Cavernous malformations of the brain stem - the clinical features and surgical approaches

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INTRODUCTION

Introduction. Cavernous malformations localized in the brain stem are considered as a separate entity in relation to other intracranial cavernoma. Clinical presentation is specific in terms of focal neurologic deficit, they show aggressive biological behavior and unfavorable clinical course, whereas localization in the brain stem naturally represents the largest surgical problem and challenge and significantly higher operational risk. Results. We report a series of 10 patients with brainstem cavernoma, operated at the Department of Neurosurgery, Clinical Center of Serbia in the period of 2008-2012. In cavernous lesions of the dorsal pons and upper cerebellar peduncle we used the approach through the fourth ventricle, in the laterally localized pontine cavernoma we used the cerebellopontine angle approach, in the cavernoma localized in the central midbrain tegmental area was used supracerebellar infratentorially approach. Conclusion. Surgical removal of the brainstem cavernoma is absolutely expedient both from the standpoint of preventing recurrent and debilitating hemorrhage and in terms of recovery of neurologic deficit. In patients with disturbed vital functions, the evacuation of the hematoma and removal of the malformation eliminate compression of effects on vital structures of the brain stem.

Key words: Cavernous, brain stem, surgical approach

INTRODUCTION

Cavernous malformations (cavernomas, cavernous angioma) belong to the spectrum of vascular malformations of the brain including also arteriovenous malformation (AVM), venous malformations (venous angioma) and capillary malformations or telangiectasias1,2. With the exception of a larger AVM that are being diagnosed with cerebral angiography, other vascular malformations including small and/or thrombosed AVM elude angiographic visualization and traditionally referred to as “cryptogenic” or “angiographically occult”4. Cavernous malformations are well-limited lesion without plug-nerous tissues, multilobularnog looks and dark red or purple color and the appearance reminiscent of mulberries3,5. Unlike AVM, cavernomas have dilated blood vessels to form arteriovenous shunts. Instead, they usually have a small feeding artery associated with peripheral caverns that are regularly seen in microsurgical dissection and can cause significant intraoperative bleeding6. Cavernous malformations are considered as congenital vascular lesions, although in recent years there have been described the occurrence of de novo malformations7. They occur mostly sporadic but not rare, may be familiar disease with an autosomal dominant model of inheritance and partial penetration. They are usually solitary lesions but may be multiple, especially in familial forms8. Cavernous malformations have dynamic behavior with intraleisional and extraleional hemorrhage and thrombosis and in time they are larger. They may be asymptomatic but are more often they are symptomatic and are manifested by epileptic seizures, haemorrhages and focal neurologic deficits9,10. In a smaller number they cause massive and catastrophic bleeding, or after the first hemorrhagic episodes usually show a pronounced tendency to recurrent hemorrhages that can cause serious invalidity or death outcome. According to aggregate data, cavernous malformations make 8-15% of all intracranial vascular malformations and 13% of all malformations localized posterior fossa11. In the overall population, the incidence of CNS cavernomas varies from 0.4% to 0.9%. According to various sources, the incidence of cavernous malformations in the brain stem varies widely in the range from 9 to 35% and averaging 17% of all intracranial cavernoma. Additional surgical stimulus was gained by a deeper acquaintance of topographic and morphological relations of lesions and functional structures which led to the identifi-
cation of safe input zones in the brain stem\textsuperscript{16-18}. In the last twenty years has significantly increased the number of operated patients, a larger surgical series were published, it has been achieved a general agreement about the goals of the operation, approaching attitudes about indication and timing for the surgery and the surgical technique is described in detail \textsuperscript{6,14,15,20-32}.

**MATERIALS AND METHODS**

In the period 2008-2012, on our clinical department we observed 13 patients with cavernous malformations of the brain stem, of which 10 underwent direct surgical excision of malformations. Three patients suffered one hemorrhagic episode after which there was a complete neurological recovery and are left to the natural course of the disease. One of them is eighteen year old girl with a dorsal pons cavernoma which did not had a new hemorrhage during four years of follow-up and that in the meantime, put forward a normal pregnancy with naturally delivery. The other two patients with small and deep lesions have been a year without new clinical episode and then they lost to further follow-up. One of them had a familial form of multiple cavernoma in different regions of the brain. For the surgery, patients were selected who are also fulfilled two conditions: a) lesions on MRI image reaches the ventricular or pial surface of the brainstem, or to at least be accessed outside of important functional structures and b) that, intermittently or continuously, there is a progression of symptoms and-or neurologic deficit.

**RESULTS**

In the operated group of patients there were six women and four men, aged 32-59 years (mean 43.9 years). According to the clinical course one of the patient which is 46 years old stands out. He was treated for 18 years under the diagnosis of disseminated neurodegenerative diseases until discovering cavernoma. A retrospective analysis of the course of the disease has shown that during this period suffered at least six subtle clinical episode with a discrete neurological progression (Table 1, case 9). Five patients had only one hemorrhagic attack, and two patients had suffered two or three hemorrhagic episodes which means that nine patients underwent a total of 19 hemorrhages. Only one patient (case 7) with a malformation in the dorsal part of the pons, in addition to focal neurologic deficit developed subarachnoid hemorrhage which is manifested clinically and confirmed by findings of hemorrhagic CSF at lumbar puncture. An initial symptoms and signs were different in correlation with the localization of the lesion, and nine out of 10 patients had more than one symptom or sign. The main symptoms were headache, nausea and-or vomiting (4 cases), vertigo (3 cases) and different sensations related to the trigeminal nerve (4 cases). Among the cranial nerves the most frequent was isolated or combined dysfunction of abducens nerve and facial nerve in the form of diplopia or peripheral paresis of the facial muscles (five patients), and verti
cal gaze palsy (2 patients). Pyramidal signs in the form of spastic hemiparesis were registered in half of patients, signs of cerebellar dysfunction (difficulty in walking, cerebellar ataxia) in 2 cases and difficulty swallowing in 2 cases. In patients with exophytic cavernous malformation in the cerebellopontine angle (case 5), the clinical presentation was in the form of tinnitus, vertigo and hypoaesthesia ipsilateral half of the face. The clinical evolution of the first symptoms until surgery in these nine patients averaged 6.3 months (minimum of two weeks and a maximum of 12 months). Clinical progression of symptoms and neurological deficits in 5 patients developed under intermittent model with incomplete remissions and exacerbations, and with the same number of patients, the course was continuously progressive. In eight cases, the clinical course can be assessed as mildly progressive, in two cases it had an extremely aggressive form in the form of dysphagia and respiratory insufficiency that developed during the two weeks since the first hemorrhagic attack (case 3), respectively, after three hemorrhagic episodes in two months (case 10).

### 4.1 Characteristics of cavernoma

In 60% of our surgical cases cavernous malformation was localized in the pons and in its lateral part in 3 patients, in the dorsal part of the floor of the fourth ventricle in two patients and in the central part of the pons in 1 patient. Among the lateral pontine cavernomas, two were typical intrinsic lesion, in the third case (case 5) malformation is a broad and superficial resulted from the pons directly below the origin of the trigeminal nerve roots and the larger portion was lying exophytic in the cerebellopontine angle (Figure 1). This is the only case in which before the operation were not made MRI visualization, the surgical exploration has been undertaken based on CT images, which, along with clinical presentation, suggested extraxial tumor in the cerebellopontine angle. Intraoperative cavernoma in this case and confirmed by histopathological examination. Two patients malformations was located at the junction of the fourth floor of the chamber and the superior cerebellar peduncle predominantly localized in peduncul, in both cases. In one case, cavernoma occupied the lateral and superficial part of the midbrain tegmentum and also in one case had the medulla oblongata localization inside. In relation to the surface of the brainstem, 4 cavernous lesions were transparent under the fourth chamber and in the remaining 6 cases the lesion was covered with a thin or thick layer of nervous parenchyma. According to the grading-system Zabramski, in seven cases of malformations was followed by subacute hematoma (type I lesions), while the remaining three cases had intralesional fields of hemorrhage and thrombosis (type II)\textsuperscript{33}. Cavernous malformations of the brain stem were solitarnie lesions in 9 out of 10 patients. In last case, in addition to the cavernoma in the pons we diagnosed an asymptomatic malformation in the right parieto-posterior region of the cerebrum, which was also surgically removed and histologically confirmed after two months of pontine le-
**Table 1**

**OUR SERIES OF SURGICALLY TREATED BRAINSTEM CAVERNOMA (2008-2012)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Year of birth</th>
<th>Initial clinical presentation</th>
<th>No of episodes</th>
<th>Clinical course</th>
<th>Localization</th>
<th>Morphological type</th>
<th>Surgical approach</th>
<th>Postoperative condition</th>
<th>Periodic monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DM</td>
<td>M</td>
<td>Headache, vomiting, Vertigo, Disruption walk</td>
<td>Three</td>
<td>Intermittent 4 months</td>
<td>Upper cerebral pendulems</td>
<td>Zabramski Type II</td>
<td>Suboccipital approach through IV chamber Above lesions</td>
<td>Improved</td>
<td>3 years and 9 months</td>
</tr>
<tr>
<td>2</td>
<td>CB</td>
<td>M</td>
<td>Hemiparesis</td>
<td>One</td>
<td>Progressive 2 years</td>
<td>Medulla oblongata</td>
<td>Zabramski Type III</td>
<td>Suboccipital approach through IV chamber Above lesions</td>
<td>Impaired</td>
<td>Exitus letalis after 13 days</td>
</tr>
<tr>
<td>3</td>
<td>TR</td>
<td>M</td>
<td>Hemiparesis, Paresis n. VII, Difficulty swallowing</td>
<td>One</td>
<td>Progressive 2 years</td>
<td>Dorsal pons</td>
<td>Zabramski Type I</td>
<td>Suboccipital approach + C1 laminectomy Through postero-lateral sulcus</td>
<td>Unchanged</td>
<td>3 years and 2 months</td>
</tr>
<tr>
<td>4</td>
<td>VM</td>
<td>F</td>
<td>Headache, Nausea, 1/2 facial hypoesthesia</td>
<td>One</td>
<td>Progressive 9 months</td>
<td>Lateral pons</td>
<td>Zabramski Type I</td>
<td>Combined petros Anterolateral surface of the pons</td>
<td>Improved</td>
<td>2 years and 1 month</td>
</tr>
<tr>
<td>5</td>
<td>UZ</td>
<td>F</td>
<td>Vertigo, Tinnitus unilat. 1/2 facial hypoesthesia</td>
<td>One</td>
<td>Progressive 12 months</td>
<td>Pons-cerebellopontine angle</td>
<td>Zabramski Type II</td>
<td>Retromastoideus the cerebellopontine angle above lesions</td>
<td>Unchanged</td>
<td>2 years and 8 months</td>
</tr>
<tr>
<td>6</td>
<td>TN</td>
<td>F</td>
<td>Vertigo, cerebrail ataxia 1/2 facial hypoesthesia, Paresis vert. views</td>
<td>Two</td>
<td>Intermittent 2 months</td>
<td>Lateral pons</td>
<td>Zabramski Type I</td>
<td>Retromastoideus the cerebellopontine angle Anterolateral surface of the pons</td>
<td>Improved</td>
<td>1 year and 9 months</td>
</tr>
<tr>
<td>7</td>
<td>SE</td>
<td>F</td>
<td>Headache, vomiting, Paresis n. VII, Hemiparesis, the syndrome SAH</td>
<td>One</td>
<td>Intermittent 3 weeks</td>
<td>Dorsal pons</td>
<td>Zabramski Type I</td>
<td>Dorsal pons</td>
<td>Unchanged</td>
<td>1 year</td>
</tr>
<tr>
<td>8</td>
<td>MS</td>
<td>F</td>
<td>Headache, vomiting, Paresis n VII, Hemiparesis 1/2 facial hypoesthesia, Paresis vert. views</td>
<td>Two</td>
<td>Intermittent 6 months</td>
<td>Tegmentum mez.</td>
<td>Zabramski Type I</td>
<td>Subtemporo-transsensatorial Through lemniscal triangle</td>
<td>Unchanged</td>
<td>1 year and 5 months</td>
</tr>
<tr>
<td>9</td>
<td>TH</td>
<td>M</td>
<td>Vomit, Paresis n.VII Multiple simpt.and signs (encephalomyelitis?)</td>
<td>Six</td>
<td>Intermittent 18 years</td>
<td>Upper cerebral pendulems</td>
<td>Zabramski Type I</td>
<td>Suboccipital approach through the IV chamber Above lesions</td>
<td>Impaired</td>
<td>2 years</td>
</tr>
<tr>
<td>10</td>
<td>KS</td>
<td>F</td>
<td>Paralysis n VII, Hemiplegia, Difficulty swallowing</td>
<td>Three</td>
<td>Progressive 2 months</td>
<td>Pons paracent.</td>
<td>Zabramski Type I</td>
<td>Suboccipital approach through the IV chamber Through suprafacial triangle</td>
<td>Improved</td>
<td>3 years</td>
</tr>
</tbody>
</table>
small field of dilated capillary vessels that are highly regarded as telangiectasia.

4.2 Surgical Approaches

Cavernous lesions of the dorsal pons and upper cerebellar peduncul (a total of 5 cases)) were approached through the fourth ventricle, through a lower midline suboccipital craniectomy. For this approach we have a long-standing habit of surgical patients to be set in a sitting position. We opened the fourth ventricle by telovelar microsurgical approach (five cases). On the floor of the fourth ventricle in the three cases we had clear surgical corridor to enter the lesion through the flange and or pathological stained fields above the malformation. In the other cases, a longitudinal incision is made through the median sulcus, approximately seven millimeters, just above the facial colliculus and above venous anomalies identified on the floor of the ventricle. In the latter case, a longitudinal incision is made in the same length suprafacial triangle. Postoperatively, in the first case there was no additional neurological deficit that would be concerning the plane of entry into the brain stem. In the second case was registered additional abducens nerve palsy, which is completely withdrawn within two postoperative weeks. For operations of lateral pontine lesions (3 cases) we used approach to the cerebellopontine angle, with the patient in a sitting position. This approach was performed through standard retromastoid retrosigmoid craniectomy (2 cases) and combined through suboccipital-subtemporal craniotomy (presigmoid variant of petrosal approach) in one case. Cavernous lesions in two occasions was reached through a small field on the flange anterolateral surface of pons, between the origin of V and VII-VIII cranial nerve. In the third case, the exophytic part of the malformation in the cerebellopontine angle itself presented a input field in cavernoma. For cavernoma in the lateral part of the midbrain tegmentum is derived medium variant subtemporal craniotomy with incision tentorium. Following the identification of the lateral mesencephalic sulcus and related mesencephalic vein, an incision made in lemniskal triangle through which they entered the cavernous lesion (case 8). In the case of lesions in the medulla oblongata is made medial suboccipital craniectomy with resection of the lower back arch of the atlas. In the medulla oblongata at the level of separation of the lower cerebellar peduncul we have identified two darkly painted fields 5mm in diameter. Since there was no prominence on the surface of the medulla, we conducted a longitudinal incision length of 3 millimeters through the posterolateral sulcus. At a depth of 5 millimeters has not been reached the expected gliose capsule of lesion and so we dropped from further exploration (case 2). From a total of 10 surgically treated cases of brainstem cavernoma at 8 besides accompanying evacuation of hematoma was performed a total removal of the vascular stroma of malformation. In neither case was an attempted dissection of the surrounding gliose layer of the adjacent parenchyma. The radicality of surgical excision in two cases documented intraoperative photograph in three cases based on the control MRI images. In the remaining three cases, the conclusion about the radicality of the operation is based only on our intraoperative impression since, for reasons that are out of this topic, it was not possible to make a control MR studies. In patient with a lesion in the cerebellopontine angle, which was operated only on the basis of CT images, intraoperative finding was unexpected, so only partially removal of the malformation was done. We planned second surgical act that the patient refused. In all these patients the diagnosis was verified by histopathological examination. As previously described, in one case we made the medulla oblongata exploration, but it was dropped from searching of malformations.

DISCUSSION

Dandy was the first neurosurgeon who performed the operation of pontine cavernoma although the diagnosis has not been established preoperatively. Since then, several authors describe the encouraging results related to the surgical treatment of brainstem cavernoma. Cavernous malformations of the brain stem have a higher rate of bleeding compared to other localizationsof cavernoma. Porter and colleagues have shown that the risk of hemorrhage 5% per year and rehemorrhage about 30%23. Fritschi and colleagues have also come to the conclusion that the rate of the initial hemorrhages is 2.7%, rehemorrhage around 27%30. In our series, the risk of hemorrhage, 6% and 30% of rehemorrhage. Most authors agree that asymptomatic or accidentally discovered cavernomas of the brainstem should be treated surgically, especially if the lesions are small and covered by a large ring of healthy parenchyma. For symptomatic cavernoma of the brain stem, especially if they tend to bleed, surgical resection should be carried out before mass effect or bleeding again cause severe neurologic deficit. Wang and colleagues have set the indications for surgical treatment11: a progressive neurologic deficit, drastic clinical picture presented coma or cardio-respiratory failure, NMR verified acute and subacute hemorrhage, all cavernomas or hematoma which are located superficially, less than 2 mm from the pial surface. Bertalanffy and colleagues believe they should operate only cavernoma who manifested by bleeding and neurological deficit. Most neurosurgeons operate brainstem cavernoma in the subacute stage. When the patient's condition is stable, when the hematoma is organized and until there is a greater mass of reactive gliosis. However, the review of the current literature, the time of the operation ranges from a few days of bleeding, from 1 to 4 weeks after the hemorrhage until over 7 weeks the attack of hemorrhage34.35. Lewis et al, avoid surgery in the acute phase because gliose edematous tissue and tissue cavernoma not clearly determined. In our series, 64% of patients underwent surgery within 1 to 3 months after hemorrhage. We think it is much easier
The surgery can be performed in the subacute and the acute or chronic phase of the disease. According to Bertalanffy - the choice of surgical approach is essential for the successful operation\textsuperscript{36}. The largest number of neurosurgeons elect surgical approach to the relationship cavernoma and the pial or ependymal a surface area of the brainstem. Brown and colleagues described the “two point method” in the selection of the most adequate approach\textsuperscript{36}. They set up a single point in the center of the cavernoma and the other end to a place where she herself lesion nearest the surface of the brain stem. The line that connects these two points is taken as a safe surgical corridor. If the associated venous anomaly located in this corridor, Zimmerman and colleagues are of the view that complete approach should be modified in in order to avoid lesions of venous anomalies\textsuperscript{37}. Ferroli and associates of 52 patients with brainstem cavernoma, 21 are operated midline suboccipital approach, 17 retrosigmoid, 6 supracerebelar infratentorially, 3 farleteral access and two patients used a different approach\textsuperscript{38}. Also, they are of the opinion that the use of the anterolateral approach is safer than access through the IV chamber. In our series, we used a midline suboccipital approach in 60\% of cases and retromastoid approach in 20\%. Other approaches we used in 20\% of cases. Surgical technique for the resection of brain stem significantly influences the outcome after surgery. Surgical technique is extensively described and three standards were adopted: 1) the complete removal of cavernoma; 2) avoidance of lesions associated venous malformations; 3) allowing hemonisering glise ring of parenchyma intact. In microsurgical technique is necessary very careful coagulation and resection of pathological blood vessels; excellent knowledge of the anatomy of the brain stem; meticulously preoperative planning of resection. Intraoperative monitoring somato-sensory potentials is recently used increasing in surgery of brainstem cavernoma. Some authors have reported that these forms of electrophysiological monitoring are useful in the prevention of postoperative neurological deficit\textsuperscript{24,31}.

CONCLUSION

Surgical removal of the brainstem cavernoma is absolutely expedient both from the standpoint of preventing recurrent and debilitating hemorrhage and in terms of recovery of neurologic deficit. In patients with disturbed vital functions (breathing, swallowing), evacuation of the hematoma and removal of the malformation eliminate life-threatening compression of effects on vital structures of the brain stem. Patients with superficial localized cavernomas and progressing neurologic deficit should undergo surgical treatment. In cases of deep lesions, which are covered with a considerable layer of nervous tissue injury, it is necessary to careful preoperative planning of safe entry into the brain stem, without damage to the vital functional structures

SUMMARY

Uvod. Kavernozne malformacije lokalizovane u moždanom stablu se izdvajaju kao poseban entitet u odnosu na ostale intrakranijalne kavernome. Klinička prezentacija je specifična, u vidu lokalnog neurološkog deficita, pokazuju agresivnije biološko ponašanje i nepovoljniji klinički tok, dok lokalizacija u moždanom stablu prirodno predstavlja najveći hirurški problem i izazov i op-terećena je značajno većim operativnim rizikom.

Rezultati. Prikazujemo seriju od 10 pacijenata sa kavernomom moždanog stabla operisanih u Klinici za neurohirurgiju KCS u periodu 2008-2012 godine. Kavernoznim lezijama dorzalnog ponsa i gornjih cerebelarnih pedunkulusa korišćen je pristup kroz četvrto komor, kod lateralno lokalizovanih pontinih kavernoma korišćen je pristup kroz pontocerebelarni ugao, za kavernome lokalizovane u tegumentumu mezencefalon korišćen je supracerebralni infratentorialni pristup.

Zaključak. Hirurško odstranjevanje kavernoma moždanog stabla je apsolutno svrshodno kako sa stanovišta prevencije ponavljanih i onesposobljavajućih hemoragija tako i sa stanovišta oporavka neurološkog deficita. Kod bolesnika sa poremećenim vitalnim funkcijama, evakuacija hematoma i odstranjevanje malformacije eliminišu kompre-sivni efakt na vitalne strukture moždanog stabla.

Ključne reči: kavernomi, moždano stablo, hirurški pristup

BIBLIOGRAPHY