Patients with infiltrative sphenopetroclival meningiomas, which propagate in orbit and infratemporal fossa, constitute a special group. Only a few such cases are described in the literature [5, 9, 19, 30, 38, 55]. Such tumors differ from “classical” sphenopetroclival meningiomas by their clinical-topographic features. For example, oculomotor disorders can be a symptom of lesions in the posterior cranial fossa, the cavernous sinus, or orbit. The surgical approach regarding tumors that spread into the orbit and infratemporal fossa also has its own characteristics. These result from the need to expand access in removing the tumor from the adjacent structures of the outer skull base. Therefore, we propose a grouping of such observations in a special category, and, relying on target diagnosis and treatment, call these tumors, which spread into the orbit, middle cranial fossa, infratemporal fossa, and region of the petroclival junction, orbitosphenopetroclival meningiomas (OSPCM). The term could not be found in the literature, but a characterization and analysis of our own data, cited below, justify, in our opinion, the allocation of a classification unit in this case. The widely distributed craniofacial and cranio-orbital meningiomas, meningiomas of the middle cranial fossa (meningiomas of the cavernous sinus and the wings of the sphenoid bone), and sphenopetroclival meningiomas are close to OSPCM in their topographical anatomical and clinical characteristics.

The term “orbitosphenopetroclival meningiomas” is used here for the first time. This explains the absence of publications in the literature on the topic. As this takes place, the number of papers devoted to topographically similar tumors is a reflection of the huge interest in the problem of treatment of common tumors of the skull base: first and foremost, cranio-orbital and sphenopetroclival meningiomas.

A. Cranio-orbital meningiomas

1. Original growth, histology, and epidemiology

Cranio-orbital meningiomas usually occur in the dura mater of the wing of the sphenoid bone. They grow intraosseously and cause significant hyperostosis of the rear and side walls, as well as the roof of the orbit, and the floor of the middle cranial fossa. This results in tumor invasion of the orbit region [56, 71]. There can also be optic nerve sheath meningiomas that spread into the cranial cavity, and meningiomas originating from orbital peristeum. Cranio-orbital meningiomas are subdivided into three groups: the lateral (46%), medial (44.4%), and common ones (9.6%) [3, 4]. Lateral hyperostotic meningiomas involve the superior and inferior orbital fissures, the base of the middle cranial fossa, as well as the infratemporal and pterygopalatine fossa. Medial hyperostotic cranio-orbital meningiomas affect the anterior clinoid process, the optic canal, the superior orbital fissure, and the ethmoid sinus. This type of tumor is characterized by visual disorders of varying severity. Common hyperostotic cranio-orbital meningiomas include the features of the lateral and medial ones.

Meningiomas of this localization constitute 9--16% of all intracranial meningiomas [44, 71]. Cranio-orbital meningiomas occur more frequently (up to 17 times more) in women [12, 58, 59, 63, 64]. The clinical manifestation of the disease occurs mainly at 40--50 years of age [65]. Histologically, most cranio-orbital meningiomas are of the first degree of malignancy according to the WHO classification [63]. Significant tumor infiltration of the dura mater, muscles of the infratemporal fossa, and mucosal tissues of the orbit have been histologically confirmed in all specimens of invasive meningiomas. In all cases, hyperostosis is tumor invasion: failure to remove the tumor is directly related to the risk of recurrence [1].

2. Clinical manifestations

Exophthalmos is the leading symptom in the majority of patients (55--93%) with cranio-orbital meningiomas; its appearance results from hyperostosis and tumor infiltration of the contents of the orbit and the cavernous sinus [11]. Besides, visual acuity is reduced in 45--77% of patients. This is frequently accompanied by the emergence of a defect in sight field. Fundoscopy has revealed atrophy of the optic nerve in 16--32% of patients and
swelling in 6–31%. Deformation of the temporomalar region (44%), retrobulbar headache (17–29%), oculomotor disturbances (6–11%), and ptosis (0–6%) are other common symptoms [59, 63–65]. Tearing, which is associated with outflow obstruction at the nasolacrimal canal of irritation or ciliary ganglion, chemosis, and trophic disorders appear with an increase in the size of the intraorbital tumor.

The analysis of the symptoms that accompany the tumors affecting the bone base of the middle cranial fossa shows that the most pronounced clinical symptoms of tumor penetration into the narrow bony space, optic canal, the superior and inferior orbital fissures, the round or oval foramina, etc. manifest as a visual impairment, ocular motor disorders, and dysfunctions of the trigeminal nerve. The symptoms appear very early and more significantly if the tumor has failed to destroy the bone skull base, and, especially, if it has not produced in them any hyperostotic changes around the respective orifices and channels, which are most characteristic of meningiomas [2]. One can select the groups of clinical symptoms which are characteristic of lesions in the corresponding anatomical regions. Hence, propagation of the tumor in the ethmoid sinus or frontal sinus, except for anosmia, may result in difficulty in nasal breathing, emergence of discharge from the nose, and nose deformity. With propagation of the tumors in the rear cells of the ethmoid sinus (the bones of which are involved in the formation of the channel walls of the optic nerves), reduced vision is possible. Under propagation of the tumor in the nasopharynx, a changed in voice and nasal tone or twang ensue, and difficulties in swallowing and pain can be observed. In the case of propagation of meningioma into the nasal cavity, otolaryngologists can observe it as a pale-pink semicircular bulging of thick consistency in the upper parts of the nose, covered with normal mucosa.

With propagation of the tumor into the orbit through its medial wall (which is formed by the frontal process of the maxilla, the lacrimal bone, orbital plate of the ethmoid bone, and the body of the sphenoid bone), the disease manifests itself in exophthalmos, impaired eye movement, reduced vision, and various pain syndromes. The neoplasms of the medial regions of the middle cranial fossa, grown into the orbit, can exhibit almost identical clinical manifestations. The topography of the process is determined by computed tomography. The most probable area of original growth of the tumor can be determined relying on the dynamics of the appearing symptoms. Hence, intraorbital tumors usually debut sufficiently rapidly (even if the volume of the neoplasms is small) with clinical features of surrounding lesions of the orbit, while in case of intracranial distributed tumors, lesions of the cavernous sinus and middle medial fossa appear. In tumors emanating from inside the cavernous sinus, exophthalmos may appear later than other symptoms, following the appearance of intraorbital invasion. In middle-cranial fossa meningioma affecting the round orifice, the maxillary nerve (the second branch of the trigeminal nerve) is affected. In the propagation of the tumor into the region of the foramen oval, the mandibular nerve (the third branch of the trigeminal nerve) is affected; this manifests in impaired sensation in the lower jaw and hypotrophy of the chewing muscles. The clinical presentation of lesions in the infratemporal fossa at advanced stages of the disease manifests itself in face deformation, jaw joint blockage of various severity, and impaired sensation in the area of the second and third branches of the trigeminal nerve. These can come together with conductive hearing loss, which occurs due to the compression of the cartilaginous portion of the Eustachian tube in the infratemporal fossa, and a disruption of taste on the anterior two-thirds of the tongue due to the impact on the tympani, extending to the infratemporal fossa.

3. Surgical treatment

The aim of surgical treatment is to perform the maximum tumor resection with decompression of the optic nerve and tumor resection of the tumor-affected bone (hyperostosis or thinning due to destruction). According to P. Saeed et al. [58], the goal is to restore visual acuity and reduce exophthalmos, but not perform radical resection of the tumor. As a rule, removal of cranio-orbital meningiomas is performed through the frontotemporal, simple pterional, or orbitozygomatic approaches [18–20]. V. Lund et al. [37] have reported on the effective application of endonasal decompression of the medial wall of the orbit in 12 patients and decompression in 8 patients with opticopathy and reduced visual acuity due to cranioorbital meningioma.

4. Results of surgical treatment

Resection of cranio-orbital meningioma reduces exophthalmos in the early postoperative period in 77–96% of patients [56, 58, 64, 65, 71]. However, other experts, relying on MRI data, have shown that significant exophthalmos remains after surgery in 53% of patients [64]. Prolonged dysfunction of the venous outflow and fibrosis, leading to lesser mobility of the orbit contents, could be the culprit here [58]. Visual acuity can be improved after surgery in 30–80% of patients; however, up to 9% of patients exhibit a permanent postoperative decrease in visual acuity. A study by P. Saeed et al. [58] showed stabilization or improvement in visual acuity for 2 or fewer lines in the Snellen chart in 40 (61%) patients; 15 of them had a visual acuity of 0.8 or higher and 3 patients suffered preoperative amaurosis on the affected side. Visual acuity improved in 20 (30%) patients; for more than 4 lines and more than 2 lines in the Snellen chart in 8 and 12 of the patients, respectively. However, in 6 (9%) cases, visual acuity dropped. In 16 (84%) out of 19 patients who voiced preoperative complaints regarding the retrobulbar pain, the pain disappeared after surgery. U. Schick [65] reported postoperative improvement in 12 (30.8%) out of 39
patients with poor visual acuity and improvement, according to the perimetry data, in 10 (35.7%) out of 28 patients with the visual field defect. However, in 2 (2.6%) patients, a decrease in visual acuity was observed in the postoperative period, including blindness in 1 patient with originally low acuity.

5. Complications

At the moment, mortality under surgical treatment of cranio-orbital meningiomas is close to zero. However, postoperative complications, such as blurred vision and transient (6–49%) or resistant dysfunction of cranial nerves (7–18%), are still common [12, 26, 52, 56, 58, 66]. U. Schick (2009) published the results of surgical treatment of 77 patients with cranio-orbital meningiomas. Mild and severe postoperative complications emerged in 14.3% and 4% of the patients, respectively. One patient developed a brain abscess, 8 (10.4%) had postoperative liquorhea, which healed after lumbar drainage. In 3 (3.9%) patients, epileptic seizures were observed during the first weeks after surgery. In 4 (5.2%) patients, after separating the upper rectus muscle and the muscle lifting the eyelid, transient diplopia was discovered. Among the neurological complications, there was a single (1.3%) case of oculomotor paresis, a case of abducens nerve palsy, one case of trigeminal neuralgia in the innervation area of the second branch, and 3 (3.9%) cases of hypoesthesia in the innervation area of the third branch of the trigeminal nerve. Two (2.6%) patients showed severe postoperative complications in the form of aphasia and hemiparesis [65]. A similar frequency of onset of complications was observed in the study by P. Saeed et al. [58]. Accumulation of cerebrospinal fluid under the aponeurosis was observed in 5 (7.6%) out of 66 patients who had undergone resection of cranio-orbital meningiomas; in one case a revision and lumbar shunting were required. Transient ophthalmoparesis was observed in 2 patients who had undergone resection of the lateral orbital wall. Postoperative diplopia occurred in 40 patients; it was either transient or permanent in 32 (48.5%) and 8 (12.1%) cases, respectively. Stable dysfunction of cranial nerves in the form of oculomotor nerve palsy was observed in 6 (9%) patients. Two patients exhibited palsy of the sixth and fourth cranial nerves; palsy of the trigeminal and facial nerves were observed in 6 (9%) and 3 (4.5%) cases, respectively. S. Oya et al. [52] mentioned in their study such complications as hypoesthesia (resulting from the dysfunction of the trigeminal nerve) in 9 (23%) patients; oculomotor nerve palsy and seizures, in 3 (7.7%) and 2 (5.1%) cases, respectively.

6. Radicability of resection, frequency of relapses

The radicality and clinical effect of surgery are the main criteria in assessing the effectiveness of a surgical treatment of skull base tumors. The radicality of the removal of infiltrative meningiomas of the skull base is evaluated by the criteria established in basal surgery [64]. Total resection means the complete removal of the tumor; only infiltration of the cavernous sinus and the clinched process remain. Postoperative remnants of the tumor can be detected by neither CT scanning nor MRI. Under subtotal resection, small fragments of the tumor that infiltrate the main vessels, cavernous sinus, the optic nerve sheath in the channels and the orbit, and oculomotor nerves are detected. These remnants of the tumor are observed in control radiological studies. Macroscopic tumor fragments in partial tumor resection can be visualized using X-ray contrast methods in the postoperative period.

The relapse frequency of cranio-orbital meningiomas after surgical treatment is 14–39% [52, 56, 58, 65], or 8–25%, according to other sources [19, 20]. The reason behind such a high frequency is the fact that total resection of the tumor in the area of the functioning anatomical structures of the orbit, in the cavernous sinus, and near the cranial nerves and blood vessels appears impossible. The infiltration by the tumor of the superior orbital fissure also often makes it impossible to perform a total resection of oculomotor nerves leaving their functioning intact [71]. Thus, a residual tumor in many patients remains after surgery to remedy cranio-orbital meningioma. According to P. Saeed et al. [59], total resection has been possible only in five (7.6%) out of 66 patients. Fifteen out of 61 patients with residual tumor underwent radiotherapy after surgery. A relapse was observed in 11 (17%) patients. The median time between the surgery and the recurrence was 46 months (10–108 months). The relapse in 4 patients was accompanied by a decrease in visual acuity and an increase in exophthalmos, while just a slight (<3 mm) rise in exophthalmos was observed in the other four patients. S. Oya et al. [52] reported on total tumor resection, near-total resection, and subtotal resection in 15, 20 (51.3%), and 4 (10.3%) out of 39 patients, respectively. A relapse was observed in 7 (17.9%) patients within 40.7 months (on average) after the surgery. Total resection of the tumor was performed by S. Honig et al. [26] in 10 out of 30 cases. Eight patients underwent a course of adjuvant radiotherapy. Another eight (26.7%) patients relapsed. In the study by U. Schick et al. [65], total resection of the tumor was performed in 42 (54.5%) patients. The remaining 35 (45.5%) patients underwent subtotal resection; tumor fragments were left in the orbit and the cavernous sinus in 8 and 12 cases, respectively. Infiltration of the superior orbital fissure and extensive infiltration of the skull base were observed in 12 and 3 patients, respectively. Nine patients underwent a course of adjuvant stereotactic conformal radiotherapy. Ten (13%) patients had a tumor relapse. P. Scarone et al. [64] performed total tumor resection (Simpson grade II) in 27 (90%) out of 30 cases. The remaining 3 patients underwent subtotal resection. The radicality of the resection was limited by the fact that the tumor had invaded the dura mater at the level of the superior orbital fissure, infiltrated the orbital tissues, and invaded the
cavernous sinus in 17 (57%), 4 (13%), and 2 (7%) patients, respectively. In the study by F. Ringel et al. [56], total tumor resection was performed in 15 (24%) out of 63 patients. MRI data showed no continued tumor growth after subtotal resection in 4.5 years of follow-up in 29 (61%) out of 48 patients.

Cranio-orbital meningiomas often cause hyperostotic changes in the bone, which are determined by tumor invasion [23]. The need for the resection of hyperostosis renders radical resection a more difficult task [5]. Radical resection without a high risk of complications seems possible in less than half of the patients with cranio-orbital meningiomas. Meanwhile, the development of transient or persistent neurological disorders is observed in a significant number of cases. In this regard, some authors [56] believe that the appropriateness of surgical intervention should be determined by the clinical manifestations of the disease in the patient, and it should be primarily directed towards optic nerve decompression (in the case of reduced vision) and the elimination of exophthalmos.

B. Sphenopetroclival Meningiomas

1. Sources of growth, histology, epidemiology

Sphenopetroclival meningiomas are meningiomas which locate in the area of the petroclival junction and exhibit parasellar and endosellar propagation [82]. Due to its rarity, this type of meningioma is usually not classified separately but lumped with petroclival meningiomas.

Petroclival meningiomas, similar to the meningiomas of other areas, are observed in women and men at a ratio of 3:1 [32]. The average age of manifestation is the middle of the fourth decade [75]. The study by T. Kawase et al. [29] describes the results of treatment of 10 patients with sphenopetroclival meningiomas; the average age of the patients was 55 years; the male to female ratio was 1:4.

The published articles focused on surgical treatment of petroclival meningiomas usually indicate only the degree of malignancy of meningiomas according to the WHO classification, and rarely do they provide information on the prevalence of various histotypes. In the study by S. Nishimura et al. [50], meningotheliomatous meningioma was the most common histological type of meningioma in the clivus and top of the pyramid (16 cases). Fibroblastic, angiomatous (one with signs of atypia), and mixed types were also observed in 3, 2, and 3 cases, respectively. A. Spallone et al. [72] described fibroblastic, endotheliomatous, and transitional meningiomas in 12, 13, and 6 cases, respectively. According to the dissertation by V.N. Szymansky titled “Meningiomas of posterior or skull base fossa: clinical presentation, diagnosis and surgical treatment,” all petroclival meningiomas (130 observations) belong to the group of benign meningiomas (Grade I) [6]. Yet, data from the literature [13, 75] lead us to conclude that the majority of petroclival meningiomas are of malignancy degree I according to the WHO classification, while anaplastic and atypical meningiomas occur in rare cases.

2. Clinical manifestations

These tumors are characterized by slow growth and may remain undetected for a long time. Sphenopetroclival meningioma in most patients manifests in headache, cerebellar disorders (69–87%), and dysfunction of cranial nerves (90–95%). Among other cranial nerves, the trigeminal nerve is the most commonly affected (43–68%): its damage manifests in facial hypoesthesia and weakness of the chewing muscles or trigeminal neuralgia, which in some cases occurs on the contralateral side. Vestibular-cochlear (31–75%) and the facial (11–67%) cranial nerves are also frequently affected. Bulbar symptoms appear under caudal growth or large tumor size. Bulbar disorders are observed in 7–38% of cases: they are less frequent in patients with dysfunction of oculomotor nerves (VI – in 11–77% ; IV – in 14–26%; and III – in 11–38% of cases), despite the proximity and mandatory inclusion of these nerves in the tumor. Symptoms of cerebellar lesions caused by its compression are observed in 69–87% of cases. Most patients exhibit cerebellar dysfunction in the form of disturbance of statics and coordination and symptoms of increased intracranial pressure. Brain stem compression manifests itself in signs of impaired corticospinal tracts in the form of spastic paraparesis in 8–38% of patients (ipsilateral paraparesis results from the dislocation and compression of the opposite pedicle of the brain stem with the free edge of the tentorium or foramen magnum, or with contralateral paraparesis) and somatosensory disorders in 3–31% of patients. The impaired vision caused by lesions in the optic nerve is also observed (2–33%). Edema of the optic nerve disc (usually mild) is observed in most cases (77%). Nausea, vomiting, mental disorders caused by intracranial hypertension (which can result from the mass effect of the tumor), and obstructive hydrocephalus also appear in patients [13, 27, 36, 46, 67, 72]. Occlusive hydrocephalus, oral-brainstem symptoms, ipsilateral lesions of the cranial nerves develop early at the rostral location of the tumor, while cerebellar symptoms emerge later.

3. Surgical treatment

The aim of surgical intervention is to reduce the tumor size and eliminate the compression on the brain stem. Sphenopetroclival meningiomas are located deep in a field with a complex anatomy, surrounded by multiple important neural and vascular structures, and they have an infra- and supratentorial localization. These anatomical features make surgical treatment of these tumors very challenging. The orbitozygomatic approach can be used to remove sphenopetroclival meningiomas [61]. T. Kawase et al. [29] have proposed using the anterior transpetrosal-transtentorial approach, which consists in standard access to the middle cranial fossa in combination with resection of the anterior part of the pyramid.
The removal of sphenopetroclival meningioma can also be performed in two steps using different combinations of the infra- and supratentorial approaches [60, 67]. Suboccipital retrosigmoid and transpetrosal accesses are among the most widely employed ones in surgical access to these tumors [13, 21, 36, 57, 62]; each one has its own advantages and disadvantages.

4. Results of surgical treatment

Complications

Despite the progress achieved in surgical techniques, the frequency of postoperative complications in the surgical treatment of petroclival meningiomas remains relatively high. First, there is the dysfunction of cranial nerves, which is transient in 41% of cases and resistant in 20–32% of cases. Second, dysfunction of cranial nerves of the oculomotor group was observed in 9–17% of patients [36, 45, 46, 67]. T. Kawase et al. [29] published the results of the surgical treatment of 10 patients with sphenopetroclival meningiomas. The postoperative period was satisfactory in 8 patients; however, there was a case of postoperative liquor rhoea and one case of hydrocephalus. Five patients developed paresis, while dysfunction of the nerves of the oculomotor group, paresis of the facial nerve, and a new persistent neurological deficit emerged in 5, 1, and 8 cases, respectively.

The study by J. Yang et al. [81] provides data on the results of surgical treatment of 25 patients with large and giant petroclival meningiomas. Seventeen of them were characterized by parasellar spread. The postoperative complications included a new rise in neurological deficit (that existed before the surgery) in 16 (64%) patients; in particular, palsy of the oculomotor nerve, dysfunction of the trigeminal nerve, abducens paresis, bulbar paresis, transient aphasia, and hemiplegia in 11 (44%), 10 (40%), 8 (32%), 2 (8%), 5, (20%) and 5 (20%) patients, respectively. The hemiplegia was transient in 3 cases. Six (24%) patients exhibited the formation of subgaleal hematoma and intracranial hypertension resulting from excessive traction of the temporal lobe. Meningitis and transient liquor rhoea developed in 3 (12%) and 1 patients, respectively.

In the surgical treatment of large petroclival meningiomas (> 3 cm in diameter), Yamakami I. et al. [80] observed the emergence of a new resistant dysfunction of cranial nerves in 7 (35%) out of 20 patients: the oculomotor, trochlear, abducens, and facial nerves in 2 (10%), 5 (25%), 2 (10%), and 3 (15%) patients, respectively. Other persistent neurological deficits occurred in 5 (25%) patients: the locked-in syndrome, cerebellar ataxia, and hemiparesis in 1, 1 and 3 patients, respectively. There was also a case of transient aphasia resulting from the venous infarction of the left temporal lobe, a case of liquor rhoea requiring plastic surgery, and pneumonia in 1 patient.

V.N. Shymansky [6] notes that the Karnofsky index (KI) always drops after surgery in patients with PCM regardless of the radicality of tumor resection. An uncomplicated postoperative course was observed in 68 (52.3%) patients: there was no rise in the new neurological deficit before surgery. A complicated postoperative course was observed in 37 (28.5%) patients. The course of postoperative period was aggravated in 25 (19.2%) patients. The mortality of tumor removal amounted to 7 (5.39%) out of 130 cases. Relying on the group of complications, the development of hemiparesis in the early and late postoperative periods was observed in 6 (6.9%) and 2 (2.3%), cerebellar disorders in 0 and 1 (1.1%), bulbar disorders in 7 (7.9%) and 6 (6.7%), hearing loss in 14 (15.7%) and 13 (14.6%), paresis of the facial nerve in 30 (33.7%) and 12 (13.5%), destruction of the trigeminal nerve in 9 (10.1%) and 20 (22.5%), and oculomotor disturbances in 15 (16.9%) and 3 (3.4%) cases, respectively.

H. Jung et al. [28] concluded that remnants of petroclival meningiomas grow slower than the original petroclival meningioma; 5-year absence of tumor progression was recorded in 60% of cases. Therefore, subtotal/partial resection is a more favorable strategy in the modern surgical approach to the treatment of petroclival meningiomas in elderly patients or in patients with tumor infiltration of the cranial nerves, arteries, brain stem, and sphenoideal sinus.

5. Radical surgery/frequency of relapses

Relying on the experience of the Burdenko Neurosurgical Institute, V.N. Shymansky [6] noted that the onset of recurrence in a group with PCM after incomplete removal of the tumor occurs within 5 years on average. In 89 patients with petroclival meningiomas, total and subtotal/partial removal were possible in 6 (6.7%) and 16 (17.9%), respectively. The mortality of tumor resection was 7 (5.39%) out of 130 cases.

T. Kawase et al. [29] were able to perform radical resection of tumors in 7 out of 10 patients; such aggressive resection led to the emergence of a persistent neurological deficit in 80% of the patients. The tumor recurred after subtotal resection in one of 3 patients.

In the study by J. Yang et al. [81], resection was also performed in 17 (68%) of 25 patients, and the frequency of neurological complications was likewise high (64%).

At the moment, the approach to the surgical treatment of sphenopetroclival meningiomas has changed. There is a tendency towards an intentional reduction of the radicality of the resection in order to reduce the risk of neurological complications. Thus, I. Yamaki et al. [80] performed total resection in only 8 (40%) out of 20 patients with large petroclival meningiomas. MRI data showed continued tumor growth in just 3 (15%) patients; the interval between the resection and the tumor recurrence was 37–74 months. Subtotal/partial resection is more favorable in elderly patients or in patients with tumor infiltration of the cranial nerves, arteries, brain stem, and sphenoideal sinus.
C. Methods of adjuvant treatment of common meningiomas of the skull base

1. Radiation therapy

Radiotherapy is the most important treatment option in patients with common meningiomas of the skull base, including patients with OSPCM. Radiosurgery is employed when tumors are smaller than 30 mm in diameter. It remains an open question as to whether all patients with a residual tumor should undergo radiotherapy immediately after surgery, or only patients with an identified further growth should do so. Based on the results of long-term studies, it appears that irradiation allows to successfully manage the growth of subtotally removed meningiomas [8, 22, 43, 76, 78]. Success in long-term (10–20 years) control over benign meningiomas and atypical forms is 70–90% and 50–70%, respectively. The goal of radiation therapy is to prevent further growth of meningiomas. As a rule, tumor shrinkage, a clinically stable disease, and improvement are observed after radiotherapy in 15–40%, 50–80%, and in about 30–40% of cases, respectively.

During irradiation of meningiomas of the skull base, it is especially important to keep safe the anatomical structures that are sensitive to radiation (visual pathways, brain stem, eyeballs, lacrimal gland, and the pituitary gland), which may localize next to the tumor or inside of it. Due to high precision in the delivery of the radiation dose, conformity (compliance of the form of dose distribution to the shape of the tumor), the high dose gradient and the option of fractionation, modern methods of radiotherapy allow one to avoid damaging functionally important structures. With larger tumors and when functionally important organs are located inside the tumor, dividing the radiation treatment into steps can significantly reduce potential risks.

According to many experts [16, 31, 33, 42, 49, 54, 68], radiosurgery is the optimal method for the treatment of small meningiomas. The doses can range from 12–16 Gy; the most often employed dose is 14 Gy [34, 47]. Radiosurgery [using a Gamma Knife unit or other devices based on the LINAC (linear accelerator LInear ACCELERator)] has been proposed to treat tumors located farther than 1–2 mm away from the optic nerve and/or optic chiasm, with a volume of less than 14 cm³ (about 3 cm in diameter) [31, 42, 54, 83]. It has been reported that the probability of a 5- to 10-year control over the tumor growth rate using stereotactic radiosurgery is 90–95% [16, 42, 43, 49, 68]. Late complications, namely, neuropathy of the cranial nerves, are observed in 1–10% of patients. The rare late complications include pituitary insufficiency, radiation injury, and ischemic complications [16, 42, 43, 49, 68].

The use of fractionated irradiation is considered optimal in treating large meningiomas and when functionally important organs are located inside the tumor [39, 70]. The irradiation mode of classical fractionation is commonly used. This means providing a fraction per day 5 days a week, with a fraction value of 1.6–2.5 Gy to achieve an effective dose of 50–54 Gy. The irradiation mode of hypofractionation is less frequently employed: the dose per fraction is increased up to 3–8 Gy, and the total number of fractions is usually 2–7. The mode is best used between the standard fractionation and radiosurgery. Unfortunately, only a few published works have been devoted to the latter procedure, and there is a lack of studies on the irradiation of OSPCM. For this reason, data on irradiation in the classical mode of fractionation will be provided further.

Irradiation of meningioma in the conventional mode of fractionation allows one to exert control over tumor growth in 92–100% of the cases [15, 17, 35, 40, 68]. As this takes place, a decrease in tumor size is observed in 14–53% of cases [15, 25, 53, 68]. The wide scattering of the frequency of tumor reduction is associated with the difference in the criteria for determining the tumor response. Although the main goal of the treatment is to exert control over the growth of the tumor, irradiation allows one to achieve clinical improvement in 20–71% of cases [15, 17, 35, 40, 68]. As this takes place, irradiation using the mode of standard fractionation is associated with a small frequency (0–17%) of persistent complications [15, 17, 35, 40, 68]. These include neuropathies of cranial nerves, swelling of the brain matter and radiation necrosis, hypothalamic-pituitary disorders, ischemic complications resulting from the damage done to the internal carotid artery and its branches, as well as minimal likelihood of developing secondary tumors.

A fractionated dose of irradiation can be delivered to a target using the stereotactic method, which allows more precise immobilization and a three-dimensional coordinate system for better limitation of the tumor and reduction of preset errors. There exist many commercial systems that enable delivery of a fractionated stereotactic radiation dose with a 2- to 5-mm expansion of GTV (tumor gross volume) with relation to the PTV (planning tumor volume). Several studies have demonstrated an excellent local control rate of growth (90–100%) with a minimal risk of late complications [7, 10, 15, 41]. Although the risk of neurocognitive decline caused by the standard procedure of irradiation is considered low, the use of the stereotactic method can further reduce this risk [7, 10, 15, 41]. The data presented above refer to the more common photon irradiation. Irradiation with a flux of particles is also used for meningiomas, and it has its own advantages. Because of the ability of the particle flux to release the bulk of its energy into a strictly defined area (Bragg peak), the load on normal tissues is significantly reduced as compared with photon irradiation [14, 69]. The biological effect of the use of protons and neutrons may be greater than that from the use of photon irra-
radiation. Proton therapy has been used very successfully in skull base meningiomas, with satisfactory control over growth and minimum toxicity to the body being its hallmarks [24, 51, 77, 79]. Difficulty consists in the fact that the equipment for producing the proton beam requires considerable space. The cost of irradiation therewith becomes almost prohibitive. Radiotherapy and radiosurgery, along with microsurgical removal, are an important step in the treatment of skull base meningiomas and allow one to exert control over tumor growth in 92–100 and 91–100% of cases. This is done with a low rate of complications in 0–17 and 0–10.5% of cases, respectively [15, 17, 34, 35, 40, 48, 54, 68, 73]. Irradiation also leads to clinical improvement in 20–71% of patients with radiotherapy and 25–66% of cases after radiosurgery.

2. Drug therapy

OSPCM are prone to continued growth, primarily due to the infiltrative nature of their growth. We have studied numerous publications focused on attempts to treat common, medically recurrent meningiomas of varying degrees of malignancy. Unfortunately, from the standpoint of evidence-based medicine, there have been no results allowing the effective use of one or another drug in clinical practice. There have been attempts to use cytostatics, inhibitors of sex hormones, blockers of the receptors of somatotropin and insulin-like growth factor 1, hydroxyurea, calcium channel blockers, interferon-alpha, erlotinib and gefitinib, imatinib, Avastin (bevacizumab), and inhibitors of cyclooxygenase-2 (celecoxib). The photodynamic therapy appears to show promise, with the use of 5-minolevulinic acid, but the problem has yet to be studied.

Conclusion

Thus, the progress achieved through neurosurgical techniques, the use of modern approaches in conjunction with endoscopy and neuronavigation, the achievements of neuroanesthesiology and resuscitation, and the widespread use of adjuvant therapies (stereotactic radiosurgery and radiotherapy), certainly have recently significantly improved results in the treatment of patients with advanced craniofacial meningiomas and led to an increase in the average survival rate. Developing an optimum treatment requires a careful analysis of the results of the treatment, which would include the assessment of the overall and disease-free survival rate for the whole group and for different histological types of tumors, and assessment of the neurological, psychological status of patients in the delayed period. A proper assessment of tumor spreading patterns is highly important for the determination of a treatment strategy.

Because of the increase in the follow-up period, the evaluation of the quality of life and social adaptation of patients becomes an important task. However, there are obvious difficulties associated with treating this group of patients. Thus, the desire to maximize radical removal of the tumor is accompanied by a high risk of postoperative complications in the form of a persistent neurological deficit and disability, or even death of the patient. Performing subtotal resection allows one to reduce the risk of complications, but it increases the relapse frequency.

Radiosurgery or radiotherapy of residual tumors exhibit a high degree of control over tumor growth, accompanied by a risk of post-radiation reactions with damage to critical parts of the brain. A study of the potential of chemotherapy, growth inhibitors, and hormonal agents regarding benign meningiomas is underway, but in reviewing evidence-based medicine, encouraging results have yet to appear. Many studies have evaluated the outcome of therapy for patients with meningioma of varying degrees of malignancy who underwent different treatments. However, while the criterion for potential efficacy of a drug for benign meningiomas can be an improvement in progression-free survival for 6 months for more than 50% of cases, the criterion for the more malignant meningiomas remains uncertain [23]. The use of effective methods of chemotherapy or a combination of chemotherapy/radiation is complicated due to lack of understanding of the signaling pathways affecting the growth of meningioma, the apoptosis of tumor cells, and intraosseous invasion. Thus, the problem of common craniofacial infiltrative meningiomas is usually associated with studying molecular oncobiology in comparison with pathomorphological and clinical data, and elaborating additional methods for treating meningiomas, which are not amenable to surgical treatment and radiotherapy.

On this basis, treatment of a group of patients with tumors of predominantly orbitosphenopetresclival localization that had formed for decades and who were initially treated with non-radical surgery methods is a challenge, even for the most advanced neurosurgical centers. Rather high rates of postoperative mortality and complications still remain. In such a context, in patients with a long history and significant tumor spread it would be reasonable to use a combination of all available methods, as well as palliative surgery to preserve vital functions (saving vision, providing the nasal breathing, mouth opening, preventing intracranial hypertension, and pain relief). The rational and consistent use of all possible methods and a “sensible” approach to the patient could allow one to preserve and extend his life, with better social adaptation and higher quality of life. A careful analysis of retrospective and prospective groups of patients with OSPCM may allow one to determine the clues for each method of treatment at a certain stage of the disease and, therefore, makes such a study as ours relevant.
REFERENCES


