, \( p=0.646 \)). The cellular composition of CSF and the protein content in CSF, which was within 0.22—392‰ (1.2±1.1; 95% CI 0.6—1.8), were known for 16 (50%) patients of the study group. The average value exceeded the upper normal threshold (0.35‰) [7]. The mean cell count was 7.7±10 (95% CI 2.4—13) cells/microliter of CSF, being close to the normal range.

**Discussion**

The analysis of the largest individual surgical series of patients operated on for spinal cord IMTs at all age groups (341 patients, 586 operations) detected 34 (6.3%) patients with concomitant HC. This number differs from the only similar paper published 26 years ago, which was also based on individual surgical series of Professor F. Epstein et al. [2]. The cited paper assessed 171 patients; a significant part of them were examined and operated on before the advent of MRI. The paper reported on symptomatic HC in 15% of patients with IMTs, which is much higher percentage compared to our data. It is possible that this is mainly due to the predominance of children in the series described by F. Epstein. Our data also confirm the association of IMTs and HC exactly for the pediatric age group. Other papers are devoted either to individual clinical cases or discuss pathophysiological mechanisms of HC development in patients with IMTs [1, 3, 5, 6, 8].

There are several theories explaining HC development in patients with IMTs [1, 3]:

— viscosity theory — IMT increases protein content in CSF, which affects resorption process;

— fibrinogen theory — IMT increases CSF fibrinogen levels. Fibrinogen is converted to fibrin and causes resorption site obliteration;

— hydrodynamic theory — IMT separates the spinal and intracranial subarachnoid space, which reduces overall elasticity of the central nervous system and increases intracranial pulse pressure;

— occlusion theory — a particular case of cervico-medullary IMT causing occlusion at the level of Magendie foramen and the IV ventricle;

— theory of neoplastic arachnoiditis — in some cases, IMT is accompanied by subarachnoid tumor dissemination impairing CSF resorption.

Our data definitely confirm the possibility of HC development through occlusion theory in patients with cervico-medullary tumors, which supports probable pathogenetic relationship between HC and tumor location. Thus, the occurrence rate of cervico-medullary tumors was 13.2% in the control group, while it was 59.4% in the study group. The theory of neoplastic arachnoiditis was also confirmed in our study [3]. In patients with hydrocephalus and IMT, signs of subarachnoid metastasis of the tumor were observed in 25% of cases, in the control group — only in 0.2%. The available limited data on the composition of CSF support the theory on the role of elevated protein levels in HC development in patients with IMTs.

The main limitation of this paper is that it is retrospective and cannot establish cause-and-effect relationships, but only indicates possible associations between the events. Unfortunately, prospective study is impossible because of the low prevalence of IMTs (about 1% of all tumors arising in the central nervous system) [9, 10] and low...
(most likely, no more than 10%) occurrence rate of HC in patients with IMTs. The best thing to do is to conduct a qualitative analysis of a large modern retrospective series of patients.

Conclusion

These data confirm possible pathogenetic relationship between intramedullary tumors and HC. The occurrence rate of HC requiring treatment in our group of 541 patients was 6.3%. HC combined with IMTs is characteristic of pediatric patients and cervico-medullary tumor location. Tumor dissemination in 90% of cases leads to HC and commonly requires shunt surgery (87.5% of cases). In the presence of cervico-medullary tumor and HC, there is a high (about 50%) probability of HC resolution by tumor resection. Therefore, such patients should be admitted as soon as possible to clinics with substantial experience in surgical treatment of IMTs. When rapid admitting of patients to such hospitals is impossible and in the presence of severe life-threatening occlusion symptom, a reasonable option should be ventriculoperitoneal shunt implantation with subsequent admitting of the patient to a specialized clinic.

Authors declare no conflict of interest.

REFERENCES


Received: 05.10.16

Commentary

This paper is focused on a very rare condition — a combination of intramedullary tumors (IMTs) of the spinal cord and hydrocephalus (HC), which occurs in about 15% of cases in pediatric patients with IMTs [1]. A detailed and useful review of the literature describing various theories on the pathogenesis of HC formation (HC combined with tumor dissemination in 90% of cases) that supports the theory on impaired cerebrospinal fluid resorption because of blastomatous process proposed by R. Maurice-Williams, J. Lucey in 1975 [2]. This explains the pathogenesis of HC development in patients with tumor location at the thoracic and lumbar spine, mainly ependymomas and ependymoblastomas, including in adult patients [3]. The paper presents a detailed discussion of the results from a thorough analysis of the authors’ own material using statistical estimations. The authors retrospectively reviewed a series of 541 patients with spinal cord IMTs and for the first time presented data on the occurrence rate of HC requiring surgical treatment. The article is interesting because it concerns a rare clinical condition for which no prospective multicenter studies are currently available.

V.S. Klimov (Novosibirsk, Russia)

REFERENCES


Central diabetes insipidus (CDI) is a neuroendocrine disease, the pathogenesis of which is associated with abnormal secretion of the antidiuretic hormone. One of the specific causes of CDI is neurosurgical resection of chiasmatic-sellar region (CSR) tumors.

Material and methods. Examination and treatment of patients were performed at a hospital for 7—14 days after surgery and then were continued after discharge. During treatment, the following tests were performed: a daily fluid intake and excretion volume, serum levels of sodium, potassium, and glucose twice a day, morning urine specific gravity, and Zimmntsky's test.

Results. Twenty-three patients with CSR tumors (11 craniopharyngiomas, 10 pituitary adenomas, 1 skull base chordoma, and 1 CSR meningioma) and CDI after neurosurgical treatment received desmopressin. On treatment, a thirst decrease, a reduced rate of diuresis, a reduced amount of excreted urine, and normalization of the sodium level were observed in all patients. In 12 patients (with pituitary adenoma, skull base chordoma, and meningioma) with transient CDI, desmopressin therapy was discontinued upon regression of symptoms 7—30 days after surgery. Eleven patients with permanent CDI continued to receive the drug at a dose of 1 to 4 doses per day. All patients well tolerated the drug without significant adverse effects.

Conclusion. Therapy with desmopressin in the form of a nasal spray (vazomirin) in patients with transient and permanent CDI after resection CSR tumors of various histological nature (craniopharyngiomas, pituitary adenomas, meningiomas, and chordomas) was effective and safe in the early postoperative and long-term postoperative periods.

Keywords: central diabetes insipidus, neurosurgery, desmopressin, craniopharyngioma, pituitary adenoma.
The purpose of this paper is to study the efficacy and safety of desmopressin in patients after resection of chiasm-sellar region (CSR) tumors.

**Material and methods**

The efficacy and safety of vazomirin were evaluated in the early postoperative period during hospital stay of patients at the Burdenko Neurosurgical Institute within 7—14 days after surgery (median, 12 days) and after discharge in the long-term period from 25 days to 3 months (median, 30 days).

Inclusion criteria:
- patients operated for CSR tumors were above 18 years of age;
- polyuria more than 3.5 l per day;
- morning urine specific gravity less than 1,010.

Exclusion criteria:
- surgical patients with complicated postoperative period requiring stay at the intensive care unit;
- fasting glucose level more than 7.0 mmol/L;
- sodium level in blood is less than 135 mmol/L.

All patients with panhypopituitarism were receiving glucocorticoid and thyroid hormone replacement treatment.

The following analyses were performed during treatment in the early postoperative period: daily fluid intake and excretion volume, measurement of sodium, potassium and glucose levels in blood serum twice a day (at 08:00 and 17:00) and evaluation of morning urine specific gravity (at 08:00).

After discharge from hospital, the following analyses were conducted: assessment of 24-h fluid intake and excretion volume. Serum levels of sodium, potassium and glucose were measured once (at 08:00) and Zimnitsky’s test of urine was performed 30 days after discharge. Desmopressin was discontinued for 24 h as a test regimen in order to estimate water-electrolyte metabolism and assess the reasons for continuing treatment with vazomirin. When thirst and polyuria appeared, the treatment was resumed.

Semi-quantitative scale was used to estimate thirst: 1 point — no thirst, 2 points — periods of dry mouth, 3 points — chronic feeling of mouth dryness, periods of thirst during a day, 4 points — chronic feeling of thirst.

**Results**

Twenty three patients (12 women and 11 men aged 19—64 years (median, 48 years) with CSR tumors (11 craniopharyngiomas, 10 pituitary adenomas, 1 skull base chordoma, 1 meningioma) with CDI after neurosurgical treatment were examined. Seventeen patients were operated on with transnasal and 6 — transcranial approach.

Preoperatively, 4 patients with craniopharyngiomas were diagnosed with CDI; when admitted to the Burdenko Neurosurgical Institute these patients received a tablet
form of desmopressin. Symptoms of CDI in form of thirst and polyuria from 4,200 to 9,300 mL/day (median 5,850 mL) were noted immediately after surgery in 21 patients (Table 1). Hypernatremia (147—161 mmol/L) was observed in 13 patients and sodium level was within normal range (138—145 mmol/L) in 10 patients.

All patients received therapy with vazomirin (all doses delivered were intranasal). The dose of vazomirin was increased when daily polyuria was more than 3,000 mL and/or urine output rate was >300 mL/h. In most (12) cases, two intranasal doses were used in the early postoperative period to relieve CDI symptoms. In 8 cases, vazomirin dose was increased to 4 doses (taken twice a day), in one — up to 5 doses (taken 3 times a day). In 2 cases, one dose was sufficient (Table 3). All patients after endonasal surgery received vasoconstrictive drops to reduce edema of the nasal mucosa and hence intranasal desmopressin was used in most cases. However, 4 patients with marked edema of the nasal mucosa needed sublingual administration in the first postoperative day.

On treatment, daily diuresis was 2,400—3,800 mL (median, 2,750) (Fig. 4). Taking into account possible spontaneous regression of CDI, vazomirin was indicated depending on urine output rate. Secondary to application of desmopressin and adequate drinking regimen (at least 2 L/day), sodium level normalized in all patients. There were no episodes of hyponatremia in any of these patients. All patients tolerated well desmopressin; no significant adverse effects were noted. Vazomirin treatment was abolished in 12 patients (pituitary adenoma, skull base chordoma and meningioma) with a transient form of CDI, when symptoms regressed in 7—30 days after surgery.

All 11 patients with craniopharyngioma, with chronic CDI continued to receive 1 to 4 doses of desmopressin per day after discharge (Table 2).

Three patients with craniopharyngioma, who received a tablet form of desmopressin preoperatively, preferred intranasal vazomirin after discharge as a more convenient form of medication that is also independent of eating. Moreover, all these patients had panhypopituitarism, which required a permanent use of glucocorticoid and levothyroxine tablets. Therefore, the patients preferred intranasal desmopressin vazomirin instead of a tablet form due to “reduced number of taken tablets”.

---

Fig. 3. a — pituitary stalk craniopharyngioma; b — MRI, sagittal and frontal views (preoperative); c — condition after complete resection of craniopharyngioma, pituitary stalk is not visualized; d — MRI, sagittal and frontal views (postoperative).
A pharmacoeconomic analysis estimated the average cost of medications (vazomirin, minirin and sublingual minirin tablets) on April 25, 2017 taking into account prices for vital medications, Moscow regional extra charge and value added tax (Table 4).

The average therapeutic dose of vazomirin was calculated for the patients included in the study. A comparative analysis was carried out in a group of previously operated patients who received tablet forms (minirin and sublingual minirin tablets) postoperatively. The groups were similar in nosological forms of tumors, age and gender of patients.

Here are some case reports.

Case report No. 1

A female patient A., 35 years old, was admitted to the Burdenko Neurosurgical Institute with complaints of visual impairment, headache, and absence of menstrual cycle.

Medical record: amenorrhea since 32 years, deterioration of vision over 6 months, headache. Magnetic resonance imaging (MRI) of the brain revealed craniopharyngioma of suprasellar location invading into the third ventricle. Neuro-ophthalmological examination revealed a decrease in visual acuity: OD=0.4, OS=0.6 and bitemporal hemianopsia.

The patient underwent surgery: transcranial resection of pituitary stalk craniopharyngioma. The source of growth tumor, pituitary stalk, was detected intraoperatively. Craniopharyngioma was removed with pituitary stalk excision. After surgery, visual acuity improved to 0.8 on both eyes and visual fields restored. Tumor remnants were not revealed on a series of control computed tomography (CT).

In the first postoperative day, symptoms of diabetes insipidus were developed: thirst and polyuria appeared. The volume of daily urine was 5,600 mL. Na — 154 mmol/L (135—145), K — 3.7 mmol/L (3.5—5.0), urine specific gravity — 1,001 g/L. In addition, the patient was diagnosed with panhypopituitarism; glucocorticoid and thyroid medications were prescribed.

Vazomirin in form of a nasal spray was administered when urine output rate exceeded 300 mL/h. The maximum dose per day was 4 intranasal doses, which were taken twice a day (at 09:00 and 21:00). On treatment, symptoms of CDI regressed. Urine output rate reduced when urine output rate exceeded 300 mL/h and 24-h urine volume was 2780 ml. The patient was discharged on the 7th day after surgery in satisfactory condition.

At follow-up examination at the Burdenko Neurosurgical Institute in 1 month after surgery requirement of pituitary stalk excision led to persistent symptoms of CDI and hypopituitarism apparently because this impaired trafficking of hypothalamic hormones, including ADH, into the pituitary gland. Administration of vazomirin restored water and electrolyte balance, stabilized the patient’s condition and significantly improved quality of life.

Case report No. 2

Patient I., 30 years old, was admitted to the Burdenko Neurosurgical Institute with complaints of headache and visual impairment.

It is known from anamnesis that since 27 years the patient had symptoms of diabetes insipidus (thirst, frequent urination up to 7 liters per day) and hypopituitarism disorders (weakness, decreased libido, erectile dysfunction, and tendency to arterial hypotension of 90—100/60 mm Hg, deterioration of appetite, nausea, and 7 kg of weight loss). CDI and panhypopituitarism diagnoses (secondary hypothyroidism, adrenal insufficiency, hypogonadism and growth hormone deficiency) were confirmed on examination. Brain MRI revealed a cra-
niopharyngioma of endosuprasellar location. The patient refused from a surgery at that time and was treated with oral glucocorticoids, thyroid drugs and desmopressin tablets at a dose of 0.4 mg/day. The treatment significantly improved the patient’s condition (thirst sensation alleviated, diuresis reduced to 3,500—4,500 mL, body weight increased by 5 kg, blood pressure normalized, appetite and performance improved), but headache aggravated, visual fields and visual acuity markedly deteriorated during the last year.

Neuro-ophthalmology examination revealed reduced visual acuity: OD=0.5, OS=0.09 and bitemporal hemianopsia. MRI showed an increase in the size of cranioopharyngioma and appearance of a large cystic component.

The patient underwent surgery: endonasal endoscopic resection of pituitary stalk cranioopharyngioma. No tumor remnants were detected on a series of control CT scans.

On control examination postoperatively, neuro-ophthalmologist noted expansion of visual fields and improved visual acuity: OD to 0.6, OS to 0.2.

Since there was no evident signs of edema at the nasal mucosa due to application of vasoconstrictive drops on the first postoperative day at the hospital, intranasal vazomirin was indicated to the patient for a urine output rate of>300 mL/h and glucocorticoid and thyroid hormone replacement therapy was continued. The maximum dose of vazomirin per day was 2 intranasal doses, which were taken twice a day (at 09:00 and 21:00). The patient’s condition remained satisfactory. A 24-h urine volume was 2,600—3,200 mL. Na — 143 mmol/L (135—145), K — 3.9 mmol/L (3.5—5.0), glucose — 4.8 mmol/L (4.1—5.9), urine specific gravity — 1,012 g/L.

Since the patient was on the long-term (chronic) intake of glucocorticoid and thyroid hormones, he preferred intranasal vazomirin after discharge due to “lower number of tablets and as a more convenient method of drug application, which is independent of eating time”.

Case report No. 3

Patient K., 46 years old, was admitted to the Burdenko Neurosurgical Institute with complaints of visual impairment and headache.

Medical record: the above complaints bothered the patient for 10 months. MRI and hormone blood tests revealed hormone-inactive pituitary adenoma of an endosuprasellar location. No hypopituitary disorders and symptoms of diabetes insipidus were observed.

Neuro-ophthalmologic examination revealed decreased visual acuity: OD=0.7, OS=0.5 and bitemporal hemianopsia.
The patient underwent surgery “resection of pituitary adenoma by endoscopic endonasal approach”. Pituitary adenoma with a dense architecture infiltrating the pituitary gland was revealed intraoperatively. A series of control CT scans did not detect any intracranial complications or evident tumor remnants.

Thirst sensation, frequent urination up to 5,800 mL/day, and an increased urine output rate of >300 mL/h developed postoperatively. Because of marked edema of the nasal mucosa after endonasal surgery, 4 doses of sublingual vazomirin per day were indicated. Intranasal vazomirin was used since the third day after surgery along with application of vasoconstrictive drops, with the maximum dose per day — 2 doses (at 09:00 and 22:30). The treatment reduced daily diuresis to 2,600 mL.

After 7 days, desmopressin was abolished due to a reduction in urine output rate. The patient was discharged on the 8th day in a satisfactory condition with regressed symptoms of diabetes insipidus (daily urine output at discharge did not exceed 3,000 mL) and vazomirin was abolished.

On control examination at the Burdenko Neurosurgical Institute 1 month after surgery, the patient had no complaints. Daily diuresis was 1,500—1,700 mL, urine specific gravity — 1,020 g/L.

Therefore, the patient was diagnosed with transient diabetes insipidus, whose genesis is probably associated with edema in the area of an operative wound and/or insignificant intraoperative injury to the pituitary gland, which caused temporary deficiency of ADH followed by complete restoration of its secretion.

**Conclusions**

Therapy with vazomirin in patients with CDI after resection of the chiasm-sellar region tumors with different histological natures (craniopharyngiomas, pituitary adenomas, meningiomas and chordomas) was effective and safe and its favorable effects were shown:

— vazomirin can be used in the early postoperative period, including in patients with swallowing impairment;
— dose adjustment/discontinuation of desmopressin treatment is possible depending on a situation in the early postoperative period;
— first instillation of vasoconstrictor nasal drops and then intranasal desmopressin can be used in case of disturbed nasal breathing after transnasal surgery;
— sublingual desmopressin can be used in patients with marked impairment of nasal breathing after transnasal surgery;
— systematic application of desmopressin in patients in the long-term postoperative period with a chronic form of diabetes insipidus;
— desmopressin application is independent of eating and intake of other tablets;
— desmopressin does not cause significant adverse effects;
— a positive psychological effect due to “reduced number of taken tablets” in patients who need continuous treatment with glucocorticoid and thyroid tablets;
— cost of vazomirin spray compared to vazomirin tablets is reduced by 45—48% in patients after resection of the chiasm-sellar region tumors.

Authors declare no conflict of interest.

**REFERENCES**


Received: 26.04.17
Commentary

This paper by L.I. Astaf’eva is focused on a common complication associated with neurosurgical treatment on the brain — central diabetes insipidus (CDI). The mechanisms of CDI pathogenesis based on modern data are described in detail at the beginning of the article. Afterwards, the efficacy and safety of vazomirin in patients after resection of the chiasm-sellar region tumors conducted by the author are assessed. Twenty three patients with CDI after neurosurgical intervention with transient and chronic CDI were examined. Both the early and long-term postoperative (after discharge) periods were analyzed. The patients were examined before and after vazomirin application. The efficacy and safety of treatment with desmopressin, including in the long-term postoperative period is shown. The author also conducted a pharmacoeconomic analysis of several variants of CDI therapy.

This paper has a high practical significance. It is known that CDI often occurs after neurosurgical interventions on the hypothalamic-pituitary area and requires treatment. This paper shows the efficacy and safety of CDI treatment with an intranasal form of desmopressin. Outpatient follow-up (after discharge of a patient from the hospital) expands the range of specialists who will benefit from this work, since outpatient healthcare professionals encounter patients after discharge from the hospital who have different forms of CDI. The author also reports cases of examination and treatment of patients with diseases of the chiasm-sellar region, which will help medical practitioners in their work.

The study design is fully consistent with the purpose of the study and modern requirements for scientific work; significant results were achieved and reasoned conclusions were made.

The author used current published data from the leading researchers working in this field.

The material is well-connected. This is a high-level study. The results can be recommended for clinical practice and are of interest to different physicians (neurosurgeons, endocrinologists, critical care physicians, therapists).

I.V. Komerdus (Moscow, Russia)
The Extended Endoscopic Endonasal Transsphenoidal Approach in Surgery for Epidermoid Cysts of the Chiasmatic Region

D.V. FOMICHEV, P.L. KALININ, M.A. KUTIN, O.I. SHARIPOV, I.V. CHERNOV

Burdenko Neurosurgical Institute, Moscow, Russia

Surgical treatment for epidermoid cysts of the chiasmatic region is a challenge because of the tendency to a massive spread of epidermoid masses through the cerebrospinal fluid pathways and a significant lesion deviation from the midline.

Purpose. To analyze capabilities of the extended endoscopic endonasal transsphenoidal approach in surgery for epidermoid cysts.

Material and methods. The study included 6 patients with epidermoid cysts of the chiasmatic region who were operated on using the extended anterior endoscopic endonasal transsphenoidal approach at the Burdenko Neurosurgical Institute in the past 5 years.

Results. Epidermoid masses were completely removed in 5 patients; in none of the cases, complete removal of the epidermoid cyst capsule was achieved. There were no cases of vision deterioration and the development of new focal neurological symptoms. One female patient developed hypopituitary disorders in the postoperative period. There was no recurrence of epidermoid cysts during follow-up.

Conclusion. Removal of epidermoid cysts of the chiasmatic region using the extended anterior endoscopic transsphenoidal approach may be an alternative to transcranial microsurgery.

Keywords: epidermoid cyst, cholesteatoma, extended endoscopic endonasal transsphenoidal approach, transsphenoidal surgery.

The epidermoid cyst (EC), which is also referred to as cholesteatoma, is a rare intracranial neoplasm that accounts for less than 1% of all intracranial neoplasms [1]. Most often, intracranial ECs are located in the air cells of the petrous pyramidal of the temporal bone, extending into the cerebellopontine angle and the chiasmatic region.

Pathogenesis of ECs is most often associated with pathological processes in the inner ear area (chronic inflammation, trauma) and hemorrhages leading to impaired drainage of the air cells of the temporal bone [2, 3]. There are also congenital ECs that are believed to arise from ectodermal epithelial fragments during the formation of secondary cerebral vesicles or those remaining in the cavity of the closing neural tube [4].

Macroscopically, ECs have undulating, shiny, light-gray surface and small-lobed inner structure with layered creamy content consisting mainly of keratohyalin. Due to external similarity they are sometimes called “pearl” tumors. They have a tendency to encase the main vessels and cranial nerves, spreading through the cerebral cisterns of the skull base. The microscopic structure of the cyst walls is represented by exfoliating stratified keratinized squamous epithelium on a thin basal membrane. The cavity of the cyst is represented by a keratinous substance with inclusion of crystalline cholesterol. Unlike dermoid cysts, ECs do not contain dermal buds, such as hair follicles and sebaceous glands.

Diagnosis of ECs is based on the data of computed tomography (CT) and magnetic resonance imaging (MRI). According to CT data, ECs have lower density than the CSF (up to –30 units H) or the density close to it and they do not accumulate the contrast. In 15—20% of cases there are petrifications in the cysts. In MRI studies in T1-mode ECs are most often hyperintensive, while in T2-mode they are iso-intensive compared to the CSF.

The clinical presentation of ECs is associated with compression effect of the cyst content on the basal parts of the brain and cranial nerves, and it is nonspecific and includes headache, vision deterioration, symptoms of brain stem damage, epileptic syndrome.

Until recently, surgical treatment of ECs of the chiasmatic region relied only on transcranial approaches [5, 6]. However, over the last dozen of years rapid development of endoscopic techniques and improvement in extended transsphenoidal endoscopic endonasal approaches led to drastic changes in the approaches to surgery of suprasellar neoplasms, including ECs of the chiasmatic region [7—12].

Our search in the PubMed database using keywords “cholesteatoma” and “epidermoid cyst” did not yield any results for publications devoted to excision of ECs of chiasmatic localization using extended transsphenoidal endonasal endoscopic approaches. The available publications are mainly devoted to various aspects of diagnostics and treatment of ECs of the cerebellopontine angle and the temporal bone.

The purpose of this work is to analyze capabilities of the extended endoscopic endonasal transsphenoidal approaches in surgery for epidermoid cysts.

Material and Methods

The present study included 6 patients with ECs of chiasmatic localization, who were operated on in the Burdenko Neurosurgical Institute by the authors of this article over the last 5 years using anterior extended transsphenoidal endoscopic endonasal approach.

e-mail: DFomichev@list.ru
All patients were examined according to the same protocol before and after the surgery, which included standard laboratory tests, studies of hormonal, neurological, neuro-ophthalmologic, and endocrinological status and X-ray studies (CT, MRI).

Clinical symptoms are represented by chiasmal syndrome of varying severity (4 patients), cranial pain syndrome (2), and hypopituitary disorders (1). Clinical characteristics of the patients are presented in Table 1.

In 4 cases, the endoscopic endonasal surgery was the primary treatment for a newly diagnosed EC. Two patients had been previously operated on in the Burdenko Neurosurgical Institute for ECs: Patient No 3 using para-median approach to a cholesteatoma of the cerebello-pontine angle, and patient No 5 using subfrontal approach to EC of the chiasmatic region.

Surgical Technique

Advanced endonasal surgeries are impossible without well-coordinated “four hands” work by a surgeon and an assistant trained in such operations.

Extended transsphenoidal endonasal operations consist of several stages: nasal, sphenoidal, removal of the tumor and plastic surgery to close the formed skull base defects. At the nasal and sphenoidal stages, standard approach to the bottom of the Turkish saddle and the plane of the sphenoid bone is performed and these stages end with trepanation of these bone structures. It is followed by the opening, using a micro-scissors or a scalpel, of the dura mater of the sphenoid bone and the bottom of the Turkish saddle. At this stage, it is necessary to carefully coagulate the upper intercavernous sinus with mono- or bipolar coagulation.

Removal of the epidermoid cyst tissue is carried out by various curved suctions, curettes and dissection instruments under the control of 30°, 45° and 70° endoscopes. Most often, the cholesteatomas have moderate density and are easily removed by conventional suction, but in a number of cases, especially in repeated surgeries, they can be dense and layered. It is this case the removal of the cholesteatoma is carried out by exfoliating it with curettes and dissecting instruments.

Instrumental manipulations are carried out in the space between the posteroinferior surface of the chiasma and the diaphragm of the Turkish saddle. If the distance between the chiasma and the diaphragm of the saddle is small, it is advisable to dissect the pituitary tissue and the diaphragm of the saddle in the anteroposterior direction while retaining the stalk of the pituitary gland in order to increase the surgical access zones.

It should be kept in mind that the epidermoid masses are permeated by vascular-nervous structures of the chiasmatic region (anterior cerebral and posterior connective arteries, optic and oculomotor nerves), which can be significantly displaced relative to their normal anatomical position during the intervention and drastically atrophied.

It is necessary to try to achieve the maximum possible excision of the capsule of the epidermoid cyst in order to reduce the incidence of tumor recurrence. However, tight fusion between the capsule on one hand and the brain and vascular-nervous structures on the other, as well as the high risk of damage to the latter, often prevents complete excision of the thin capsule of the cyst.

The degree of EC removal is also affected by significant lateral spread of epidermoid masses. Cholesteatomas that extend into the cavity of the third ventricle are easily removed by various suction, since the main volume of the cyst is located along the trajectory of the anterior expanded transsphenoidal approach. If the epidermoid masses spread to the posterior cranial fossa, the back of the Turkish saddle and the clivus can be resected, ensuring sufficiently wide corridor to remove the retrosellar portion of the EC. However, the opportunities for EC removal in case of significant lateral spread under the basal surfaces of the temporal lobes are limited by the position of the internal carotid arteries.

The sealing of the extensive skull base defects is a particularly important stage during extended operations [11—14]. We consider the previously described “sandwich” method of sealing [7, 8] to be the best one among numerous variants of closing the defects of the skull base which we have tried. We use a multilayer plastic surgery: first a fragment of the wide fascia of the thigh is inserted intradurally beyond the edges of the bone defect; then the fascia is fixed in the cranial cavity by the auto-fragment, cut from the septum of the nose, so that the edges of the fascia are in the cavity of the sphenoidal sinus. Further, this layer is fixed with 1—2 mL of fibrin-thrombin glue (Evicel ETHICON, Inc), and the second layer of fascia is laid on the adhesive layer. The layer of fibrin-thrombin glue can be repeated, after which the sphenoidal sinus is plugged with autofascia taken from the thigh of the patient. In some cases, mucoperioidal flap on the feeding pedicle is used as one of the layers in the plastic surgery. The entrance to the sphenoidal sinus is closed with an expanded Foley catheter or an elastic swab for a period of 3—5 days. External drainage of the CSF is carried out through the lumbar drainage for 3—4 days after the operation. The stages of the removal of EC of the chiasmatic region using anterior extended endoscopic endonasal transsphenoidal approach in patient No 2 are shown in Fig. 1.

Results

Radicality

Total removal of the epidermoid masses was achieved in 5 patients. In 1 case, a small fragment of the tumor which extended laterally under the basal parts of the temporal lobe, remained.

The main problem in the removal of ECs is the difficulty of excising a thin capsule of the cyst, which is tightly fused to the basal parts of the brain and vascular-nervous structures. In all the cases, we failed to achieve complete excision of the EC capsule during the surgery; its fragments always remained because their removal was fraught with damage to adjacent vascular-nervous structures.
Table 1. Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>№</th>
<th>Gender, Age, years</th>
<th>Clinical symptoms before the surgery</th>
<th>Dynamics of clinical symptoms after the surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F, 32</td>
<td>Chiasmatic syndrome</td>
<td>No changes in vision, onset of hypocorticoid-ism</td>
</tr>
<tr>
<td>2</td>
<td>M, 20</td>
<td>Chiasmatic syndrome</td>
<td>Restoration of vision</td>
</tr>
<tr>
<td>3</td>
<td>F, 50</td>
<td>Continued EC growth in the chiasmatic region 3 years after the removal of EC of the cerebellopontile angle using para-median approach. Chiasmatic syndrome, hypocorticoid-ism, diabetes insipidus</td>
<td>No changes in vision, no changes in hypopituitary disorders</td>
</tr>
<tr>
<td>4</td>
<td>F, 41</td>
<td>Headache</td>
<td>Regression of headache</td>
</tr>
<tr>
<td>5</td>
<td>F, 53</td>
<td>Recurrence of EC in the chiasmatic region 17 years after removal of the EC of the cerebellopontile angle using sub-frontal approach. Chiasmatic syndrome</td>
<td>No changes in vision</td>
</tr>
<tr>
<td>6</td>
<td>F, 32</td>
<td>Headache</td>
<td>Regression of headache</td>
</tr>
</tbody>
</table>

Fig. 1. Stages of removal of the epidermoid cyst of the chiasmatic region from anterior expanded transsphenoidal endoscopic endonasal approach using a 30° endoscope.

a — the bottom of the Turkish saddle and the sphenoid plane area are trepanized. DM of bottom of the saddle and plane (1) is opened, beginning of removal of epidermoid masses (2). b — a stage in removal of the epidermoid cyst: 1 — left ICA, 2 — left ACrA, 3 — epidermoid masses, 4 — suction; c, a stage in removal of the epidermoid cyst: 1 — left ICA, 2 — left ACrA, 3 — ACA, 4 — right ACrA, 5 — epidermoid masses; d, a stage in removal of the epidermoid cyst: 1 — left ACrA, 2 — ACA, 3 — right ACrA, 4 — walls of the ventricle III, 5 — interthalamic adhesion.
Fig. 2. An example of the total removal of the giant epidermoid cyst of the chiasmatic region in patient No 2.
a, b — CT in the frontal and sagittal projection before the surgery; c, d — MRI in T1-mode in the frontal and sagittal projection before the surgery. Giant epidermoid cyst of the chiasmatic region is visible; e,f — MRI in T1-mode in the frontal and sagittal projection 6 months after the surgery. Total removal of the tumor is visible. Plastic materials are located in the sellar region and in the projection of the sphenoidal sinus.
Dynamics of clinical syndromes and symptoms

Table 1 presents the dynamics of pre-operative clinical symptoms and syndromes of the disease. We have no cases of deterioration in vision or onset of new visual disorders after the surgery. One patient with gross visual impairment noted complete restoration of visual function in a short period after the surgery. In case we observed an onset of hypopituitary symptoms in the form of hypocorticism after the surgery. Two patients reported regression of the cranial pain syndrome that was present before the operation.

There were no cases of new development of any new focal neurological symptoms after the surgery.

Complications

In the postoperative period patient No 1 reported the onset of recurrent nasal liquorrhea, which required repeated endoscopic endonasal procedures for plastic surgery of skull base defects using autologous and heterologous materials, as well as external lumbar drainage of the CSF.

There were 2 reported cases (Patients No 1 and No 6) of development of bacterial meningitis, which required specific antibacterial therapy with identification of the pathogen.

The follow-up period has been traced to the present day in 4 patients. There were no case of EC recurrence.

Fig. 2 presents an example of the total removal of EC of giant dimensions from the chiasmatic region in the patient No 2.

Discussion

Our experience of endonasal endoscopic operations in various pathologies of the chiasm-sellar region (pituitary adenoma, craniopharyngioma, meningioma, choroidoma, malignant tumors of the skull base, etc.) amounted to more than 6,000 surgeries over the past 12 years. We have conducted the excision of more than 230 different suprasellar tumors (craniopharyngioma, meningiomas, gliomas, etc.) from the anterior extended transsphenoidal approach, wherein the standard craniotomy of the bottom of the Turkish saddle was supplemented by resection of the plane of the sphenoidal bone and posterior portions of the ethmoidal labyrinth, including 6 patients with EC of the chiasmatic region.

Despite the very low incidence of ECs of the chiasmatic region, their surgical treatment is a challenge because of the tendency to a massive spread of epidermoid masses through the cerebrospinal fluid pathways and a significant lesion deviation from the midline. Therefore, the issue of adequate surgical approach to ECs of the chiasmatic region is highly relevant.

Currently, there are two approaches to surgical treatment of suprasellar tumors, which include ECs: transcranial microsurgical (subfrontal, pterional) and extended transsphenoidal endoscopic intranasal approaches [5, 9, 15—18].

Both approaches have advantages and disadvantages. The advantage of the extended transsphenoidal approach is, first of all, the ability to avoid brain traction during the surgery, and secondly, direct transnasal access to suprasellar neoplasm under the conditions of good illumination and much better overview of the operating field. All this contributes to less traumatization of the diencephalic region and visual pathways, which promotes the favorable course of the postoperative period.

The main limitation of the endoscopic endonasal approach for this pathology is the significant lateral spread of ECs, which prevents removal of epidermoid masses from under the basal parts of the temporal lobes.

In addition, it is necessary to consider a number of disadvantages inherent in all endoscopic transsphenoidal operations. First of all, they require considerable time for additional training of a neurosurgeon in particularities of endonasal anatomy and for development of new, completely specific endoscopic manual skills while working with a two-dimensional image provided by an endoscope. Secondly, stopping of both venous and arterial bleeding is a major challenge in the endoscopic endonasal surgeries and requires delicate work of the entire surgical team and, first of all, “four hands” of a surgeon and an assistant.

It is necessary to strive for the maximum possible excision of the EC capsule in order to avoid recurrence of the tumor. However, our experience convinces us that it is impossible to completely excise a thin epidermoid capsule covering the basal parts of the brain and the neurovascular structures of the chiasmatic region without the risk of damage to the latter. Therefore, it is difficult to state with certainty that an EC has been completely excised; more often it is possible to radically remove only the epidermoid masses (in 5 out of 6 cases), leaving the capsule fragments on the vessels and nerves. No recurrence of the cysts was observed in our cohort patients despite the fragments of the epidermoid capsule left in place, although it is possible that this observation is due to the relatively short follow-up period (the average duration of the follow-up period is 36 months).

The dynamics of clinical symptoms in patients with EC, operated from the anterior expanded transsphenoidal endoscopic approach, is quite favorable: there were no cases of vision deterioration and the development of new focal neurological symptoms. Only one patient developed hypopituitary disorders in the postoperative period, which were associated with dissection of the pituitary gland during the surgical approach.

Complications after the removal of EC using the extended transsphenoidal approaches are non-specific and represent the main issues associated with extended transsphenoidal surgery: nasal liquorrhea and meningitis. It should be kept in mind that the plastic surgery of the skull base defects is an extremely important stage in the extended transsphenoidal surgeries, since it is necessary to achieve the maximum sealing via multilayer plastic surgery using the full range of available plastic materials, both autologous and heterologous in nature (autofascia, fragments of the wide fascia of the thigh, mucosal periosteal flap on a feeding pedicle, analogues of dura mater, inducers of duro- and osteogenesis, collagen plates, fi-
High risk of infectious postoperative complications in patients operated on from the extended transsphenoidal approaches necessitates the use of antibiotic prophylaxis with a wide range of drugs, both during and after the surgery, as well as careful adherence to aseptic conditions.

**Conclusion**

The data accumulated by us indicate that the removal of ECs of the chiasmatic region using the anterior expanded transsphenoidal endoscopic endonasal approach is an effective and low-trauma technique that ensures the maximum possible removal of neoplasms and relatively low rates of postoperative complications.

Therefore, the extended transsphenoidal surgeries to remove ECs of the chiasmatic region may be a real alternative to transcranial microsurgery.

**Authors declare no conflict of interest.**

---

**Commentary**

The article is devoted to one of the important issues in transsphenoidal endoscopic surgery: the removal of epidermoid cysts of the chiasmatic region. The authors present proper analysis of the submitted material. The study was conducted on a small set of patients, which may be explained by the fact that not all such patients are included in the study or by the fact that significant proportion of patients was operated on transcranially. The pathology under consideration is quite rare and, therefore, the generalization of the experience gained by the authors is of practical importance for relevant specialists. The authors’ conclusions are justified and follow from the logic of the work. There are no remarks from our side. The work can be accepted for publication.

*V.Yu. Cherebillo (St. Petersburg, Russia)*
Craniofacial Tumors Blood Supply


Burdenko Neurosurgical Institute, Moscow, Russia

Because of the spread to different anatomical regions, craniofacial tumors (CFTs) usually receive blood supply from several arterial systems, and CFT removal is often accompanied by abundant blood loss.

**Purpose.** The study purpose was to develop an algorithm of diagnostic angiography for planning surgical treatment of CFT patients.

**Material and methods.** Complex preoperative angiography was performed in 72 patients with craniofacial tumors, aged 10 to 78 years (mean age, 45.5 years), who underwent surgical treatment at the Burdenko Neurosurgical Institute in the period from 2012 to 2015. At the first stage, blood supply to tumors was quantified using SCT perfusion. Then, depending on an assessed degree of tumor vascularization, direct angiography or modern minimally invasive angiographic techniques (3D TOF HR MR angiography, SCT angiography) were applied.

**Results.** In 12 cases of hypervascular tumors, accessible afferents were preoperatively embolized through the external carotid artery, which was accompanied by an increase in the blood supply to tumors via alternative routes of the external and internal carotid arteries. The obtained data were used to plan the surgical approach. A comparative analysis of the SCT perfusion data and the expression level of endothelial markers in histological specimens revealed no significant correlation.

**Conclusion.** The study demonstrated the importance of a comprehensive assessment of the blood supply to CFTs in planning of the surgical treatment and enabled the development of algorithms for preoperative angiographic diagnosis, depending on the baseline clinical and radiological data.

**Keywords:** craniofacial tumors, skull base, angiography, blood supply.

### Abbreviations

APA — ascending pharyngeal artery  
ICA — internal carotid artery  
MA — maxillary artery  
PDTA — posterior deep temporal artery  
CFT — craniofacial tumor  
MRI — magnetic resonance imaging  
MRA — magnetic resonance angiography  
CCA — common carotid artery  
SCT — spiral computed tomography  
SCT-AG — spiral computed tomographic angiography  
ECA — external carotid artery  
STA — superficial temporal artery  
ADTA — anterior deep temporal artery  
ACA — anterior cerebral artery  
EA — ethmoid artery  
MCA — middle cerebral artery  
MMA — middle meningeal artery  
CBF — cerebral blood flow  
CBV — cerebral blood volume  
TBF — tumor blood flow  
TBV — tumor blood volume

Craniofacial tumors (CFTs) are a heterogeneous group of neoplasms sharing the topographic characteristics and differing in the histological structure and vascularization degree. For example, meningiomas, juvenile craniofacial angiofibromas, capillary hemangiomas, and some malignant tumors are masses with intensive blood supply, while chondroid tumors and chordomas are hypovascular neoplasms [1—4]. Because of the spread to different anatomical regions, craniofacial tumors (CFTs) usually receive blood supply from several arterial systems, and their removal is often accompanied by abundant blood loss. Intraoperative bleeding, on the one hand, limits the radicalness of surgery and, on the other hand, increases the risk of postoperative functional deficits due to injury to normal tissues under complicated orientation conditions.

One of the main ways to prevent intraoperative blood loss and, therefore, to minimize postoperative functional
disorders and increase the extent of craniofacial tumor resection is planning of surgical management based on analysis of the peculiarities of tumor blood supply. Knowledge of the angio-architectonic features of these neoplasms, depending on the histological structure, location, dissemination, and direction of growth, facilitates choosing the optimal algorithms for their pre- and intra-operative devascularization. The vascular anatomy variants of the craniofacial region in health are studied in sufficient detail. Tumor growth significantly changes the blood supply. Newly formed vessels with anastomoses develop, and venous outflow pathways change, which along with the intensity of blood supply to the tumor stroma should be considered when preparing for surgery.

The study purpose was to develop an algorithm for angiographic diagnosis for planning the surgical management of patients with craniofacial tumors.

**Material and methods**

In the prospective study, we selected 72 patients aged 10 to 78 years (mean age, 45.5 years) with advanced craniofacial tumors of a different histological structure. All patients underwent primary or repeated surgical treatment in the Department of Craniofacial Surgery of the Burdenko Neurosurgical Institute between 2012 and 2015. The distribution of patients by the histological tumor patterns is shown in a diagram (Fig. 1).

In all patients, the diagnosis was established based on the data of magnetic resonance imaging (MRI) or contrast-enhanced spiral computed tomography (SCT). In the preoperative period, patients underwent a detailed angiographic examination. The tumor blood supply was quantitatively evaluated by SCT perfusion on a 64-slice GE Optima 660 scanner using the Perfusion Long protocol, with low-dose axial SCT being preliminarily performed to identify the area of interest. In this case, we used a highly concentrated iodine-containing drug (350—370 mg/mL) solution injected into the median cubital vein using an injector. The data were processed on v. 4.2 and v. 4.4 Advantage GE workstations using Perfusion 2.0 and 3.0 software. Absolute values of the tumor blood flow (TBF, mL/100 g/min) and tumor blood volume (TBV, mL/100 g) were determined. Because the data were processed on different workstations, analysis of the perfusion data was based on normalized values of tumor blood flow (nTBF) and blood volume (nTBV), i.e. the values reflecting the ratio of tumor parameters to those of the intact white matter, expressed as coefficients.

For detailed qualitative assessment of blood supply and evaluation of the possibility of preoperative embolization in the presence of clinical and radiological signs of hypervascular tumors (angiofibromas, meningiomas, some malignant processes), patients underwent direct selective angiography, in some cases, extended with high-resolution magnetic resonance angiography (MRA) or spiral CT angiography (SCT-AG). In the other cases, only minimally invasive angiographic studies (MRA and SCT-AG) were performed. Direct selective angiography was performed using AdvantX DLX GE Healthcare and Allura Xper FD20/10 Philips Healthcare systems. High-resolution magnetic resonance angiography in 3D TOF HR and TRICKS modes was performed on GE Signa HDxt 3.0 T and 1.5 T scanners with 16.0 and 15.0 software versions, respectively, and GE Signa Optima 450 w 1.5 T with a 24.0 software version. In the case of tumors poorly contoured in the native mode, 3D TOF MRA was performed after administration of a contrast agent, which improved visualization of the tumor stroma and vasculature. SCT angiography using standard and dynamic modes was performed using GE LightSpeed 16-slice and GE Optima 660 64-slice CT scanners. The results were processed on v. 4.2 and v. 4.4 Advantage Windows GE workstations.

The extent of tumor vascularization at the histological level was analyzed in the Laboratory of Pathomorphology using expression of endothelial markers CD 31 and CD 34.

Embolization of tumor vessels originating from the ECA system was performed in 12 cases: 7 patients with angiofibromas, 2 patients with meningiomas, 1 patient with schwannoma, and 2 patients with rhabdomyosarcomas. Embolization of afferent vessels originating from the ICA is not used in routine practice due to a high risk of ischemic complications. To remove hypervascular CFTs, we also used blood-sparing techniques: isovolemic hemodilution, instrumental reinfusion of autorythrocyes, plasmapheresis of autologous plasma, and transfusion of donor blood components.

Statistical data processing was carried out by methods of descriptive statistics and correlation analysis using the Statistica 8 software package.

**Results**

**Juvenile craniofacial angiofibromas** are highly vascularized tumors present exclusively in males. Embolization of accessible afferent vessels is recommended before angiofibroma removal. In previously described series, preoperative embolization was performed in 83—100% of cases [5—7]. There are several topographic classifications of angiofibromas, but the U. Fisch’s classification [5, 6] is most relevant to the goals of our study. The study included 10 male patients with angiofibroma: 4 patients with Fisch stage 2, 5 patients with Fisch stage 3, and 1 patient with Fisch stage 4 tumors. The age of patients ranged from 12 to 37 years (mean age, 19.7 years; median age, 22.5 years).

SCT perfusion revealed very high normalized tumor blood flow and volume values. The main sources of blood supply to angiofibromas were the maxillary artery (MA), ascending pharyngeal artery (APA), ascending palatine arteries, and, in most cases, cavernous and petrosal seg-
ments of the internal carotid artery (ICA), as well as branches of the ophthalmic artery (OA). Given frequent involvement of the contralateral carotid arterial system, even in the case of lateralized tumors, direct angiography was always performed bilaterally. In 5 cases, patients with lateralized tumors underwent embolization of afferent vessels from the external carotid artery (ECA) system on the ipsilateral side, with one of the patients having MA embolization during previous treatment. In 4 cases, embolization of tumor afferent vessels was performed bilaterally. The high-resolution MRA data were consistent with the direct angiography data.

Sometimes, embolization of the MA was accompanied by an increase in blood supply from cavernous ICA sources. In these cases, major blood loss occurred during resection of the parasellar tumor portion. Other alternative sources may be the facial artery, superficial temporal artery (STA), and transverse facial artery. In the case of advanced tumors with Fisch stage 3 and Fisch stage 4, the ICAs, like the ECAs, were involved in feeding the tumor by afferent vessels from the OA, cavernous ICA (inferolateral trunk), and middle cerebral artery (MCA). In one case with the main tumor blood supply from the MMA and an additional blood supply from the ICA, embolization of the former artery was performed; after this, there was contrast enhancement of the deep temporal arteries and transcranial afferent vessels from the pterygopalatine MA, as well as an increase in contrast enhancement from the cavernous ICA (Fig. 3). Removal of the tumor was accompanied by intensive bleeding, probably due to an increased role of additional sources.

Meningiomas. A detailed angiographic examination was performed in 30 patients (20 females and 10 males aged 19—78 years (mean age, 52.7 years; median age, 54.5 years)) with craniofacial meningiomas. Histologically, meningiomas were meningotheliomatous or mixed in most cases (26), atypical in 3 cases, and anaplastic in one case. For convenience of analysis, all patients were divided into 5 topographic subgroups. According to the SCT perfusion data, high values of tumor blood flow and volume were detected in all cases.

In most patients with crani-orbital meningiomas (12), the ECA branches were the major source of blood supply. The afferent vessels were the orbital, frontal, and parietal branches of the middle meningeal artery (MMA), anterior and posterior deep temporal arteries (ADTA and PDTA, respectively), and branches of the pterygopalatine segment of the MA, often anastomosing with the cavernous ICA. In one case, there was a meningo-lacrimal type of orbit blood supply on the tumor side where the lacrimal artery was an extension of the orbit branch of the MMA and had no anastomoses with the OA. The ICA was involved in feeding the tumor by means of afferent vessels from the OA, cavernous ICA (inferolateral trunk), and middle cerebral artery (MCA). In one case with the main tumor blood supply from the MMA and an additional blood supply from the ICA, embolization of the former artery was performed; after this, there was contrast enhancement of the deep temporal arteries and transcranial afferent vessels from the pterygopalatine MA, as well as an increase in contrast enhancement from the cavernous ICA (Fig. 3). Removal of the tumor was accompanied by intensive bleeding, probably due to an increased role of additional sources.

Fig. 1. Distribution of patients by tumor histology.
Fig. 2. A 18-year-old male patient S. Diagnosis: juvenile craniofacial angiofibroma on the right
a — contrast-enhanced MRI in the axial projection; b — contrast-enhanced MRI in the frontal projection; c — according to SCT perfusion, the tumor is characterized by high values of blood flow; d — blood volume; e — direct angiography of the right CCA; f — the right ECA; in the lateral projection, afferent vessels from the MA (red arrows), petrous segment of the ICA (blue arrow), and APA (yellow arrow) are visualized

See continue of the Figure on the next page
In a group of patients with advanced craniofacial meningiomas (8 cases), the ECA system was also the dominant source of tumor blood supply in 5 patients. In 2 cases, equivalent blood supply from the ECA and ICA systems was found. The main afferent vessels from the ECA were the orbital, frontal, and parietal branches of the MMA, with hypertrophied anastomoses between the orbital branches of the MMA and the OA system being present in some cases. The blood supply also involved the hypertrophied ADTA and PDTA, APA, and also afferent vessels from the pterygopalatine MA via transcranial anastomotic branches to the cavernous ICA. Sources from the ICA included branches of the OA (including recurrent meningeal arteries) and cavernous segment as well as the MCA.

In patients with sphenoid wing meningiomas with extensive hyperostosis (6 cases), the major tumor blood supply was provided from the ICA in 2 cases, from the ECA in 2 cases, and equivalently from the ICA and ECA systems in 2 cases. The sources of tumor feeding from the ECA were the hypertrophied frontal and orbital branches of the MMA, extensively anastomosing with the OA system, cavernous branches of the ICA, and pterygopalatine segment of the MA, as well as the deep temporal arteries, accessory meningeal artery, and transcranial branches of the pterygopalatine MA anastomosing with the cavernous ICA. The ICA was involved in tumor feeding through the cavernous segment, meningeal branches of the OA, tentorial artery of Bernasconi-Cassinari, MCA, and anterior cerebral artery (ACA). One patient underwent preoperative embolization of tumor afferent vessels from the

Fig. 2. A 18-year-old male patient S. Diagnosis: juvenile craniofacial angiofibroma on the right (continued).

\(\text{g — direct angiography of the right CCA; h — right ICA in the lateral projection after embolization of the right MA, an increase in blood supply from the cavernous ICA (red arrows) and petrous (blue arrows) ICA is seen; i — angiography of the left CCA in the lateral projection before embolization of the MA; j — after embolization of the MA, there is a significant decrease in blood supply to the tumor (indicated by arrows).}\)
Fig. 3. A 62-year-old female patient S.
Diagnosis: hyperostotic cranio-orbital meningioma on the left. Contrast-enhanced MRI in the axial projection (a) and MRA in the frontal projection (b). MRA identified the afferent vessel from the MMA on the left (indicated by an arrow). SCT perfusion revealed high values of blood flow (c) and volume (d). Comparison of the data of direct angiography of the ECA before (e) and after (f) embolization of the MMA demonstrates an increase in contrast enhancement of the afferent vessels from the pterygopalatine MA (red arrow) and deep temporal arteries (blue arrow).

See continue of the Figure on the next page
MMA; after this, an increase in contrast enhancement of transcranial anastomoses between the MA and ICA was observed, but there was no increase in blood supply to the tumor from the cavernous branches.

In a group of patients with large meningiomas of the anterior cranial fossa with extracranial spread (3 cases), the dominant source of blood supply was the ICA system, namely the afferent vessels from the ethmoid arteries (EAs). Additional feeding was provided from the anterior meningeal and anterior cerebral arteries, anastomotic branches from the MMA system, as well as from terminal segment of the MA through the pterygopalatine arteries — in contrast to the transcranial anastomoses between the MA and the ICA in the previous groups. During removal of tumors, the primary task was to exclude the main afferent vessels from the EA on a hyperostotically altered matrix, which significantly reduced bleeding.

In the case of optic nerve meningioma (1 case), the main source of tumor feeding was the OA; additional blood feeding was provided from the infraorbital and meningeal arteries. The neoplasm was removed via the supraorbital approach, which enabled control of not only afferent vessels from the OA system but also anastomotic branches from the MMA.

In the case of meningiomas, MR angiography enabled identification of afferent vessels of different caliber and intratumoral anastomoses. In some cases, the technique was not less informative than direct angiography (Fig. 4). SCT angiography enabled visualization of afferent vessels only from the ECA system, in particular the MMA, which was probably associated with coincidence of the contrasting phase for distal feeding arteries from the ICA and that for tumor vessels. However, the technique enabled assessment of the topographic relation-

**Table 1. SCT perfusion-based distribution of tumors**

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>nTBF (mean)</th>
<th>nTBV (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High degree of perfusion</td>
<td>&gt;10</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Angiofibroma</td>
<td>43.29</td>
<td>30.44</td>
</tr>
<tr>
<td>Renal cell carcinoma metastasis</td>
<td>34.08</td>
<td>54.61</td>
</tr>
<tr>
<td>Olfactory neuroblastomas</td>
<td>12.47</td>
<td>11.94</td>
</tr>
<tr>
<td>Cranio-orbital meningiomas</td>
<td>11.41</td>
<td>10.04</td>
</tr>
<tr>
<td>Sphenoid wing meningiomas with extensive hyperostosis</td>
<td>10.4</td>
<td>10.45</td>
</tr>
<tr>
<td>Advanced craniofacial meningiomas</td>
<td>10.2</td>
<td>10.01</td>
</tr>
<tr>
<td>Middle degree of perfusion</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Malignant meningiomas</td>
<td>≥5</td>
<td>≥5</td>
</tr>
<tr>
<td>Anterior cranial fossa meningiomas with extracranial spread</td>
<td>9.27</td>
<td>7.98</td>
</tr>
<tr>
<td>Primary craniofacial cancer</td>
<td>2.28</td>
<td>2.43</td>
</tr>
<tr>
<td>Low degree of perfusion</td>
<td>&lt;5</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Breast cancer metastases</td>
<td>3.44</td>
<td>5.61</td>
</tr>
<tr>
<td>Neurofibromas and schwannomas</td>
<td>2.88</td>
<td>3.79</td>
</tr>
<tr>
<td>Sarcomas</td>
<td>1.16</td>
<td>1.58</td>
</tr>
<tr>
<td>Cavernous hemangiomas</td>
<td>0.63</td>
<td>0.98</td>
</tr>
</tbody>
</table>

**Table 2. Comparison of perfusion parameters and the expression level of endothelial markers in different tumors**

<table>
<thead>
<tr>
<th>Tumor</th>
<th>nTBF</th>
<th>nTBV</th>
<th>CD31/CD34</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiofibroma</td>
<td>32.80</td>
<td>19.62</td>
<td>++</td>
</tr>
<tr>
<td>Mixed meningioma</td>
<td>15.41</td>
<td>14.04</td>
<td>++</td>
</tr>
<tr>
<td>Olfactory neuroblastoma</td>
<td>14.28</td>
<td>13.41</td>
<td>++</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>8.76</td>
<td>10.32</td>
<td>+</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>7.61</td>
<td>6.91</td>
<td>++</td>
</tr>
<tr>
<td>Breast cancer metastases</td>
<td>3.44</td>
<td>5.61</td>
<td>+/++</td>
</tr>
<tr>
<td>Cavernous angioma</td>
<td>0.7</td>
<td>1.04</td>
<td>+++</td>
</tr>
</tbody>
</table>
ships between meningiomas and main intracranial vessels.

We analyzed perfusion data obtained for intra- and extracranial tumor components, depending on blood supply sources. Comparison of the distribution of perfusion parameters for tumors fed predominantly from the ECA and from all other vessels revealed no statistical differences. However, the parameters for the extracranial tumor components equally fed from the ICA and ECA or predominantly from the ICA were higher than the others in groups (U-test).

Primary craniofacial cancers. The study included 8 patients aged 35—68 years with cancers of the midline and lateral craniofacial localization.

According to the SCT perfusion data, high values of tumor blood flow and volume were detected in most

Fig. 4. A 50-year-old female patient A.
Diagnosis: cranio-orbital hyperostotic meningioma on the right. Contrast-enhanced MRI in the axial projection (a, b). MR angiography in the axial projection (c) revealed the tumor afferent vessel from the MMA (red arrow), anterior deep temporal artery (blue arrow), and hypertrophied recurrent meningeal branch of the OA (yellow arrow).

See continue of the Figure on the next page
cases. Exceptions were 2 cases of lacrimal gland adenocarcinoma where the values were low. Direct angiography revealed tumor afferent vessels from the OA, MMA, MA, APA, STA, and less often from the ACA and MCA. In this group, MRA revealed sources of tumor feeding from the ECA system, and SCT angiography enabled assessing the topographic relationships between the tumor and the main arteries, as well as the extracranial pathways of venous drainage. In previously operated patients who underwent MA ligation, hypertrophy of alternative blood supply sources, such as the APA and cavernous ICA, were detected.

In the case of lateral cranio-orbital tumors (lacrimal gland adenocarcinoma), the dominant source of blood supply was the ECA system, and the main sources of blood supply were coagulated at the surgical approach stage. The blood supply of midline tumors involved the ICA and ECA from the ipsilateral or both sides. Tumors were removed through open or transnasal endoscopic approaches, which was accompanied by significant bleeding.

Neurofibromas and schwannomas. The group consisted of 6 patients aged 32 to 65 years. Histologically, tumors were grade 1 and 3 schwannomas in 4 cases and grade 1 and 2 neurofibromas of the trigeminal nerve branches in 2 cases. All tumors were located predominantly extracranially (in the orbit, maxillary sinus, and pterygopalatine and infratemporal fossae), extending extradurally into the middle cranial fossa, which corresponded to type D (Samii classification), type A (Ramina classification), and type ME 1—3 (Kawase classification) [8—10].

In all cases, the blood supply was mainly from the ECA; rarely, additional sources were branches of the ICA. The main afferent vessels were the MA, APA, and OA (orbital tumors). Rarely, additional sources were branches of the cavernous and petrous ICA. According to the SCT perfusion data, the mean blood flow and vol-

---

**Fig. 4.** A 50-year-old female patient A (continued).

MR angiography in the frontal projection (d) identified the tumor afferent vessels from the MMA (red arrow), anterior deep temporal artery (blue arrow), and MCA (green arrow).

Diagnosis: cranio-orbital hyperostotic meningioma on the right. Contrast-enhanced MRI in the axial projection (a, b). MR angiography in the axial projection (c) revealed the tumor afferent from the MMA (red arrow), anterior deep temporal artery (blue arrow), and hypertrophied recurrent meningeal branch of the OA (yellow arrow). MR angiography in the frontal projection (d) identified the tumor afferent vessels from the MMA (red arrow), anterior deep temporal artery (blue arrow), and MCA (green arrow).
Fig. 5. A 65-year-old female patient V. Diagnosis: bilateral craniofacial neurofibromas. Contrast-enhanced MRI in the axial projection (a, b). The right orbitozygomatic approach; removal of an infratemporal fossa neurofibroma. The tumor (NF), soft tissues of the orbit (OR), and squama of the temporal bone (T/B) are indicated. Sequential coagulation of tumor afferent vessels from the maxillary (c) and ophthalmic (d) artery systems (indicated by arrows) was performed.
ume values were low (2.88 and 3.79, respectively), and there was no tumor’s own vasculature. In one case, the tumor blood flow and volume were significantly different from the mean values in the group (8.76 and 10.32, respectively); the tumor’s own vasculature originating from the MA system was revealed; the MA was embolized. During removal of tumors, feeding sources were sequentially excluded from the MA and OA systems (Fig. 5).

Hemangiomas. The group included patients with cranio-orbital cavernous (4 cases) and craniofacial capillary (1 case) hemangiomas. During SCT perfusion, cavernous angiomas demonstrated low mean values of tumor blood flow and volume (0.63 and 0.98, respectively). During their removal, small tumor afferent vessels from the OA system were sequentially coagulated, with preservation of distal non-anastomosing branches. Direct angiography in a patient with disseminated capillary hemangioma revealed multiple feeding sources from the ECA; after their embolization, the role of the ICA in tumor blood supply was significantly increased.

Sarcomas. The study included 6 patients with advanced craniofacial sarcomas, aged 10 to 63 years. Low values of tumor blood flow and volume were detected in sarcomas, but because of tumor spread, 5 patients underwent direct angiography. In 4 of these, there was no tumor’s own vasculature, and the main sources of tumor feeding were multiple small peripheral afferent vessels, mainly from the ECA. The role of the ICA in tumor feeding was more significant in patients who underwent MA ligation during previous treatment (3 cases). In 2 cases (rhabdomyosarcoma), important tumor afferent vessels from the MA and APA systems were identified; the latter were embolized.

In most cases, moderate diffuse bleeding, apparently due to involvement of multiple small peripheral afferent vessels in the blood supply, was intraoperatively observed.

Olfactory neuroblastomas. The study included 2 patients with Kadish stage C olfactory neuroblastoma (tumor spread beyond the sinonasal tract) [11, 12], one of whom was operated on earlier. SCT perfusion revealed high values of tumor blood flow and volume. According to direct selective angiography, the main sources of tumor feeding were the EAs; additional sources were anastomotic branches from the distal MA. During MRA, the afferent vessels from the ECA were better visualized than those from the ICA.

During tumor resection through the frontal sinus, the stroma was dissected in a horizontal plane to enable an approach to hypertrophied EAs, coagulation of which significantly decreased the intensity of bleeding.

Metastases. The sources of blood supply to metastatic craniofacial tumors can be afferent vessels both from the ICA and ECA system, which is most often associated with the primary site location. In a study by M.A. Stepanyan et al. [13], out of 163 patients with metastatic skull base tumors, 8 patients underwent embolization of tumor afferent vessels from the ECA system.

A group of patients with metastatic CFTs consisted of 2 patients with renal clear cell carcinoma metastases and one patient with breast cancer metastasis. According to the

---

**Fig. 6.** Distribution of normalized blood flow (nTBF) values in different tumors.
SCT perfusion data, the mean values of tumor blood flow and volume in patients with renal carcinoma metastases were 34.08 and 54.61, respectively, being among the highest values in this study; the parameters in the female patient with breast cancer metastasis were low, 3.44 and 5.61, respectively.

Previously, at another hospital, one of the patients with a midline craniofacial metastasis of renal carcinoma underwent bilateral ECA ligation due to intensive bleeding at an attempt of transnasal biopsy. Direct angiography revealed abundant tumor vasculature with blood supply from hypertrophied OA branches on both sides. The ECA was fed through collaterals from the vertebral arteries and retrogradely, but there were no tumor afferent vessels coming from the ECA. Resection of the tumor was accompanied by intense bleeding from hypertrophied EAs.

**Perfusion data and expression of endothelial markers**

Based on the mean values of normalized perfusion data, tumors were conditionally divided into three types: with a high (nTBF>10.0), medium (5.0<nTBF>10.0), and low (nTBF<5.0) perfusion degree (Table 1).

The distribution of mean normalized values of blood flow and volume in different tumors is shown in Figures 6 and 7.

The degree of tumor vascularization at the histological level was evaluated based on expression of endothelial markers CD31 and CD34 (Fig. 8). The results were evaluated using a semi-quantitative method. The intensity of staining (expression) was assessed as weak, moderate or high, which was quantitatively expressed as +, ++, and ++++, respectively. Comparison of perfusion parameters (nTBF and nTBV) and the expression level of endothelial markers are presented in Table 2.

A correlation analysis between SCT perfusion parameters and expression of endothelial markers revealed only a weak inverse relationship between the tumor blood volume (nTBV) and the intensity of marker accumulation k=−0.43. It is obvious that there is no clear correlation between functional and morphological parameters of tumor vascularization. In our opinion, this may be associated with the histobiological features of tumors, their angioarchitecture. In this case, the extent of blood supply to the tumor is determined not by the number of vascular elements, but by the features of their morphology.

**Discussion**

The issue of blood supply of advanced skull base tumors has been addressed in a number of works of domestic and foreign authors. Studies by A. Valavanis (1993), A. Gruber, P. Lasjaunias, and A. Berenstein (1983), and J. Pryor, J. Hirsch, and R. Hurst (2012) have described the blood supply features of hypervascular tumors, such as meningiomas, juvenile angiofibromas, capillary hemangiomas, etc. as well as presented the results of successful embolization of tumor afferent vessels in large series of patients. In Russia, this problem has been studied by S.R. Arustamyan (2002), D.V. Svistov (2008), E.M. Burtsev, I.Kh. Ryabkin, and others.
In most similar studies, the classification of material has been based on the topography of tumors. In this case, qualitative and quantitative parameters of tumor vascularization have been proved to largely depend not on the location but on the histological nature. There are reports of using SCT perfusion in the differential diagnosis of skull base tumors [14]. In this paper, the histological classification of clinical material was used.

According to our data, highly vascularized tumors included juvenile craniofacial angiofibromas, meningiomas, renal cell carcinoma metastases, olfactory neuroblastomas, and some types of carcinomas. Lacrimal gland adenocarcinomas, breast cancer metastases, and some sarcomas and schwannomas were characterized by a moderate degree of vascularization. Tumors with a low degree of blood supply included cavernous hemangiomas, most sarcomas, schwannomas, and neurofibromas, giant cell tumor, and leiomyoma. After embolization of accessible afferent vessels from the ECA system, the role of alternative sources from both the ECA and ICA increased. There were no complications of direct angiography and embolization of tumor afferent vessels.
In all cases, a full correlation between perfusion and direct angiography data was found. An analysis of the relationship between SCT perfusion data and expression of endothelial markers in histological samples (CD31/D34) revealed no significant correlation.

In the case of meningiomas and angiofibromas, MR angiography enabled identification of afferent vessels from the ECA and ICA systems, intratumoral anastomoses, and topographic relationship between the tumor and the main vessels. In some cases of advanced meningiomas, SCT angiography visualized afferent vessels from the ECA, in particular the MMA. In other cases, the techniques enabled highly accurate assessment of the topographic relationships between tumors and the main vessels. Direct selective angiography in the 2D perfusion mode was for the first time used in such a study, which provided a detailed picture of blood supply reorganization in tumors after embolization of their afferent vessels.

On the basis of obtained data, we developed an algorithm for preoperative angiographic examination of patients with CFTs. At the first stage, we recommend applying SCT perfusion. If there is evidence of a hypervascular nature of the tumor, direct selective angiography is necessary to evaluate the angioarchitecture and advisability of embolization. If meningioma is suspected, an alternative may be MRA that enables identification of the main sources of tumor feeding, including those suitable for embolization. In the case of low perfusion parameters, MRA is more preferable for assessing the topographic relationships between tumors and the main vessels of the craniofacial region. An alternative may be dynamic SCT-AG (Fig. 9).

**Conclusion**

The topographic location and developmental features of craniofacial tumors often underlie their blood supply from different arterial systems. One of the most important problems associated with resection of these tumors is intraoperative bleeding. In our opinion, preoperative comprehensive assessment of blood supply to CFTs is necessary for planning surgical treatment. In this case, stepwise diagnostics of both quantitative and qualitative characteristics of vascularization should be performed. The obtained data will provide the basis for making a decision on ways of intraoperative blood loss prevention, advisability of preoperative embolization, and need for applying blood-sparing techniques (autologous plasma preparation, autoreinfusion of blood) as well as on the algorithm for intraoperative tumor devascularization.

Authors declare no conflict of interest.
REFERENCES


Commentary

Craniofacial tumors are common skull base lesions with a varying degree of blood supply provided simultaneously from different arterial systems. Tumor resection is sometimes associated with significant intraoperative bleeding, which complicates differentiation of crucial structures as well as increases the duration and reduces the radicalness of surgery. Detailed angiographic evaluation in the planning of surgical treatment of craniofacial neoplasms is an extremely important stage because it provides information on the quantitative and qualitative characteristics of blood supply, main afferent vessels, and tumor’s own angioarchitecture. The obtained data are used to conclude on the use of procedures for blood loss prevention, e.g., preoperative embolization, autohemotransfusion, etc.

The authors performed SCT perfusion in combination with various angiographic techniques in a large series of patients with craniofacial tumors of various histological types. They developed a classification of tumors based on perfusion characteristics and described features of blood flow reorganization after embolization or ligation of accessible tumor afferent vessels. Several angiographic techniques were used for these types of tumors for the first time. The authors developed algorithms for preoperative evaluation of blood supply of craniofacial tumors based on native X-ray data. For the first time in similar studies, a correlation analysis of the tumor SCT perfusion data and the expression level of endothelial markers was performed, which enabled evaluation of the relationship between the functional and morphological parameters of blood supply.

It should be noted that the quantitative parameters of blood flow in the tumor were assessed only by SCT perfusion. In the future, it would be necessary to evaluate the capabilities of non-contrast MRI perfusion in this category of patients with subsequent comparison of the results.

The study is of great research and practical interest in the field of surgery of skull base tumors because it promotes development of the main concept — a high extent of resection with minimal functional deficit.

A.Kh. Bekyashev (Moscow, Russia)
A Malignant Peripheral Nerve Sheath Tumor Derived from the Auditory Nerve: a Case Report and a Literature Review

V.N. SHIMANSKIY, K.V. SHEVCHENKO, M.V. RYZHOVA, S.V. TANYASHIN, D.A. ODAMANOV, V.K. POSHATAEV

Burdenko Neurosurgical Institute, Moscow, Russia

We present a rare clinical case of a patient with a malignant peripheral nerve sheath tumor developed from the auditory nerve as well as a literature review, including 30 reported cases of this disease.

Keywords: malignant peripheral nerve sheath tumor, auditory nerve.

Abbreviations:
- MPNST — malignant peripheral nerve sheath tumor
- MRI — magnetic resonance imaging
- CT — computed tomography

Malignant peripheral nerve sheath tumor (MPNST) belongs to a rare and heterogeneous group of mesenchymal malignancies, which are considered as a sarcomatous process in most publications. This group of tumors accounts for 5—10% of all soft tissue sarcomas with an estimated incidence of 1 person per 1 million population per year [1—4].

The last revision of the WHO morphological classification defines two subtypes of malignant peripheral nerve sheath tumors: epithelioid MPNST and MPNST with perineural differentiation, which are believed to be sufficiently different in terms of clinical course. Other MPNST subtypes, such as Triton’s tumor, glandular MPNST, etc., which were previously considered as individual pathologies, are currently regarded as histological variants [5]. MPNST may develop either primarily from the cells of the peripheral nerve sheath, or due to malignantization of neurofibromas and schwannomas [3]. Most MPNSTs develop in soft tissue from the proximal part of the peripheral nerves of the upper and lower extremities and most commonly involve sciatic nerve, brachial plexus, and sacral plexus. Cranial nerves are the source of tumor growth in less than 5% of cases [3, 6, 7]. Intracranial MPNSTs typically involve facial and auditory nerves [2, 4].

The incidence of auditory nerve MPNST is 1 case as against 1041 cases of vestibular schwannoma [1]. Up to 50% of MPNSTs develop in patients with neurofibromatosis [8, 9].

It should be noted that there are only scarce literature data on intracranial MPNSTs, in particular on tumors derived from the acoustic-facial group of nerves. Most publications report case studies and only a few papers analyze series of observations [1, 4].

Type 1 neurofibromatosis (NF) and previous radiotherapy are the main risk factors for MPNST. Lifetime incidence of MPNST in patients with type 1 NF is 8—13% [10]. Most publications [8, 9] report cases of malignantization of benign neurofibromas or neuromas. The risk of vestibular schwannoma to MPNST transformation after radiotherapy is 1/500 to 1/2000 cases [11—13]. Several studies [4, 13—15] reported MPNST development without prior radiotherapy.

Differential diagnosis of MPNST includes neurinoma, paraganglioma, hemangioma, ependymoma, angiolipoma, solitary fibrous tumor, lymphoma, hemangiopericytoma, cavernoma, atypical or anaplastic meningioma, fibrosarcoma, synovial sarcoma, and melanoma.

MPNST metastasis occurs either in hematogenous way or with CSF flow [6].

Treatment of patients with this pathology primarily involves surgical resection of the tumor. The surgery is aimed at total resection, but it does not prevent recurrence. In most cases, radical removal fails due to infiltrative tumor growth. In this situation, radical resection would lead to severe disability or death. Surgical treatment should be supplemented by radiotherapy. The use of chemotherapy and its effectiveness is questioned by some specialists [1, 6].

The most recent research on MPNST reports the analysis of 24 cases of auditory nerve MPNSTs, which occurred without previous surgical and radiation therapy. [11] Sex distribution of patients was equivalent in the series of observations. The average age of patients at the time of diagnosis was 44 years, which was about 10 years lower than in patients with sporadic vestibular schwannomas [1, 16]. Clinical presentation of the disease included cochleovestibular syndrome along with facial palsy. Neuroimaging data included the following char-
characteristics: fuzzy tumor boundaries, edema of the brainstem, destructive cavities in the tumor [1].

The prognosis for patients with MPNST is extremely unfavorable. The median life expectancy since diagnosis is 3 months. The most important factors influencing treatment efficacy include total resection, radiotherapy, and female gender [17].

Case study

Patient K., 19 years old, was admitted to the Burdenko Neurosurgical Institute on 02.03.16 with complaints of dizziness, pain in the face and ear, weakness of the facial muscles, severe headache, nausea and vomiting, double vision, and face numbness.

The first symptoms, including severe lightning pain in the right ear and dizziness, occurred on 17.11.15 with underlying acute respiratory infection. Three days later, the patient also experienced severe headache with nausea, vomiting, and progressive impairment of hearing in her right ear. MRI of the brain was performed on 27.11.15 and showed changes in the right internal auditory canal.

Contrast-enhanced MRI of the brain on 02.12.15 showed the presence of intracanal tumor, spreading towards the cisterna magna and for this reason acoustic

Fig. 1. The dynamics of tumor proliferation as shown by MRI of the brain and spinal cord (the tumor is shown by arrows):

a — MRI on 27.11.2015, newly detected tumor; b — MRI on 13.01.2016, the tumor proliferates into the cerebellopontine cistern; c — MRI on 22.02.2016, the tumor proliferates to the brainstem and middle cerebellar peduncles accompanied by development of perifocal edema; d — MRI on 02.03.2016, the tumor compressed and infiltrates the brainstem, there is an intracanal tumor on the left.
neuroma was suspected. It was decided to follow-up the patient. However, the patient developed acute weakness of the facial muscles and increasing dizziness on 14.12.15. Unscheduled control MRI on 13.01.16 demonstrated almost twofold increase in extracanal portion of the tumor. Patient’s state significantly worsened during preparation for surgery, including increase in static and dynamic disturbances, increased severity of symptoms from the right cerebellopontine angle, development of bulbar disorders, and severe general cerebral symptoms. MRI of the brain on 22.02.16 showed progression of the extracanal portion of the tumors up to 3 cm. Glucocorticoid, analgesic, and antiemetic therapy resulted in stabilization of patient’s condition.

The patient was admitted to the Burdenko Neurosurgical Institute in grave condition. Clinical presentation of the disease included pronounced symptoms of involvement of the right cerebellopontine angle in the form of failure of the trigeminal, facial (paralysis of the facial muscles on the right), and acoustic (deafness) nerves, bulbar disorders, and right-sided hemiataxia. There were also severe cerebral symptoms, including headache, nausea, vomiting, and localized ear pain.

Given the rapid development of symptoms, malignant tumor was suspected. The patients underwent contrast-enhanced MRI of the brain and spinal cord at the day of admission (02.03.16). Disseminated process was...
detected with a new tumor in the left internal auditory canal and multiple foci of abnormal accumulation of contrast medium in the spinal meninges. The dynamics of primary tumor dissemination and metastasis are shown in Fig. 1 and 2.

Given the pathologic process dissemination and low Karnofsky score (40 points), we decided to carry out a palliative surgery, including extended decompression of the posterior cranial fossa from the sigmoid sinus to the middle of the left cerebellar hemisphere and craniovertebral junction, partial tumor resection, and expansive duraplasty.

The surgery was carried out on 04.03.16. The operation was conducted in the patient’s prone position on the operating table (“concord”). Midline hockey-stick-shaped incision of the skin and underlying soft tissue in the cervico-occipital area bending to the right was followed by skeletonization of the occipital bone and posterior arch of the first cervical vertebra. The occipital bone was resected above the right cerebellar hemisphere and to the middle of the left cerebellar hemisphere, the arch of the first cervical vertebra was resected. The dura mater was tense, it was opened above the craniovertebral junction and right cerebellar hemisphere. Displacement of the cerebellar hemisphere exposed a light gray structureless tumor at the cerebellopontine angle without clear boundaries with brain tissue and with a large number of vessels on its surface. Tumor resection was accompanied by intensive and difficult to control bleeding from the tumor stroma. There was no boundary between the tumor and brain tissue. Taking into account the aforementioned features of the tumor tissue, we decided to confine the operation to open biopsy. Expansive duraplasty was followed by wound suturing. The patient’s condition was temporarily stabilized. However, the symptoms began to progress a week later. Fig. 3 shown CT of the brain on the 6th day after the operation. Taking into account dissemination of the process and grave condition of the patient, radiotherapy was considered as inappropriate. The patient died on 10.04.16.

Thus, the time from onset of symptoms until tumor detection using MRI of the brain was 10 days, and the total duration of the disease until death was 136 days.

Morphological examination showed a malignant tumor with hemorrhage and necrosis. The tumor consisted of bipolar cells with long processes and polymorphic oval nuclei; the cells formed patchy alveolar structures. Mi-
Glio-fibroblast activity was observed in association with the tumor (Fig. 4). Immunohistochemical examination revealed positive expression of epithelial markers, cytokeratin AE1/3 (+++), and epithelial membrane antigen EMA (++), smooth muscle actin SMA (+++), and synaptophysin syn (+) in the tumor cells; expression of CD34 (+) in vascular endothelium. There was no expression of S100, glial fibrillary acidic protein GFAP, and common leukocyte antigen CD45 in tumor cells. There was also no expression of IN11 in tumor cells along with preserved antibody expression in vascular endothelium (Fig. 5). Labeling index of U-67 proliferative marker was more than 90% (Fig. 6). The differential diagnosis included atypical teratoma-rhabdoid tumor, epithelioid sarcoma, and epithelioid malignant peripheral nerve sheath tumor. Conclusion: considering patient’s age and nature of tumor growth and proliferation, immunohistochemical data are more consistent with the diagnosis of “epithelioid malignant peripheral nerve sheath tumor” (WHO grade IV). An autopsy was not carried out.

Discussion

MPNSTs are poorly explored due to the low incidence (MPNST of the acoustic and vestibular nerve are very rare) and extremely unfavorable outcome. The severity of symptoms at the early stages of the disease often facilitate diagnosis of the tumor, when it is small. The differential diagnosis, especially with acoustic neuroma, complicates surgery scheduling. At the time of surgery, patients have large tumors and signs of metastasis to the central nervous system. Surgical treatment at the early stages increases life expectancy by 1—3 years provided that the tumor was completely resected followed by radiation therapy. In the absence of surgical treatment, the patient dies on the average 3 months after the onset of the disease. The use of chemotherapy is currently a disputable issue.

Conclusion

MPNST derived from the VIII pair of cranial nerves is a rare tumor, which is very complicated in terms of surgical removal and subsequent adjuvant treatment. The absence of surgical treatment leads to death within a short time. Even total resection of the tumor does not prevent recurrence. Prognosis of the disease is unfavorable.

Authors declare no conflict of interest.
**Commentary**

MPNST is a quite rare tumor mainly derived from the nerve plexuses and nerve trunks. The main risk factors of MPNST development include malignization of benign neuromas or neurofibromas after radiotherapy and the presence of type 1 neurofibromatosis. Primary MPNSTs are extremely rare. Tumors of the trigeminal nerve and its branches rank first among intracranial MPNSTs. MPNSTs derived from the VIII pair of cranial nerves are extremely rare. The risk of malignant transformation of benign neuroma after radiotherapy is 0.05—0.2%. The world literature available for analysis reported only 30 cases of primary MPNSTs of the auditory nerve. For these reason, each patient should be examined and the pathology should be thoroughly studied. Differential diagnosis based on clinical and X-ray data is very broad, and since patients often visit a surgeon at advanced stages of the disease, surgical resection is sometimes an effective option and essential part of treatment. Maximum radical tumor resection followed by radiotherapy and chemotherapy can increase patient’s life expectancy. Surgical treatment should be as fast and aggressive as possible even in the case of small tumor and discordance between tumor size and severity of clinical symptoms. Resection enables verification of histological diagnosis and, therefore timely initiation of adjuvant treatment and guessing the prognosis.

*A.Kh. Bekyashev (Moscow, Russia)*
An Aneurysm of the Medial Posterior Choroidal Artery: a Case Report and a Literature Review

YU.A. GRIGORYAN*, A.R. SITNIKOV, A.V. TIMOSHENKOV, G.YU. GRIGORYAN

Medical Rehabilitation Center, Moscow, Russia

Introduction. Aneurysms of the medial posterior choroidal artery are very rare. To date, only 5 cases have been reported. The article presents a case of successful surgical treatment of an aneurysm of the medial posterior choroidal artery and a literature review.

Clinical case. A 57-year-old male was admitted to the Center 1 month after a massive subarachnoid hemorrhage. CT angiography revealed an aneurysm of the right posterior medial choroidal artery in the perimesencephalic cistern and resolved hemorrhage.

Treatment. The paramedian supracerebellar transtentorial approach to the lateral surface of the midbrain was used. The posterior cerebral artery was identified in the perimesencephalic cistern, and the medial posterior choroidal artery aneurysm was isolated and successfully clipped, with the parent artery being preserved. Postoperative CT and MRI scans revealed a small asymptomatic ischemic lesion in the tectal region on the right. The patient was discharged without any neurological symptoms 10 days after surgery.

Conclusion. Medial posterior choroidal artery aneurysms can be clipped using the paramedian supracerebellar transtentorial approach.

Keywords: medial posterior choroidal artery, aneurysm, supracerebellar transtentorial approach, mesencephalic infarction.

Case study

Patient P., 57 years old, was admitted on 18.05.16 with complaints of periodic headaches. It is known that sharp headache developed on 11.04.16 during a moderate physical load followed by repeated vomiting and dizziness. CT and CT angiography showed massive subarachnoid and mild intraventricular hemorrhage with moderate hydrocephalus in combination with aneurysmal dilation of the vessel in the projection of the parastemal segment of the right posterior cerebral artery (Fig. 1).

No neurological disorders were observed at admission. CT angiography on 19.05.16 showed complete regression of the subarachnoid hemorrhage and detected an aneurysm located in the right perimesencephalic cistern. MPCA branched from the PCA in the form of single trunk at the junction of P1 and P2 segments, enveloped the midbrain, being located posterior and medial to the PCA. BVR was projected above the PCA. Aneurysmal dilation of the MPCA was located in the posterior region of the perimesencephalic cistern and had a wide neck comparable to the diameter of the parent vessel.

Abbreviations

BVR — basal vein of Rosenthal
PCA — posterior cerebral artery
CT — computed tomography
CT angiography — computed tomography angiography
LPCA — lateral posterior choroidal artery
MPCA — medial posterior choroidal artery
MRI — magnetic resonance imaging
TC — tentorium cerebelli
PN — pathetic nerve

MPCA aneurysms are quite rare in international clinical practice and were diagnosed only in 5 cases [1—5]. LPCA aneurysms are more common and more than 20 cases have been reported in the literature so far [6—19].

In most cases, aneurysms of the posterior choroidal artery occur concomitantly with moyamoya disease and may present with intraventricular, parenchymal, and subarachnoid hemorrhages depending on the location in the cisternal and parenchymal-ventricular arterial segments. Aneurysms are excluded from blood flow using both endovascular method and various microsurgical approaches, including transcisternal and transventricular approaches, whose application is determined by aneurysm location with respect to CSF spaces [1—19].

The present report describes the case of the MPCA aneurysm located in the perimesencephalic cistern, which was clipped using supracerebellar paramedian approach.

© Group of authors, 2017

*e-mail: grig63@hotmail.com
which made the detected aneurysm similar to fusiform one. The neck of the aneurysm was 2 mm and the dome sized 4x3 mm was directed downwards and medially. The aneurysm was located at the site of MPCA branching in superior and posterior direction towards the midbrain (Fig. 2).

Right-sided paramedian suboccipital approach exposing the transverse sinus was carried out on 23.05.16 in patient’s sitting position. Base-to-sinus dura mater dissection was followed by arachnoid dissection along the upper surface of the cerebellar hemisphere toward the tentorial notch (Fig. 3a). Posterolateral surface of the midbrain and the trochlear nerve were identified and aneurysm was detected along the edge of the tentorial notch. The aneurysm was surrounded by dense yellow arachnoid adhesions and the lateral portion of the aneurysmal body was covered with the tentorium (Fig. 3b). Medial portion of the tentorium was coagulated with excision of a triangular flap for visualization and subsequent dissection of the aneurysm, which enabled wide opening of the mediolateral portion of the temporal lobe.

Posterior cerebral artery was isolated in the perimesencephalic cistern. Subsequent arachnoid dissection showed that the aneurysm originated from MPCA located on the lateral surface of the midbrain medial and posterior to the PCA. The aneurysm with thin walls and wide neck was located at the site where a branch bifurcated from the MPCA towards the midbrain (Fig. 3c). The arterial trunk and its branches were isolated together with the aneurysmal sac. However, clipping was accompanied by significant narrowing of the blood vessels due to the relatively wide aneurysmal neck. The aneurysm was excluded after several attempts using microclip with underlying temporary proximal clipping with minimal impact on the mesencephalic branch of the MPCA (Fig. 3d). Integrity of the dura mater was restored using continuous suture, bone flap was fixed, and the wound was closed in a standard way.

CT of the brain on the next day after surgery showed small ischemic changes in the right midbrain. Evaluation of neurological status found no additional neurological symptoms. CT angiography and MRI on 30.05.16 confirmed MPCA aneurysm exclusion from the bloodstream and the presence of asymptomatic ischemic lesion (12x12 mm) at the quadrigeminal plate (Fig. 4). No ocular motor disorders were observed throughout the hospital stay and the patient left the hospital on day 10 after surgery without neurological disorders.

Discussion

Both posterior choroidal arteries (MPCA, LPCA) branch from the PCA. MPCA bifurcates from the posteromedial surface of the proximal segment of the artery. MPCA branches from P1 segment of the PCA in 14.3% of cases; in 70% cases, artery branches in the form of a single vessel from the beginning of P2 segment and considerably more rarely it is a branch of the distal segment of the PCA. MPCA envelopes the lateral surface of the midbrain. It is located medial to the PCA, penetrates the quadrigeminal cistern, and then runs toward the epiphysis in somewhat anterior and lateral direction through the cistern of the velum interpositum, enters the vascular plexus of the third ventricle roof, reaches the foramen of Monroe along the choroidal fissure, and terminates in the vascular plexus of the lateral ventricle. MPCA is divided into cisternal and plexal segments, wherein cisternal segment includes the artery from the point of branching from the PCA to the posterior portion of the third ventricle roof. Plexal segment extends forward to the interventricular foramen, giving branches to the vascular plexuses of the third and lateral ventricles, as well as to the thalamus. The MPCA blood supply system, wherein the number of branches ranges from 16 to 34, includes the brain stem, tegmentum, lateral and medial geniculate bodies, the superior colliculus of the quadrigemina, pineal gland, medial and dorsal portions of the pulvinar. In

---

Fig. 1. CT (a) and CT angiography (b) scans of the patient P. with MPCA aneurysm (shown by arrow).
most cases (87%), LPCA originates from the posterior portions of P2 segment of the PCA in the form of two trunks and runs laterally through the pulvinar or around the superior surface of the thalamus, enters the temporal horn of the lateral ventricle through the choroidal fissure, and terminates in the vadicular plexus, where it anastomoses with terminal branches of the anterior choroidal artery and MPCA. Arterial branches are involved in the blood supply to the brain stem, posterior commissure, lateral geniculate body, crus and body of the fornix, pul-

**Fig. 2.** Three-dimensional CT angiography in a patient with MPCA aneurysm.
An — aneurysm.

**Fig. 3.** Intraoperative pictures of steps (a—d) of the paramedian supracerebellar transtentorial approach to MPCA aneurysm.
SCA — superior cerebellar artery.
vinar, superomedial nuclei of the thalamus, and caudate nucleus body [20—28].

In most of cases, MPCA and LPCA present with asymmetric intraventricular hemorrhage. Detection rate of subarachnoid-cisternal hemorrhage and parenchymal hemorrhage in the thalamus is much lower. This distribution of hemorrhage variants is due to more frequent localization of aneurysms of both posterior choroidal arteries in their distal portions, which topographically correspond to the intraventricular segments of the blood vessels near to the choroid plexus [1—19].

In the case of intraventricular aneurysms, precise identification of the parent artery sometimes becomes a challenge due to significant anastomosis of the terminal branches of the anterior and both posterior choroidal arteries in the vascular plexus of the lateral ventricle. Cerebral angiography shows intraventricular aneurysm, but aneurysmal sac contrasting, which may also occur through the collateral anastomotic pathways, significantly complicated identification of the parent artery [2, 15]. Thus, the case report by K. Ungersbock and A. Pemeczky [2] specifies that accurate attribution of an intraventricular aneurysm to one of the posterior choroidal arteries is impossible. Despite this uncertainty, the authors [12] specified MPCA aneurysm in the title of their publication.

Subarachnoid hemorrhages occur in the case of PCA aneurysm localization in the cisternal vascular segments. Massive cisternal hemorrhage was observed in the case reported in our article, which was due to location of MPCA aneurysm in the perimesencephalic cistern at the level of the distal portion of P2 segment of the PCA. T. Ohta et al. [3] described MPCA aneurysm with similar anatomical localization, wherein spontaneous hemorrhage was followed by blood detection in suprasellar cisterns and Sylvian fissures without involvement of the ventricular system. Superselective angiography with PCA microcatheterisation allowed the authors to differentiate arteries in the perimesencephalic cistern and identify aneurysm of the MPCA, branching from the PCA in the form of two separate trunks [3].

Evaluation of CT angiography may be complicated when identifying the vessels and attributing an aneurysm to a particular artery due to close adherence of the posterior cerebral artery, MPCA, and initial segments of the LPCA and BVR in the perimesencephalic cistern. In our case, interpretation of CT angiography results was also associated with some complications in differentiating the parent artery of the aneurysm. The proximity of the PCA and MPCA in the perimesencephalic cistern and overlap of aneurysm shadow with arteries in the biplanar images hindered reliable identification of the parent vessel, but the analysis of three-dimensional reformations confirmed that the aneurysm belonged to the cisternal segment of the MPCA.

The complexity of surgical treatment of the posterior choroidal artery aneurysms is due to their small size, deep location, and anatomical structural features. Intraventricular aneurysms, sometimes referred to as peripheral, often have no apparent neck and actually are fusiform aneurysms of the terminal segments of the choroidal arteries. It is difficult to evaluate the anatomical variations of the aneurysms of choroidal artery cisternal segments due to the scarcity of such cases, but in the present case, similarly to the case reported by T. Ohm et al. [3], the aneurysm had no apparent neck and involved MPCA trunk. These structural features may lead to occlusion of the posterior choroidal arteries and their branches resulting from microsurgical or endovascular aneurysm exclusion from blood flow.

There are scarce articles focusing on endovascular treatment of MPCA aneurysms and emphasizing the complexity this technique and the fact that selective exclusion of the aneurysm is impossible [3—5]. The narrow

![Fig. 4. CT (a) and MRI (b) after MPCA aneurysm clipping.](image-url)
lumen, brittle walls, and significant tortuosity of the posterior choroidal artery greatly restrict the use of endovascular surgical techniques, which in most cases resulted in aneurysm exclusion by means of parent artery occlusion [7, 13, 18, 19].

Location of the posterior choroidal artery aneurysm with respect to the cisternal and ventricular CSF spaces is a major factor determining the choice of surgical approach. In most cases, intraventricular LPCA and MPCA aneurysms were clipped through the ipsilateral or contralateral parieto-occipital interhemispheric transcortical approach. Opening of the ventricular cavity enables identification of the aneurysm based on posthemorrhagic changes in the ventricular wall at the site of choroid plexus attachment. Dissection of the parent vessel and its branches is an essential stage of aneurysm clipping, although selective occlusion of the aneurysm is not always possible due to its terminal location or fusiform structure. Transcortical approach is used much less frequently in the cases where hemorrhagic lesion is location lateral to the wall of the lateral ventricle. This endoscopically assisted surgical procedure using stereotactic navigation and tubular dilators can be initially aimed at elimination of intracerebral hemorrhage, while the subsequent inspection of ventricular walls and hematoma cavity enables identification and isolation of arterial vessels bearing the aneurysm [2, 6, 8—12, 14—17]

In the cases of aneurysm location in cisternal segments of the posterior choroidal artery, which are relatively rare, various approaches to the perimesencephalic cisterns and vessels located therein can be used [20—22, 24, 25]. Excision of fusiform MPCA aneurysm was carried out by H. Fukuda et al. [10] through the supratentorial suboccipital approach. T. Ohta et al. [3] excluded a MPCA aneurysm by proximal clipping of the artery through the pterional-zygomatic approach. In the case reported in our study, MPCA aneurysm was clipped through the paramedian supracerebellar transtentorial approach. This approach provides good visualization of the posterior cerebral artery, MPCA, and basal vein without traction of temporal and occipital lobes and with minimum caudal displacement of the cerebellum [20, 24, 25, 29—32].

Endovascular and microsurgical treatment of the posterior choroidal artery aneurysms is accompanied by various complications presenting with worsening of existing neurological deficits or the development of new pathological symptoms. Application of approaches associated with encephalotomy (transcortical) and brain tissue traction (hemispheric, infratemporal-occipital) may be accompanied by the development of specific symptoms of nervous system impairment. Other causes of worsening of neurological condition include ischemic disorders in the posterior choroidal artery system resulting from vasocostriction, compression of a thin-walled vessel by a clip placed on the aneurysm, and occlusion of arteries due to endovascular embolization. However, in most cases, microsurgical and endovascular treatment of patients with LPCA and MPCA aneurysms is successful without severe neurological consequences [1—19].

J. Neau and J. Bogousslavsky [33] described the infarction syndrome in the posterior choroidal artery system based on their own observations and literature data and noted significant prevalence of LPCA involvement. Homonymous quadrant hemianopsia, which may be accompanied by hemitropic sensitivity loss, aphasia, and memory disorders is the most common symptom of infarction in the LPCA supply area. Oculomotor disorders are the most common neurological manifestations of ischemic disorders in the MPCA system [33—35].

In the present study, no visual field defects and oculomotor disorders were detected after MPCA aneurysm clipping, but MRI detected a unilateral ischemic lesion of the quadrigemina. Impaired circulation in a relatively small MPCA blood supply area may be caused by both temporary clipping of the main arterial trunk and narrowing of its branch to the midbrain after final clamp repositioning. This neurologically asymptomatic development of midbrain injury is indicative of relatively good tolerability of the unilateral ischemia in the MPCA system due to the wide Anastomosis of the systems of the posterior choroidal arteries.

Authors declare no conflict of interest.


Received: 12.12.16
Aneurysms of the medial posterior choroidal artery (MPCA) is a quite rare pathology and therefore any new report on the issue is of great interest. The article reports a case of subarachnoid hemorrhage from the aneurysm of the cisternal segment of the MPCA and its successful microsurgical treatment using the supracerebellar transtentorial approach. The study is well illustrated with neuroimaging pictures and intraoperative photographs.

The discussion includes the analysis of literature data on the anatomical characteristics of the posterior choroidal artery, the problems of verification of the aneurysm parent vessel, methods of treatment (microsurgical and endovascular), and surgical approaches. The authors specified the role of three-dimensional reconstruction of spiral computed tomography angiography data in the identification of the hemorrhage source and choice of treatment.

The reported case is of particular interest because the patient had no symptoms of the moyamoya disease and arteriovenous malformation. This fact indicates the possibility of idiopathic genesis of aneurysms in patients not suffering from these diseases.

Aneurysms of the posterior choroidal artery are difficult to approach using both endovascular and microsurgical techniques due to the small diameter of the parent artery, as well as small size and structural features of aneurysms. Treatment of these aneurysms is associated with the risk of occlusion of the posterior choroidal artery. This complication is less dangerous in the case of distal localization of aneurysms in the plexal segment of the artery because of the pronounced network of collateral anastomoses with the branches of the anterior choroidal and lateral posterior choroidal arteries. When treating proximal aneurysms of the posterior choroidal arteries, it is important to preserved the parent artery to prevent the development of ischemic complications. In this regard, the surgical technique used by the authors is adequate: the aneurysm was excluded from the circulation, while preserving MPCA trunk. The formation of a small “clinically silent” focal ischemia in the projection of the right portion of the quadrigemina is likely to be associated with stenosis of a small branch of the MPCA trunk. Exclusion of the arterial trunk itself would lead to more severe ischemic lesions.

In our opinion, it is appropriate to conclude that the choice of treatment method preserving blood flow in the MPCA in the case of cisternal aneurysms location is of great importance.

A.S. Kheyreddin (Moscow, Russia)
Expansive Suboccipital Cranioplasty in Chiari-1 Malformation (a Case Report and Technical Notes)

A.E. KORSHUNOV, YU.V. KUSHEL

Burdenko Neurosurgical Institute, Moscow, Russia

In this case report, we describe the use of expansive suboccipital cranioplasty in Chiari-1 malformation. The technique improves the efficacy and safety of treatment for Chiari-1 malformation. The technique can be used as an adjunct treatment together with any variant of posterior fossa decompression, including duroplasty and extradural decompression.

Keywords: Chiari-1 malformation, expansive suboccipital cranioplasty.

The displacement of cerebellar tonsils through the foramen magnum accompanied by their wedge-shaped deformity, which often leads to impaired CSF circulation at the craniovertebral junction and syringomyelia, is referred to as Chiari-1 malformation (CM1). Typical clinical manifestations of AM1 include cephalalgia and myelopathy symptoms associated with syringomyelia; cerebellar disorders and symptoms of cranial nerve dysfunction are more rare. CM1 is managed using surgery aimed at normalization of CSF circulation at the craniovertebral junction. Posterior decompression of the craniovertebral junction is the most common treatment for CM1 [1], wherein resection of the squama occipitalis and the edge of the foramen magnum is carried out. The conventional variant of the operation includes bone decompression along with duroplasty, which ensures maximum efficacy of the operation but is associated with a high incidence of complications (pseudomeningocele, wound liquorrhea, meningitis) [2, 3]. Recent reports quite often describe the use of extradural technique of the posterior cranial fossa (PCF) decompression, where the risk of complications is minimal, but in some cases, surgery does not provide the desired effect, which necessitates reoperations [4]. Expansive cranioplasty technique [5, 6] was suggested in 1999 to improve surgical efficacy and safety of CM1 surgery. In this article, we describe our modification of this technique.

Case study

Complaints, clinical presentation, and the results of examination. Patient D, 16 years old, was examined in connection with complaints of persistent intensive disabling headache and cervico-occipital pain for 2 years. Additionally, patient’s relatives observed two attacks of generalized tonic seizures with loss of consciousness; EEG data did not confirm epilepsy. Ophthalmoscopy showed no signs of intracranial hypertension. MRI examination showed wedge-shaped deformity of the cerebellar tonsils and their displacement by 17 mm below the foramen magnum; no hydrocephalus, intracranial mass lesions, or syringomyelia was observed (Fig. 1a). The patient was diagnosed with Chiari-1 malformation and admitted to the hospital for surgical treatment. At admission, neurological status was characterized by spontaneous horizontal nystagmus; there were no other objective symptoms.

Surgical procedure. Patient’s head was fixed in the Mayfield head clamp under general anesthesia and the patient was moved to sitting position. Midline osteoplastic trepanation of the PCF was carried out using linear soft tissue incision followed by wide resection of the thickened and deformed edge of the foramen magnum, resection of the posterior semi-arc of the atlas (resection extent is shown in Fig. 3). Outer layer of the dura mater (DM) was dissected and tonsil tissue firmly pressed to the thinned inner layer was observed through the latter; dura mater remained tense. It was opened by Y-shaped incision preserving the arachnoid membrane. There were only a few microscopic defects in the arachnoid after dura mater opening and CSF filling the subarachnoid space leaked through these defects. The collagen matrix patch was sutured to the DM defect. TD suture was sealed with the Tachocomb plate and fibrin glue. Foramen magnum edge was resected on the free bone flap; flap thickness was reduced by grinding the inner bone plate at the area of all bone protrusions. The upper edge of the bone flap was fixed with silk ligatures, the lower edge was pulled out and fixed with two resorbable mini-plates so as to form an additional space in the caudal portion of the PCF. Soft tissue and skin were tightly sutured. Schematic representation of the operation is shown in Fig. 2.

The postoperative course. Postoperative period was uneventful, there were no complications. Computed tomography 12 hours after surgery confirmed the satisfactory position of the bone flap (Fig. 1b, c and Fig. 3). The patient was discharged home 36 hours after surgery and returned to her school studies a week later. She noted complete regression of headache and cervico-occipital pain at the control examination 3 months after the operation. There were no recurrent seizures after surgery. MRI

© A.E. Korshunov, Yu.V. Kushel, 2017

*e-mail: Akorsh@nsi.ru
**Fig. 1.** Preoperative and postoperative MRI and CT data.

a — preoperative MRI of the brain: wedge-shaped deformity of the cerebellar tonsils and their dislocation through the foramen magnum below C1 vertebral arch can be seen; b, c — CT of the brain 12 hours after the operation: it can be seen that the new bone flap position (indicated by yellow arrow) increased the diameter of the foramen magnum and the volume of the posterior cranial fossa; d — MRI 3 months after surgery: cerebellar tonsils occupy their normal position, the lumen of the large occipital cistern can be seen, and there are no signs of pseudomeningocele.

**Fig. 2.** Schematic representation of the result of the operation.

a — rear view and left-side view; b — sagittal slice (left-side view). 1 — parent bone (squama occipitalis; it is shown by dashed line in Fig. 2b); 2 — displaced bone flap; 3 — silk ligature fixing the upper edge of the bone flap; 4 — resorbable mini-plates, which firmly fix the lower edge of the bone flap in the new position (Fig. 2a shows fragments of mini-plates located beyond the bone flap indicated by dashed line.); 5 — collagen matrix flap used for duraplasty; 6 — silk ligature drawing dura mater to the bone flap.
of the brain 3 months after surgery (Fig. 1d) showed normal position of cerebellar tonsils, formed lumen of the large occipital cistern, and no signs of pseudomeningocele.

Discussion

PCF decompression is the most common method to treat CM1, where the squama occipitalis and the edge of the foramen magnum are resected [1] Conventional variant of the surgery includes duraplasty, which provides maximum effectiveness of the operation but is associated with high incidence of complications (pseudomeningocele, wound liquorrhea, meningitis) [2, 3]. Recent reports quite often describe the use of extradural technique of the posterior cranial fossa (PCF) decompression, where the risk of complications is minimal, but in some cases, surgery does not provide the desired effect, which necessitates reoperations [4]. This article describes an expansive PCF cranioplasty technique in operations for CM1 aimed at reducing the incidence of complications and ineffective interventions.

Background. Expansive cranioplasty (reconstruction) of the PCF was first described by H. Sacamoto et al. [5] in 1999 and it was successfully used by the author and other surgeons [6] in Japan to treat CM1, but it was not widely used abroad. H. Sacamoto’s method includes extensive osteoplastic trepanation of the PCF, flap bone fragmentation and remodeling followed by its fixation with silk. We modified the procedure developed by H. Sacamoto and for the first time present our version of this technique. Unlike the original technique, our variant includes less extensive dissection of soft tissues. Furthermore, only minimal reconfiguration of the bone flap is

Fig. 3. CT data 12 hours after surgery; 3D reconstruction.
a — bottom view; b — the view from within the skull cavity; c — rear and right-side view; d — rear and left-side view (bone flap is shown by dotted line).
required due to the use of mini-plates, while flap fixation is stronger and faster.

**Application scope.** Expansive cranioplasty of the PCF with rigid bone flap fixation is appropriate after any type of PCF decompression for CM1, including duraplasty and extradural decompression.

**Materials and equipment.** The described technique of PCF reconstruction in patients with CM1 requires mini-plates for rigid bone flap fixation and corresponding tools. The rest of the operating equipment and supplies are identical to those in conventional PCF decompression.

**Advantages of the method.** PCF reconstruction has the following advantages compared to conventional resection trepanation:

1) in the case of planned bone defect closure, its size is not so much limited and the surgeon can perform duraplasty in a more convenient way through a large bone window. This should improve the quality of DM suturing and reduce the risk of complications (CSF pseudomeningocele, meningitis);

2) bone flap provides support for hermetic sealing of the dura mater defect: Tachocomb used to seal DM is pressed against the DM suture, which should lead to reduced incidence of complications (liquorrhea, pseudomeningocele, meningitis);

3) rigidly fixed bone flap eliminates DM compression with soft tissue subjected to careful suturing, which is a common cause of ineffective surgery for CM1; this gives grounds to expect reduced rate of ineffective operations;

4) fixation and drawing of DM to the edge of fixedly placed bone flap moves the DM from the brain structures and facilitates reconstruction of the lumen of the large occipital cistern, which gives grounds to expect reduced rate of ineffective operations, especially when using extradural decompression (this maneuver was not used in the case reported herein).

Disadvantages of the described technique are as follows: operation cost increases due to the use of mini-plates and slight increase in the duration of the surgery. However, there are good grounds for believing that the total cost of treatment of CM1 patients does not increase (and even possibly decrease) due to lower incidence of complications and reoperations. This matter should be further studied.

**Conclusion**

We described the technique of expansive cranioplasty (reconstruction) of the posterior cranial fossa in patients with Chiari-1 malformation, which is aimed at increasing the efficacy and safety of surgery; this technique can be used as an adjunct treatment together with any type of posterior cranial fossa decompression, including duraplasty and extradural decompression.

**Authors declare no conflict of interest.**
Commentary

The article reports the case study and description of the surgical technique of expansive cranioplasty of the posterior cranial fossa (PCF) in patients with Chiari-1 malformation. The authors described in detail and exemplified by a case report the technical aspects of PCF reconstruction after the craniovertebral decompression and supplemented them with illustrations and results of neuroimaging. The discussion presents data on clinical manifestations of the disease, existing treatments, their advantages and disadvantages.

H. Sakamoto [1] et al. and other authors [2, 3] proposed technique aimed at PCF reconstruction to prevent prolapse of the cerebellum and formation of pseudomeningocele along with required increase in PCF volume. However, the proposed reconstruction techniques, such as formation of multicomponent bone flap, its rotation or shift to the level of the foramen magnum, defect closure with bone chips, etc., were unreasonably complicated from the technical viewpoint. The method modified by the authors greatly simplifies the technique. In addition to advantages of the technique described in the article, PCF reconstruction reduces postoperative pain caused by formation of adhesions between the soft tissue and dura mater containing a large amount of pain receptors [4].

The article provides a valid answer to the natural patients’ questions about currently available methods to reduce the risk of posterior decompression of the craniovertebral junction and the possibilities of avoiding postoperative cosmetic defects. I am grateful to the authors for the revived interest to the “reconstructive technique” of surgical treatment for Chiari-1 malformation and encourage its application.

A.A. Reutov (Moscow, Russia)

REFERENCES


A pineal cyst (PC) is a benign neoplasm in the pineal region, or more precisely, in the pineal body. Most cysts are incidental findings and are not associated with symptoms typical of patients seeking medical advice. Symptomatic cysts are discovered less often and, depending on the clinical picture, require different treatment approaches.

**Material and methods.** We analyzed the literature data about the clinical picture, diagnosis, and treatment of PCs for more than a century (1914—2016).

**Conclusion.** To date, there is no single approach for managing PC patients. The indications for surgical treatment of symptomatic PCs are still not fully defined. It remains unclear which PC cases should be followed-up, and how often control examinations should be performed. More research of PCs is needed to develop new approaches to treatment of PC patients.

**Keywords:** pineal cyst, epiphysis, surgical removal, headache, pineal region.

---

**General information on pineal cysts**

Pineal cyst (PC) is a benign neoplasm in the pineal region, or more precisely, in the pineal body [1—6]. Pineal cyst is a quite frequent finding in both adults and children [1—4]. The natural history of pineal cysts is poorly understood, but most authors report favorable prognosis [1—4]. PCs rarely change in size over time [1—5, 7]. Most cysts are incidental findings and are not associated with symptoms typical of patients seeking medical advice. However, some PCs can be symptomatic and cause headache, hydrocephalus, oculomotor disorders and even lead to sudden death [1—4, 7—33].

Increasing findings of PCs on neuroimaging scans, unclear clinical picture and the lack of optimal management of these tumors raises concerns over the issue of PCs.

**Material and methods**

We explored electronic medical and biological databases (Pubmed, Medline) using keywords “pineal cyst”, “pineal gland cyst”, “glial pineal cyst” to find papers over a 100-year period (1914—2016) on the clinical presentation, diagnosis and treatment of PCs. A total of 32 papers were found, which mainly present single case reports and small series of cases on surgical treatment of PCs (132 patients) and 42 papers containing data on diagnosis and clinical presentation in patients with PCs.

Summary of the published data and analysis on PCs are reviewed in 5 parts: 1) Epidemiology; 2) Morphology and etiopathogenesis; 3) Clinical symptoms; 4) Neuroimaging; 5) Treatment.

**Epidemiology**

MRI studies documented the prevalence of PCs to range between 1.5 to 10.8% [1—5, 34—37], although their prevalence in autopsy series was reported as being between 33 and 40% [35, 38]. The prevalence of PCs is higher in female than male patients (3:1), with an increased frequency at the age between 21 and 30 years [39]. An estimated 350 million people worldwide are affected by PCs and about 20% (70 million) among them may have large cysts and need surgical treatment [10].

**Morphology and etiopathogenesis**

The pineal body (pineal gland, epiphysis) is a small endocrine gland and is part of the epithalamus. Its name is derived from its shape, which is similar to that of a pinecone. The gland is typically reddish-gray in color and about 5 to 8 mm in size. The pineal gland’s histology consists mainly of pinealocytes surrounded by connective tissue. As the pineal gland can convert electrical photoreceptor signals from the retina into hormonal signals, it is considered to function as a “neuroendocrine transducer” in mammals [40]. The primary function of the pineal body is to produce the hormone melatonin by pinealocytes. The intensity of melatonin synthesis depends on light signals conveyed from the retina: melatonin secretion is stimulated by darkness and inhibited during light phase. Melatonin communicates information on the “time of day” and “time of year” and thus the pineal body is responsible for maintaining circadian rhythms [41]. Downregulation of melatonin production can impair the synthesis of gonadotropins, corticotropin, somatotropin, and thyrotropin. Cases of premature puberty [42, 43] and hypogonadism [44] associated with PCs were described.

Macroscopically, the capsule of pineal cysts was reported as transparent or yellow to dark-brown in the case of hemorrhages. Cystic contents contain watery, hemorrhagic fluid or coagulated blood, sometimes with high protein content. Histologically, PCs are composed of 3 distinct layers. The inner thin layer comprises fibrillar glial tissue sometimes containing hemosiderin, indicative...
of hemorrhage. A middle layer of pineal parenchymal tissue can contain calcium deposits. The outer layer is the thinnest layer composed of leptomeningeal tissue frequently containing Rosenthal fibers and granular bodies [5, 6, 10, 39, 45].

The precise etiology of PCs remains unclear. Several theories explaining PC pathogenesis have been suggested.

1. During brain development, the walls of the third ventricle proliferate giving rise to diverticulum — cavum pineale to form subsequently the pineal gland. Impairments during this process can cause incomplete obliteration of the cavum pineale and a cavity can be formed [10].

2. Some researchers believe that PCs can arise from ischemic degeneration of glial layer. Others have suggested that PCs result from necrotic pineal parenchyma; however, the cause of the necrosis is unclear [5, 45].

These hypotheses may account for the pathogenesis of smaller cysts which do not exceed 1 cm in diameter. Large PCs were first described by Campbell et al. in 1899. The mechanisms underlying the formation of larger and symptomatic cysts have yet to be elucidated.

3. Some researchers suggest that large PCs can result from the fusion of several smaller pineal cysts; however, this seems unlikely, since PCs do not increase their size, as shown in analysis of the natural PC history [2, 5].

4. Hemosiderin deposits in the tissues of PCs detected by microscopy after cyst resection can indicate that pineal cysts occur secondary to hemorrhage [2, 5, 8, 45—47].

5. P. Klein and L. Rubinstein [5, 39] suggest hormone-dependent nature for PC growth and development based on a higher prevalence of PCs in female patients, particularly during puberty, and an age-related decrease in incidence of cysts. A gender-related difference described in many papers is explained by the action of hormones involved in the menstrual cycle or gestation.

Clinical symptoms

The majority of PCs, about 80%, are small — less than 10 mm in diameter [10]. Such cysts are often asymptomatic. Larger cysts (>15 mm in diameter) can lead to neurologic symptoms. Symptomatic PCs are rare and thus reports have been rare. However, when symptoms do develop, clinical manifestations of PCs are tied to the location of the pineal gland adjacent to such deep cerebral structures, as the midbrain, the thalamus, internal veins and the vein of Galen. With the limited space within the pineal region, even an insignificant extra volume can lead to symptoms [1—4, 10—33].

Headache

According to the literature, headache is the most frequent neurological symptom in patients with PCs. It was revealed in 107 (81%) of 132 patients treated surgically. In some of these patients (26%) headache was the result of intracystic hemorrhage and hydrocephalus; in 35% — headache resulted from hydrocephalus without intracystic hemorrhage [5, 36, 45, 48—53]. C.L. Seifert et al. assessed the association between headache and PCs in a case—control study and revealed that headache occurred twice more frequently in patients with cysts compared to age-matched and sex-matched controls (51% versus 25%) and migraine (26%) was the most frequent presenting symptom in patients with cysts [53]. While there is a widespread belief that large PCs can lead to hydrocephalus with resultant headache some investigators suggest that the mechanisms producing headaches in patients with PCs are not always associated with mass effect. In support of this, many patients with PCs exhibiting compression of the quadrigeminal plate and narrowing of the Sylvian aqueduct as determined by MRI are asymptomatic. Since none of these patients had hydrocephalus and that size of PCs was not associated with symptoms in the study by Seifert et al., the investigators propose a possible role of abnormal melatonin production, rather than mass effect, to cause headaches [51, 52]. However, how much can PCs affect normal production and secretion of melatonin is still unclear [53]. Headache can also result from compression of deep cerebral veins by large PCs that leads to central venous hypertension, with clinical features resembling central venous thrombosis, which also manifests mainly as a headache. Narrowing of veins can raise venous pressure, consequently, leading to interstitial cerebral edema [54]. According to other studies [9, 11, 13], headache develops from blockage of the Sylvian aqueduct at the entry by PC (for example, in case of colloid cysts) or occurs secondary to intracystic hemorrhage.

Hemorrhage

The real frequency of hemorrhage in PCs is unknown. We analyzed published data on surgical treatment of patients with PCs and revealed that 32 (21%) patients had signs of intracystic hemorrhage on MRI [6, 27, 37, 70]. Symptomatic presentation of intracystic hemorrhage is relatively scarce. The dominating features are secondary symptoms resulting from hydrocephalus secondary to blockage or compression of the Sylvian aqueduct by a cyst [5, 13, 33, 34, 55, 56]. According to the researchers [57], the most frequent symptoms of apoplexy are acute severe headache, mainly in the frontal or occipital areas, or sudden exacerbation of chronic headaches often accompanied by oculomotor disorders. Headache was the most frequent symptom that made patients seek medical advice [24]. Other symptoms were nausea and vomiting (32%), loss of consciousness (32%), and oculomotor disorders (46%). The cause of hemorrhage in PCs is not clear. Hemorrhage may occur in patients under anticoagulant therapy [8, 33]. Other researchers [13] propose vascular malformation in cyst wall to be responsible for hemorrhage.
Oculomotor disorders

As the dorsal portions of the midbrain are compressed, the patients can present with Parinaud’s syndrome, which is characterized by paralysis of the gaze upward, retraction of the eyelids, absent response of the pupils to light but preserved reaction to convergence, and convergence-retraction nystagmus [1—4, 10—33]. Although Parinaud’s syndrome is an indication for surgical treatment of PCs [36, 45, 49, 55, 57—61], this symptom is quite rare in patients with symptomatic PCs: it was revealed only in 13 (9%) patients out of 132 in the analyzed material. Preoperative oculomotor disorders were detected in 53 (40%) patients and were mostly associated with different degrees of upward gaze paresis (less frequently — downward gaze paresis) and impaired focusing [7, 45, 55, 57, 62].

Hydrocephalus and intracranial hypertension

Large PCs can cause hydrocephalus secondary to compression or complete occlusion of the Sylvian aqueduct. Almost half (44%) of patients operated on for PCs had hydrocephalus, which was caused by intracystic hemorrhage in 33% of cases. In addition, the literature describes cases of syncope and sudden death associated with sudden blockage of the Sylvian aqueduct at the entry by a cyst [8, 9, 11—13].

Given symptom variation among patients with PCs, many researchers [6, 8, 45, 49, 53, 55—57, 60, 61] identify three types of clinical presentation of PCs with certain symptomatology:
1. paroxysmal headaches and gaze paresis;
2. chronic headache, gaze paresis, optic disc congestion, occlusive hydrocephalus;
3. hemorrhage in PCs with acute headache and occlusive hydrocephalus.

In some cases, PCs can cause non-specific symptoms, including seizures, vertigo, blurred vision, motor and sensation deficits, vomiting, ataxia, and memory impairment. Rare complications associated with PCs: secondary Parkinsonism [4] and aseptic meningitis caused by cyst rupture [62] have been reported.

Neuroimaging

Classic PCs appear as small, adequately circumscribed, unilocular masses within the pineal gland typically measuring less than 10 mm in diameter [10]. Cysts can range from 5 to 15 mm in many asymptomatic patients and can reach 45 mm in diameter in symptomatic cases [15, 37]. PCs either reside within or completely replace the pineal gland [16]. PCs typically do not exhibit compression of adjacent structures [17].

Computed tomography

On computed tomography (CT), PCs can appear as circular masses with a fine capsule. The contents of PCs are hypodense, with density similar to cerebrospinal fluid (CSF) [15, 45]. Regions of hyperdensity commonly reflect hemorrhage or capsule calcification [45]. Roughly 25—33% of PCs contain thin rim calcifications along cyst walls [18, 52]. The contents of PCs can be either homogeneous or heterogeneous and may have either a unilocular or polycystic appearance [19]. On contrast imaging, PCs exhibit contrast enhancement along cyst capsule [18]. Some small PCs are not clearly detectable on CT and require further MRI for confirmation [45]. Identification of PCs on CT is a challenge because of similar density of CSF and cystic contents.

Magnetic resonance imaging

On MRI, PCs are well-circumscribed cystic lesions with smooth margins [20, 63]. Signal intensity varies with cystic contents. Because cystic contents typically contain lipid material or protein, PCs usually have signal characteristics similar to CSF [18, 52]. Atypical configurations and imaging characteristics on MRI, most often — intracystic septations, are frequently observed [19].

On T1-weighted image, PCs appear hypointense to white matter and isointense or hyperintense with CSF [2]. About 55—60% of PCs were hyperintense relative to CSF in adjacent ventricles [18], which is mainly attributed to the lack of flow in cysts compared to the surrounding CSF, remnants of previous hemorrhage, or increased protein levels within the cystic contents [22]. The cyst wall (remnant pineal tissue) appears slightly hypointense or isointense relative to the adjacent brain [23]. On contrast imaging, roughly 60% of PCs show contrast enhancement [10] because of the lack of a blood-brain barrier in the cyst wall. The pineal tissue around the cyst is infiltrated by a contrast agent resulting in a hyperintense enhancement (<2 mm). Some authors [45, 55] reported an atypical nodular enhancement, which was more predominant posteriorly. Normally the center of the cyst does not enhance following administration of a contrast agent. However, if imaging is delayed 60 to 90 minutes after contrast agent administration, the PC enhances uniformly, including liquid components [7, 18, 64].

On T2-weighted image, PCs typically have a homogeneous appearance and are isointense or slightly hyperintense relative to CSF. The thickness of a cyst wall typically does not exceed 2 mm [15, 37, 63]. Mild increases in protein content are unlikely to alter the T2 scans in a meaningful way, and the increased signal intensity is likely due to stagnant cystic contents [15].

Although fluid-attenuated inversion recovery (FLAIR) sequences are adjusted to suppress CSF, enhancement of cystic fluids within PCs is not suppressed in the majority of cases. On FLAIR images, PCs typically appear slightly hyperintense with respect to CSF [21, 63].

In some cases, differential diagnosis between PCs and other pineal lesions, particularly, neoplastic lesions, is relatively difficult. PCs with histological proof have unique contrast enhancement and various internal appearance in 50—58% of cases [65]. Fast imaging employ-
ing steady-state acquisition (FIESTA) sequences of a high-resolution MRI can distinguish PCs from pineal tumors on scans of internal cyst features [14]. Based on MRI imaging features, D. Pastel et al. [14] identified four types of cysts from the internal structure: 1) homogeneous with fine walls; 2) polycystic with rough surface; 3) containing fine internal septations; 4) polycystic with fine internal septations.

Modern neuroimaging techniques, CT and MRI, in most cases can differentiate PCs from other pineal lesions. Differential diagnosis is mostly effective in discriminating PCs from: 1) pineal region tumors (pineocytoma); 2) arachnoid cyst; 3) epidermoid cyst.

**Treatment**

Microsurgical resection is the primary treatment for symptomatic PCs. Microsurgical removal of a symptomatic PC was first performed in 1914 by Pussep, a founder of Russian neurosurgery and head of the world’s first Department of Neurosurgery in St. Petersburg. Pussep used infratentorial supracerebellar approach developed by Krause in 1913. This approach is still most frequent one and was used to operate on 54% of the patients among the analyzed cases. This approach provides total and non-traumatic resection of a cyst and the best navigation of pineal region structures [5, 7, 45, 49, 55, 57, 60, 62].

Occipital transtentorial approach is the second surgical approach in frequency (32%) and provides complete resection of a cyst in 70% of cases. The complications associated with this approach were transient homonymous hemianopsia in 5 (18%) patients and convulsive syndrome in 1 patient from the analyzed material [7, 8].

In one case, transcoccal subchoroidal approach was applied, as the cyst spread far anteriorly to the third ventricle cavity [24].

Nowadays, minimally invasive surgical procedures are an alternative to open surgery: endoscopic transventricular resection and stereotactic cyst fenestration [67, 68]. These methods do not provide complete resection of a cyst and thus recurrent cyst can occur [7, 55, 60—71].

Endoscopic surgery in the analyzed material was only performed when hydrocephalus was present (11%) [7, 55, 72]. In all 9 cases, the operation did not lead to any complications; however, cyst remnants were detected on postoperative MRI in 3 patients [7, 55, 72], which subsequently can develop into a recurrent cyst [7, 55, 69—72]. The drawbacks of this treatment option are associated with thickened interthelial commissure, posterior parts of the cyst that are difficult to approach, capsule with abundant blood supply, small size of PCs, absence of hydrocephalus, and need to use neuronavigation for choosing an optimal trajectory in some cases [71].

F. Kreth et al. [69] noted a positive effect after surgery in only 8 of 14 patients, as well as several cases of recurrent cyst growth in the long-term postoperative follow-up [8, 69, 70].

Transient oculomotor dysfunctions of varying intensity are the most frequent manifestation associated with worsening of neurological symptoms in the early and long-term postoperative periods. A critical factor contributing to these disorders is the close association of cyst capsule with its adjacent commissura posterior, where the nerve fibers originating from the nuclei of Cajal and Darkshevich coordinating movements of the eyes are crossed. According to various data, postoperative oculomotor disorders take 7 days to 6 years to regress [7, 45, 55, 57, 62].

**Strategy of monitoring and indications for surgical treatment — questions without a definite answer**

The number of patients with incidental findings of PCs is growing steadily due to availability, accessibility, and affordability of MRI and continual advancement of neuroimaging techniques. The literature describes such patients as victims of modern imaging technology (VOMIT) [73]. The indications for surgical treatment of PCs have still not been formulated completely. Since the studies on PCs typically involve small groups with approximately 20 patients, it is unclear which PCs need follow-up in dynamics and how often control MRI should be performed.

Most patients with PCs remain asymptomatic and hence different opinions exist as to the advisability of long-term monitoring. Among 110 (72%) surveyed neurosurgeons, the majority preferred to monitor patients with PCs via clinical examinations and control MRI. Among these respondents, 8% monitored only the dynamics of clinical picture and 20% refused any follow-up [65]. For example, Marques and Rivero recommend control examinations in children in 1 and 3 years after diagnosis and end further monitoring for a stable cyst. In case of cyst growth, monitoring is continued and the patient is followed-up for another 3 years after when a cyst stabilizes its size. Since even PCs with an evident increase in size can remain asymptomatic, several authors [65, 74] recommend a follow-up examination in all adult patients at 12 months after diagnosis. This strategy also helps to discriminate a cyst from neoplasms. Patients above 60 years of age usually do not need monitoring since the size of cysts does not show any dynamics in none of the published studies.

Most patients with PCs need no surgical management. Occlusive hydrocephalus and Parinaud’s syndrome are the main indication criteria for surgery worldwide [65]. About 15% of the surveyed neurosurgeons operate on patients with non-specific symptoms: vertigo, tremor, nausea, vomiting, motor and sensation disorders, and episodes of syncope. Some authors believe that PCs can cause transient aqueductal obstruction with resultant paroxysmal headache or syncope, particularly at posture or activity changes (postural paroxysms of syncope) [8, 49].
These paroxysms are thought to be caused by forward flexion of head with resultant sudden aqueductal obstruction by a cyst and an acute increase in intracranial pressure. Current disputes concern whether PCs can cause headache without evident signs of compression of CSF duct pathways on MRI and CT. Headache is a most common reason forcing patients to seek medical advice. Headache can be the only symptom in clinical presentation associated with PCs. Most neurosurgeons do not attribute cephalic syndrome to cysts when there is no hydrocephalus [65]. In such cases, an examination by a neurologist who identifies the cause of headache and an assessment of life quality of a patient in the presence of headache, which is not alleviated with medications, are essential for further patient management. The literature contains only one paper showing successful experience of surgical treatment in 18 patients with PCs without ventriculomegaly and Parinaud’s syndrome presenting with headache [62]. Severe cephalic syndrome can also be caused by central venous hypertension. Some authors have recently revealed MRI biomarkers of central venous hypertension in patients with PCs without hydrocephalus [54]. The authors analyzed size of a cyst, grade of aqueductal stenosis and grade of compression of the quadrigeminal plate, the apparent diffusion coefficient (ADC) in deep and superficial cerebral structures. Interestingly, the proportion of space occupied by the cyst along the spleno-tectal distance (tectum-splenium-cyst ratio) and the thalamic and periventricular ADC indices were significant and correlated with severity of clinical picture.

Conclusion

In conclusion, consensus for the management of patients with PCs was only reached in case of surgery for patients with occlusive hydrocephalus and/or oculomotor disorders [1—3, 36, 45, 49, 55, 57—61]. No uniform management strategy for symptomatic patients with PCs without hydrocephalus and impaired functions of the midbrain has been developed so far. Probably, this is associated with unclear natural history of PCs: the origin of PCs, causes for cyst growth, the relationship of cysts with clinical symptoms in the absence of occlusive hydrocephalus and oculomotor disorders have not been defined. In addition, although not all neurosurgeons recommend surgical treatment of patients with non-specific complaints, the published data indicate efficacy of surgery in some cases [5, 45, 62, 67]. According to the questionnaire, only 48% of neurosurgeons noted a positive effect from surgery on PCs [65].

Subsequently, new approaches to treatment for PC patients with unclear indications for surgical treatment can be developed based on studies and monitoring. Therefore, further accumulation of case reports and analysis of more clinical data is needed.

Authors declare no conflict of interest.

REFERENCES
