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FEATURES OF THE CLINICAL COURSE OF CAVERNOUS MALFORMATIONS OF THE BRAIN IN CHILDREN

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Abstract:

Cavernous malformations (CM, cavernomas, cavernous angiomas) of central nervous system represent one of the vascular malformations options, which may form in various locations brain and spinal cord. The spectrum of clinical manifestations of this pathology quite wide - from asymptomatic carriage to severe rebleeding leading to disability or death of the patient. Thanks to ubiquity and technical improvement of modern neuroimaging methods, cavernous malformations of various parts of CNS are found more and more often, and the flow of patients to neurologists and neurosurgeons with this diagnosis, constantly increases. However, cavernomas remain rare disease, diversity of its clinical manifestations and course, complicates right choice of patient management, especially in small neurosurgical departments, with not enough sufficient experience in the treatment of this pathology.

Keywords: Cavernous malformations, cavernomas, children, electroencephalography, epilepsy, microsurgical treatment.

The presented article is aimed at studying features of cavernous malformations' clinical course in children. The article presents a discussion ofstudy results of medical examination, diagnostic methods, treatment results of 31 treated children presented in medical documents for the period of 2014-2021. The discussion presents opinions of various authors identified inliterature study of the pathology, differences from our observations and the results of their own research.

Cavernous malformations (CM) are angiographically occult vascular malformations of the central nervous system (CNS) with low blood flow, which can form in various parts of the central nervous system and occur with single and multiple manifestations [1,7,13]. CNS cavernomas can present clinically at any age, from infancy to the elderly. 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. There are several theories of the formation of CMs of the central nervous system: congenital, genetically determined, radiation-induced [11, 13]. Cerebral CMs occur in up to 0.5% of the total population [4,13]. 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 [1,5,11]. Among all vascular anomalies of the CNS in children, cavernomas range from 18 to 42%. According to many scientists, CMs in children (compared to adults) are characterized by a more pronounced hemorrhagic potential with the formation of intracerebral hematomas. The peak of detection of this pathology falls on the younger and older children's age.

PURPOSE OF THE STUDY

To study the features of cavernous malformations' clinical course in children.

MATERIAL AND METHODS

The study included 31 operated patients with cerebral CM aged 6 to 18 years, who were treated in the Republican Specialized Scientific and Practical Medical Center of Neurosurgery for the period 2014-2021. There were 18 boys, 13 girls. Among patients with CM (cavernous malformations) of supratentorial localization prevailed - 27 (87%), subtentorial - 2 (6.5%), multiple - 2 (6.5%). Table 1 shows the distribution of patients by CM localization.

Table 1
Distribution of patients by localization

Localization	Quantity	Ratio
Supratentorial	**27**	**87%**
Cavernomas of the frontal lobe	10	32,2%
Cavernous malformations of the temporal lobe	8	25,8%
Cavernous malformations of the parietal lobe	5	16,1%
Cavernomasofthethalamus	3	9,7%
Cavernous malformations of the occipital lobe	1	3,2%
Subtentorial	**2**	**4,5%**

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Cavernous malformations of the trunk	**1**	2,25%
Cerebellarcavernomas	1	2,25 %
Multiple cavernomas	**2**	**4,5%**

Neurological examination revealed cerebral symptoms, the presence of convulsions and focal signs of central nervous system damage. Cerebral syndrome in form of acute headache of varying intensity was diagnosed in children without disturbed wakefulness or its suppression to the point of stunning. Meningeal syndrome was considered positive if the patient had stiff neck and positive symptoms of Kernig, Brudzinsky. The time and features of convulsive syndrome appearance, the results of conservative treatment were revealed. To determine the type of seizures in patients with structural (symptomatic) epilepsy, a variant of the international classification of epileptic seizures was used. Epileptic seizures were divided into focal and generalized. Symptoms of damage to supratentorial and subtentorial structures of the brain, motor and sensory disorders were revealed. With subtentorial localization of cavernomas, special attention was paid to the study of the functions of the cranial nerves and cerebellar symptoms.

All patients underwent MRI of the brain before surgery and MSCT of the brain in the postoperative period. MSCT and angiographic diagnostic methods were also subjected. Electroencephalography (EEG) and acoustic evoking stem potentials (AESP) were performed in 26 patients using neurophysiological methods.

In this patient, microsurgical removal of CMs. The main indications for surgical treatment were signs of hemorrhage with or without focal neurological symptoms and convulsions.

RESULTS AND DISCUSSION

In study of patients, in 23 (74.1%) cases, the prevailing symptoms were convulsions, focal neurological deficit 6 (19.5%), acute headaches 2 (6.5%). Generalized convulsions were noted in 21 (64.5%) cases, and rare seizures waried in frequency of seizures, which accounted for 96.8% of cases. The duration of the epileptic history was also taken into account. It ranged from 1 month to 9 years, with an average of 7 months length. Of the 25 patients who underwent EEG before the operation without an attack, only 10 (40%) had epileptic activity, and in 4 epileptic activity was based on the proportions of the cavernoma localization. In 3 patients, epileptic activity originated from the median structures, in the rest patients it coincided with the side of the CM localization. In the rest of the children, the EEG revealed the phenomenon of cortical irritation in the form of dysfunction and cerebral changes. During epileptic history study, it was revealed that the duration of the epileptic history does not affect the formation of epileptic activity in the cortex, perhaps anticonvulsant therapy takes place here.

Focal neurological deficit in patients was associated with acute hemorrhage, deep (thalamic and stem) localization of caverns. In neuroradiological studies in 15 patients, signs of hemorrhage were revealed, which is typical for type 1 cavernomas according to Zabramsky's classification.

Hidden cavernomaswere found in children with multiple cavernous malformations in special SWI or SWON sequences. MSCT of the brain was performed in all patients in the postoperative period and in 8 patients before surgery in order to detect acute hematoma. Angiographic examination was prescribed in 8 patients for the purpose of differential diagnosis of other malformations of cerebral vessels. Figure 2 shows scans of neuroimaging methods applicable in the diagnosis of CM

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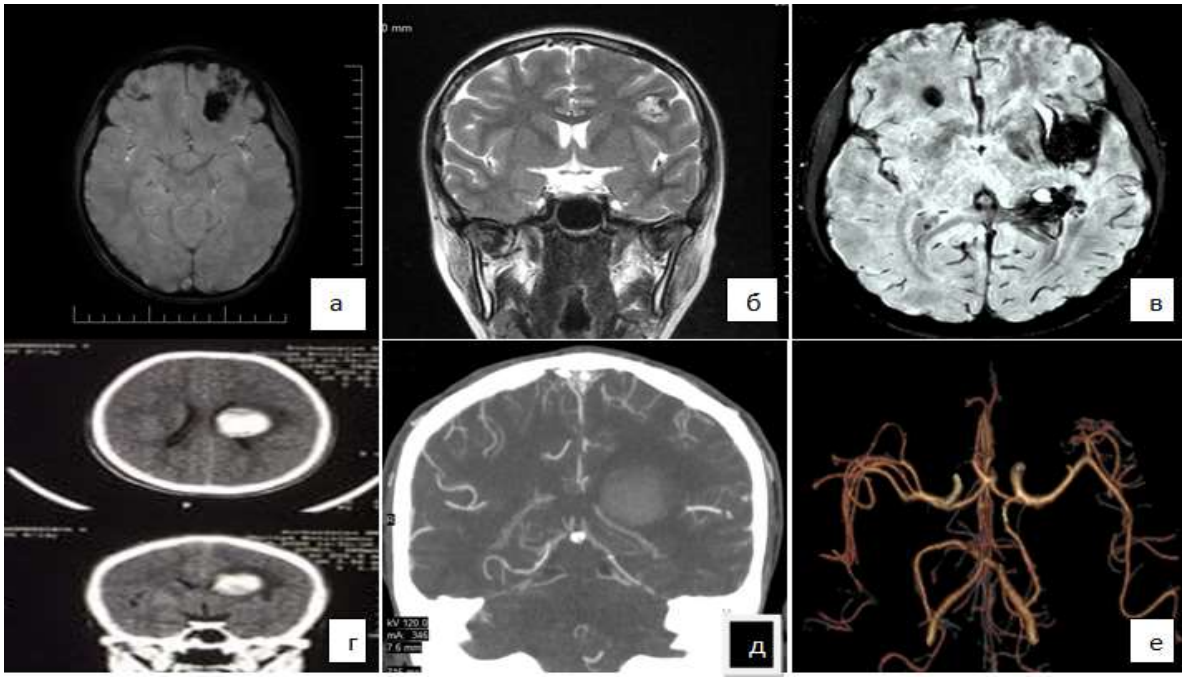

Figure 2. a) MRI axial section, Flair mode, cavernoma of the left frontal lobe. b) MRI coronary slice, T2 mode, cavernoma of the left frontal lobe. c) MRI axial section, SWI mode, multiple brain cavernomas. Cavernoma with hemorrhage of the left frontotemporal and parietal regions and cavernoma (Type IV) of the right frontal lobe. d) MSCT of the brain, axial and coronal sections, cavernoma with hemorrhage of the left thalamic region. e) MSCT angiography of cerebral vessels. f) MSCT angiography, 3D reconstruction of cerebral vessels.

All patients underwent surgical treatment of CM. The indication for surgical treatment of CM was the presence of a seizure, MRI data, signs of CM hemorrhage. When planning surgery, we analyzed the topographic relationship of CM to anatomical landmarks based on MRI images. At the stage of soft tissue incision and craniotomy, we took into account extracranial anatomical landmarks - coronary, sagittal, lambdoid sutures, occipital protuberance, mastoid process, external auditory canal, upper wall of the orbit, nasion, inion, pterion. At the stage of corticotomy, the trajectory was chosen taking into account intracranial landmarks - the superior sagittal, transverse sinuses and sinus duct, the veins of Troland and Labbe, the lateral and central sulci, and the convolutions of the lobes. This approach helped to find and remove CM with high accuracy in 30 (96.7%) patients. Depending on the depth and size of the cavernomas, we tended to take a transsulcant approach to the focus. Detection of yellow pigmentation in the area of dissection is a reliable sign indicating the approach to the cavernoma. Upon detection, a circular dissection of the CM was performed. A revision of the cavity of the removed cavernomawas necessarily carried out in order to exclude small satellite foci. In functionally insignificant areas, the dissection of the surrounding pigmented tissue and the glial zone was maximally performed. In case of localization of cavernomas in functionally significant parts of the brain, the removal of the cavernoma was limited with minimal use of bipolar coagulation. Fragments of removed malformations and surrounding glial tissue were sent for histological examination. During microsurgical removal of the cavernoma under the control of intraoperative neuromonitoring and corticography, the surrounding glial tissue, hematomas in different decay evolutions, and tissues impregnated with hemoglobin metabolites were also removed. All patients were discharged on the 7-10th day after the operation, no lethal outcomes were observed.

Analyzing histological structure of CM, 3 types of CM were identified, which is shown in Figure 3. In our observations, type I (classic) is a cavernoma, consisting of closely adjacent caverns, in the walls of which there are no muscle and elastic fibers. There are no layers of brain tissue between the caverns. The cavernoma has a clear border with the brain and a capsule. This variant was the most common and accounted for 83.8% of all cavities. Type II (mixed) is characterized by the fact that, along with tissue typical of cavernoma, poorly differentiated vessels are found, with layers of brain tissue between them. The frequency of cavernomas of this type was 13%. Type

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III (proliferative) is characterized by the presence of microscopic areas of pronounced cell (endothelial) proliferation in the CM tissue. These microfoci resemble the structure of a capillary hemangioma. This type of CM was very rare - 3.2% of cases

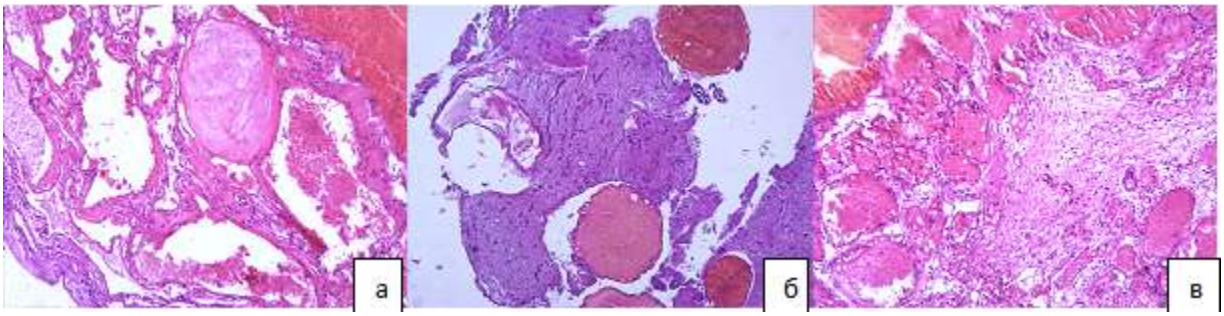

Figure 3. a) Vascular cavities of various sizes, filled with blood and separated by connective tissue septa. Consisting of closely adjacent caverns, there is no muscle and elastic fibers, the basement membrane, on which the endothelium with dystrophic changes is located. b) Pathological vessels with a deformed capillary, cavities of various sizes, filled with blood, lined with a single layer of endothelium, dystrophic changes, with layers of brain tissue between them. c) Vascular cavities of various sizes, filled with blood, lined with a single layer of endothelium, in which intercellular connections and interstitium are defective. The basement membrane, on which the endothelium is located, is also characterized by pathological changes and reactive gliosis.
Hematoxylin-eosin stain. SW. 100

Studying the catamnesis, it was revealed that convulsions were not observed in 93.1% of patients during the first 6 months, in 2 patients who had a convulsive anamnesis for more than 2 years, convulsions were noted after the surgical period, but with a significant regression of frequency. In 79.3% of patients, anticonvulsant therapy was canceled based on EEG data within 1 year after surgery. In 2 patients, focal neurological deficit persisted in the form of hemisymptomatics, which was associated with hemorrhage, and some regression was noted after surgery.

CONCLUSION

Prevailing symptoms of CM in children are convulsions, focal neurological disorders and headaches. Children with CM are more prone to hemorrhage than adults. Microsurgical removal of cavernomas and their surrounding complications is 93.1% effective in treating epilepsy due to CM.

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