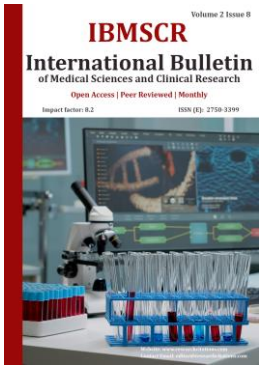

SURGICAL TREATMENT OF BRAIN STEM CAVERNOUS MALFORMATIONS

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Cavernous malformations (CMs, cavernomas) are angiographically hidden vascular malformations with low blood flow, which can be found in various parts of the central nervous system and have a sinusoidal structure [1,3,7,8]. Microscopically, they represent accumulations of sinusoids formed by a collagen skeleton, lined with a single layer of endothelium and with presence of endothelial fenestrations, as well as gaps in intercellular junctions. A characteristic feature is the absence of smooth muscle cells and elastic fibers in the walls of the cavities [1,8]. Clinical manifestations of CMs can appear at any age, but often appear between the 2nd and 5th decades of age.

According to the number of CMs, they can be single (sporadic) and multiple. The latter are detected in 10–20% of patients, and are typical for the hereditary form of the disease [6,9,10]. There are several theories of the formation of CMs of the central nervous system: congenital, genetically determined, radiation-induced [1,3,6]. About 20% of CMs are inherited due to familial mutations in CM genes, including CCM1/KRIT1, CCM2/MGC4607, and CCM3/PDCD10, while the etiology of most patients with sporadic CM remains unclear [9,10].

Cerebral CMs occur in up to 0.5% of the total population [1,2,6,9]. They account for 5–15% of all neurovascular formations and vary widely in different populations, amounting to 0.15–0.56 per 100,000 people per year [1,2,9,13]. The largest number of CMs is located supratentorially, mainly in the frontal, temporal, and parietal lobes of the brain. In the trunk - 9-35% of cases [6,9]. In the posterior cranial fossa, CMs are most often located in the brainstem, mainly in the area of the pons, less often in the midbrain, and even more rarely in the bulbar region. Isolated midbrain cavernomas are quite rare, and medulla oblongata cavernomas are the least common. Cerebellar cavernomas (8% of all cavernomas) are more often located in its hemispheres, less often in the vermis [6,9].

CMs located in the brainstem have a higher risk of hemorrhage compared to supratentorial ones. It ranges from 2.46 to 5% and increases to 60% per year after first hemorrhage [1,2,4,9]. CM hemorrhages of stem localization leads to death in up to 20% of cases. At the same time, surviving patients in most cases remain with neurological disorders, and repeated hemorrhages in this category of patients lead to an even greater deterioration of neurological disorders, up to lethality [9,10,13,15]. It is impossible to predict rebleeding from a CM in each specific case, and its successful surgical removal can permanently save the patient from possible deep disability and mortality. Therefore, such CMs of the brainstem are subject to surgical removal if they are anatomically accessible. Treatment of brainstem cavernomas has a number of features that prove the classification of this pathology as an independent group [6].

Cavernous malformations located in the deep regions and in the brain stem are not always indicated to surgical treatment. Most patients are recommended for conservative treatment, in which case the mortality rate reaches 20% [6]. Even with radiosurgery, mortality is 8.3%, the recurrence rate of hemorrhage is 59% [2,6,11,16]. A number of authors point out that in the surgical treatment of brainstem CM, it is possible to achieve regression of neurological symptoms from partial to complete with a mortality rate of 0 to 3.5% [13,16].

The purpose of this work is to study the results of surgical treatment of brainstem cavernous malformations.

Materials and methods. The analysis of the results of 17 patients, who received treatment in the Republican Specialized Scientific and Practical Medical Center for Neurosurgery for the period 2016-2022 with CM of stem structures, was carried out. There were 8 (47%) men and 9 (53%) women patients. The age of patients ranged from 12 to 43 years, the average age was 28 years, and young patients dominated, 4 patients were children. 3 patients had multiple CMs, with localization in the pons, cerebellum, temporal, frontal and parietal lobes of the brain. By localization, most of the CM were located in the pons - 16 (94.1%) patients, and in 1 patient the cavernoma with hemorrhage was localized in the midbrain.

The main diagnostic method was MRI, which has high sensitivity and specificity in relation to this pathology [4,17]. In addition to the standard T1, T2, FLAIR modes, DWI, SWI, FIESTA, MR - angio - and tractography were used. Among the patients, 4 patients came with MSCT images of the brain, where signs of hemorrhage were detected, and 2 patients underwent angiographic examination for the purpose of differential diagnosis (Figure 1). When studying MRI scans, type I was detected in 11 patients, type II in 5 and type III in 1 patient according to the classification of Zabramsky et al. (Appendix 1) [17]. To register the degree of dysfunction of stem structures caused by compression and ischemia, BSEP was performed in 9 (52.9%) patients.

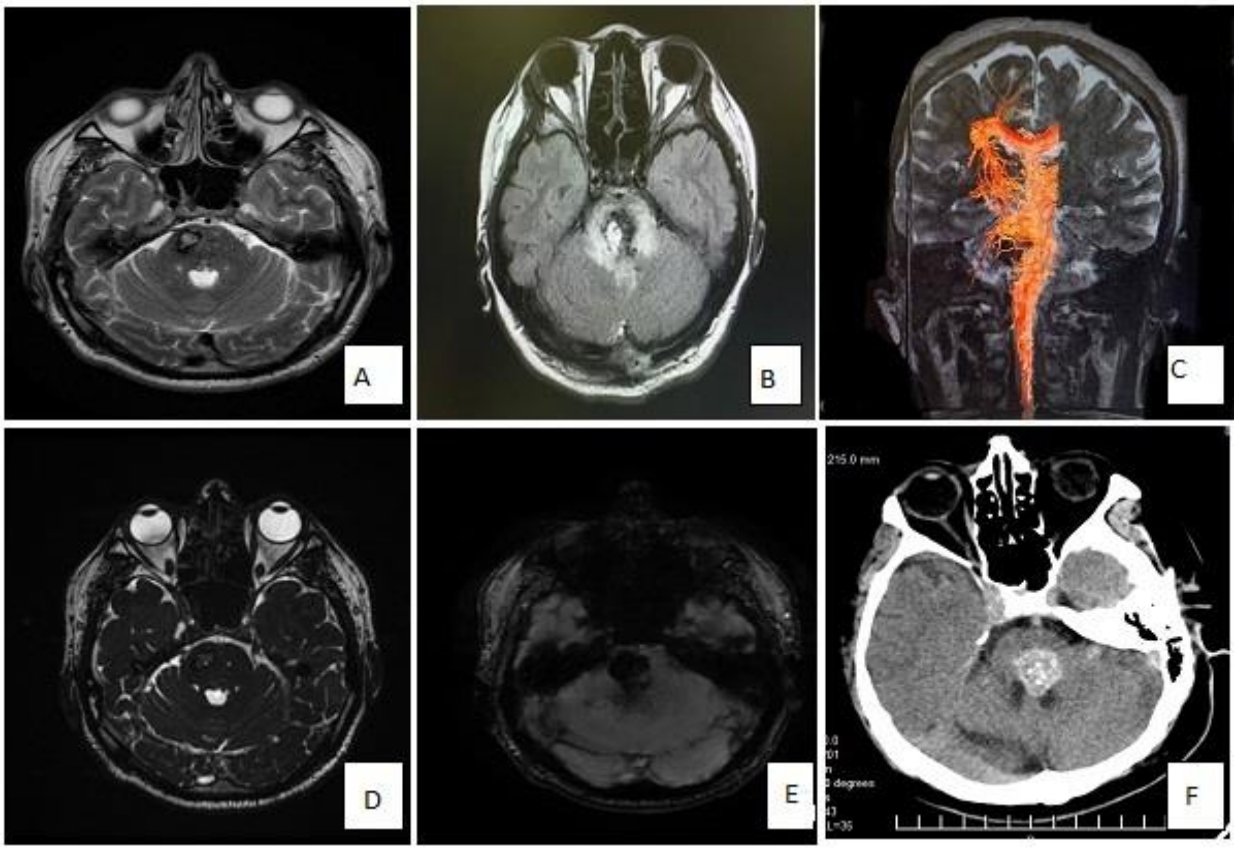

Figure 1. Interscopic diagnostic methods . a – MRI axial section T2, CM of the pons, b – MRI axial slice T1, CM with pontine hemorrhage, c – MR tractography, coronal slice, CM of the pons, d – MRI axial slice, CM of the bridge, FIESTA mode, e – MRI axial section, SWI mode, pontine cavernoma, (f) MSCT axial section, cavernoma with pontine hemorrhage.

Clinical manifestations of brainstem CM were characterized by acute development of neurological symptoms in the form of general cerebral symptoms, changes in the cranial nerves functioning (cranial nerves), cerebellar symptoms, and conduction disorders. In 2 patients, the predominant symptoms were convulsions caused by hemorrhage of the other cavernomas localized in the frontal and temporal lobes with asymptomatic course regarding CM in the pons (Table 1).

Clinical manifestations of cavernous malformations of brain stem.

Таблица 1

Symptoms	**Number of patients n -17(%)**
General cerebral symptoms (headaches, dizziness, nausea).	12 (70,6)
Focal changes in cranial nerves (paresis of the oculomotor, facial nerves)	11 (64,7)
Cerebellar symptoms (ataxia, dysdiadochokinesis)	10(58,8)
Conduction disorders (hemiparesis, hemihypesthesia)	9(52.9)
Convulsions	2(11,7)

Characteristic clinical manifestations of CM of the pons (n-16) were combined changes in CN (abducens nerve paresis in 5 (31.25%), paresis of the facial nerve in 5 (31.25%), bulbar disorders in 4 (25%) patients, hypoocusia in 1 (6.25%), facial hypesthesia in 1 (6.25%) and trigeminal neuralgia in 1 (6.25%) patient) and conduction disorders in 9 (56.25%) patients in the form of hemiparesis and semihypesthesia. Of these, 8 cases proceeded in the form of alternating symptoms. In a patient with CM localized in the midbrain, the main symptoms were cerebral symptoms with conduction disorders (hemiparesis, hemihypesthesia).

In 15 patients, according to MRI data, signs of hemorrhage of the CM of brain stem localization were determined. Studying the anamnestic data, 13 patients showed signs of repeated hemorrhage with manifestations of repeated focal brain stem symptoms. In 2 patients, with the background of hemorrhage, there was a progressive increase in symptoms with the appearance of bradycardia, so why surgical intervention was performed urgently. Whereas in 13 patients focal neurological symptoms regressed after the primary hemorrhage for quite a long time (from 4 months to 12 years).

The indications for surgical treatment were repeated hemorrhage and progressive symptoms of brainstem damage. From hospitalization to surgical treatment lasted from 1 to 4 days. Surgical removal of the CM of the brainstem was performed in 15 patients. All patients were operated on using modern methods of microsurgery. The choice of surgical approach has always been based on a thorough study of the topography of the formation according to MRI and tractography. Operational approach was carried out from the side of its closest attachment to the surface of the brainstem. In our series, to remove brainstem malformations in 5 (33.3%) cases, a median suboccipital approach was used with an approach through the IV ventricle, 9 (60%) patients underwent removal of a cavernoma through a safe interzone using a retrosigmoid approach. The lateral subtentorial supracerebellar approach was performed in the midbrain to remove the cavernoma.

The search for a malformation was greatly facilitated by the presence of posthemorrhagic changes in the brain. The cavernoma, as a rule, was clearly delimited from the medulla, which made it possible to isolate it. Internal decompression of the cavernoma by evacuating the hematoma made it possible to reduce the surgical trauma. With any localization of the cavernoma, it has always been aimed at its total removal due to the high frequency of repeated hemorrhages. Partial removal of the cavernoma was performed in one patient with background of trigeminal neuralgia with no focal brain stem changes. Microvascular decompression of the trigeminal nerve and partial removal of the cavernoma through the peritrigeminal safe interzone were performed. Removal of perifocal posthemorrhagic changes was not performed. We tried to minimize the use of coagulation. After evacuation the hematoma, additional space was formed, and the cavernous angioma was divided into fragments and removed in parts. The obtained intraoperative material was mandatory sent for histological examination, and in all cases, morphological verification of CM was obtained.

Results: Among the patients, 2 (11.76%) patients underwent surgical removal of supratentorial CM, and it was decided to dynamically observe the CM of the brain stem. The reason for this opinion was the absence of stem focal neurological symptoms and interoscopic static nature of the brain stem cavernoma in dynamics. Figure 2 shows MRI scans of one patient from 2014, 2019 and 2020.

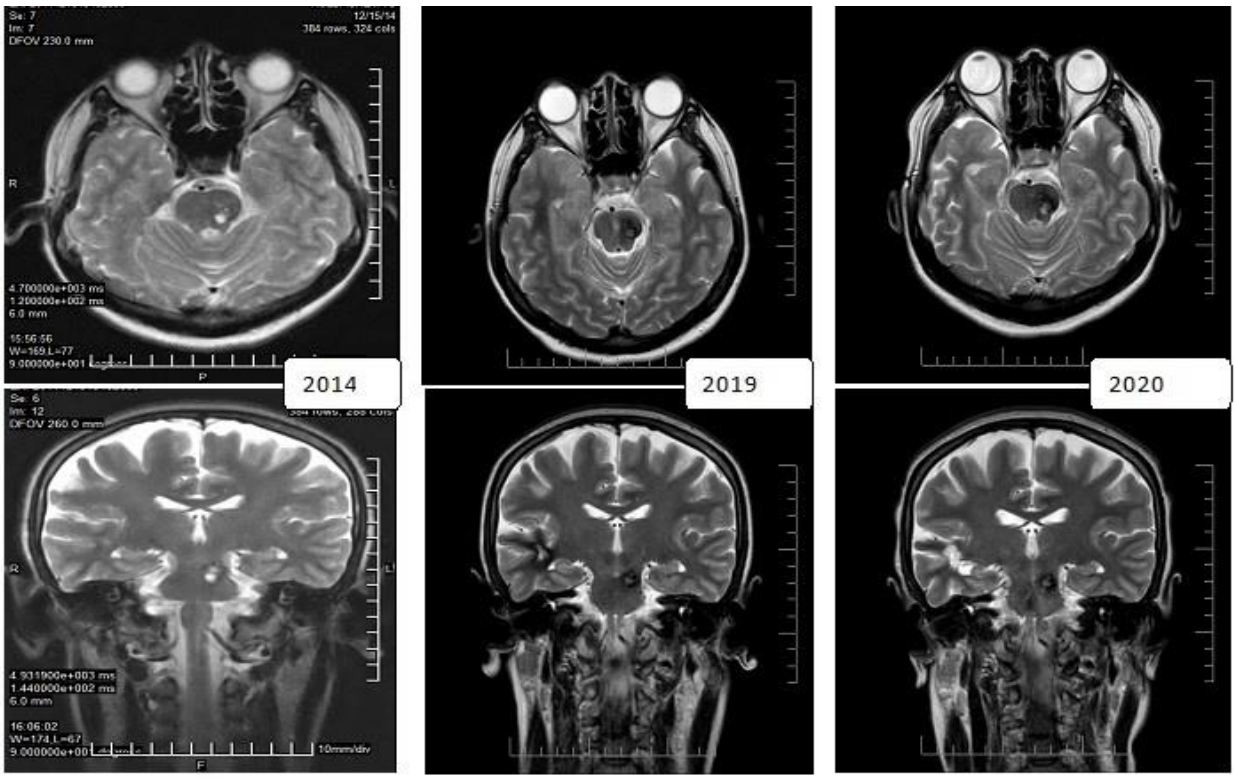

Figure 2. MRI of the brain T2, axial and coronary scans, in dynamics over 6 years (there are no data for hemorrhages of the CM of the brainstem).

Microsurgical removal of the CM of the brain stem was performed in 15 patients. At preoperative registration, in all patients who underwent BSEP, there were a slowdown in conduction at the level of CM localization with or without an ischemic component, mostly unilateral. The detection of the ischemic component correlated with the severity of neurological stem symptoms.

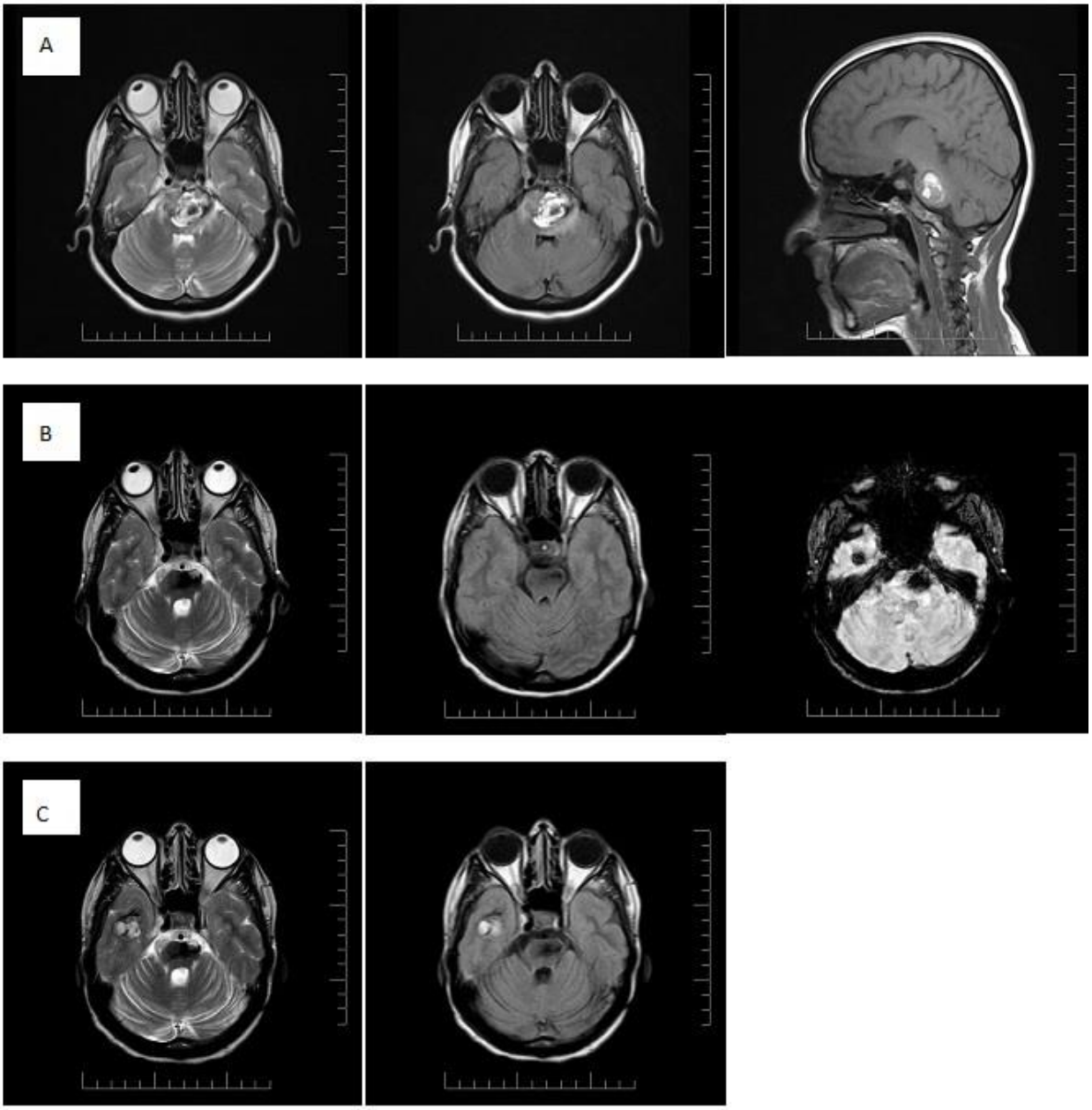

Figure 3. a – MRI of the brain before surgery (signs of cavernoma with hemorrhage of the pons). b - MRI of the brain 6 months after surgery (signs of total removal of the pontine cavernoma, left temporal cavernoma). c- MRI of the brain a year after the operation (signs of total removal of the pontine cavernoma and signs of hemorrhage of the cavernoma of the left (right) temporal lobe.

In 4 patients, surgical treatment was carried out urgently, due to the progressive deterioration of neurological symptoms and the appearance of bradycardia. In 14 (93.3%) patients, a total removal of the BM was performed (Figure 3). In the early postoperative period, only 2 (13.3%) patients had a severe postoperative course with a deepening and the appearance of new focal brainstem neurological symptoms. During the first 4-5 days, feeding was carried out through a nasogastric tube, due to the lack of swallowing. There were no lethal outcomes in the postoperative period. At discharge, the condition of the patients was assessed using the Rankin scale (Appendix 2). At the time of discharge, 8 (53.3%) patients had no significant impairment of life (Rankin 1), mild impairment (Rankin 2) was in 3 patients (20%), moderate (Rankin 3) - in 1 (6.6%), expressed (Rankin 4) – in 3 (20%).

Follow-up was collected in 11 patients, and ranged from 6 months to 3 years. In the dynamics, there is a regression of clinical symptoms in most patients. A characteristic feature was the regression of conduction disorders and peripheral disorders of cranial nerves (CN). Cerebellar changes and nuclear lesions of CN persisted as a persistent disorder.

Discussion. Clinical symptoms of CM during its manifestation occur acutely, mainly at the age of 20 to 50 years (mean age 32 years) [6,9], the patients of our group were younger, even child age. The risk of hemorrhage increases with younger age[4,5]. The main clinical manifestations depend on the location of the CM in the brain stem and the amount of hemorrhage. The leading clinical manifestations of stem CM were cerebral, cerebellar, conduction changes and dysfunction of IV, V, VI, VII–X pairs of cranial nerves [1,2,13,15], all of which were also observed in our study.

Considering the localization and manifestation of neurological symptoms after the surgical period, we proposed surgical treatment for repeated hemorrhages of the brainstem cavernoma, and for progressive worsening of neurological symptoms. Since neurological symptoms from primary hemorrhage are well treated conservatively with the achievement of complete regression of symptoms [7,9,13]. The chosen surgical strategy coincides with the opinion of other authors that CMs of the brainstem are prone to bleed in varying severity and this requires more active surgical tactics [6]. Today, well studied, developed and put into practice microsurgical approaches to the brainstem regions allow for low-traumatic and radical removal of BM.

In our series of surgical treatment of pons CMs, better results were observed with lateral approaches through safe interzones compared with median access to the CM, and there was more regression of neurological symptoms over time. In all cases, we planned and applied microsurgical approaches, taking into account localization, anatomical accessibility and the least adherence to the surface of the brainstem, using microsurgical techniques. This made it possible to achieve zero mortality with good functional outcomes in 80% of cases according to the Rankin Disability Scale [6], and patients were discharged from the hospital without additional neurological symptoms in more than 50% of cases.

Conclusions: 1. The indication for surgical removal of CM of stem structures is the progression of focal neurological and stem symptoms and/or recurrent hemorrhage.

2. Microsurgical removal of CMs of stem structures is a reliable method for preventing hemorrhage, which allows achieving good functional results in operated patients without postoperative mortality.

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