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Surgery for enlarged perivascular spaces: primary experience

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ABSTRACT

Perivascular spaces are cavities surrounding cerebral and spinal cord vessels and filled with cerebrospinal or intercellular fluid. Abnormal enlargement of these spaces can lead to neurological symptoms. Currently, there are no clear approaches to surgical treatment of this pathology. We set ourselves the task of analyzing the literature data, as well as presenting own clinical observations and sharing the experience of microsurgical treatment of this pathology.

Material and methods. We reviewed the PubMed databases between 2009 and 2024. We analyzed own small sample (*n*=5) of patients with dilated perivascular spaces who underwent microsurgical treatment between 2009 and 2024. Four patients underwent microsurgical cystoventriculostomy, one patient — microsurgical cystocysternostomy and biopsy.

Results. Microsurgical cystoventriculostomy and cyst drainage were less effective than expected. Four out of five patients developed new neurological symptoms after surgery, while baseline symptoms did not significantly regress.

Conclusion. To date, cerebrospinal fluid shunting is still the main surgical method for dilated perivascular spaces accompanied by intracranial hypertension.

Keywords: *Virchow-Robin spaces, dilated Virchow-Robin spaces, dilated perivascular spaces, surgical treatment of dilated perivascular spaces, pathologically dilated perivascular spaces.*

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Abbreviations

DWI — diffusion-weighted imaging
MRI — magnetic resonance imaging
VRS — Virchow-Robin spaces
PVS — perivascular spaces
CSF — cerebrospinal fluid

Introduction

Perivascular spaces, known as Virchow-Robin spaces, surround vessels throughout their course from subarachnoid space through brain parenchyma. These spaces are filled with cerebrospinal fluid or interstitial fluid. They are a part of normal anatomy of the central nervous system.

They are usually less than 2 mm in diameter. However, they dilate in 7.7—9.2% of cases for unclear reasons and can lead to neurological symptoms [1, 2].

Due to small incidence and unclear pathophysiological mechanisms, treatment of dilated perivascular spaces is still a subject of discussion [3—5].

In this article, we present own experience of microsurgical treatment of this pathology in addition to literature review.

Material and methods

We reviewed the Medline database (via Pubmed) using the keywords "symptomatic giant Virchow—Robin spaces", "treatment of giant Virchow—Robin spaces", "treatment of symptomatic giant Virchow—Robin spaces", "treatment of perivascular space enlargement in brain". Due to small incidence of this pathology and small number of appropriate studies, we expanded the period from 2009 to 2024. Earlier articles of particular scientific value were separately included in analysis [6—8].

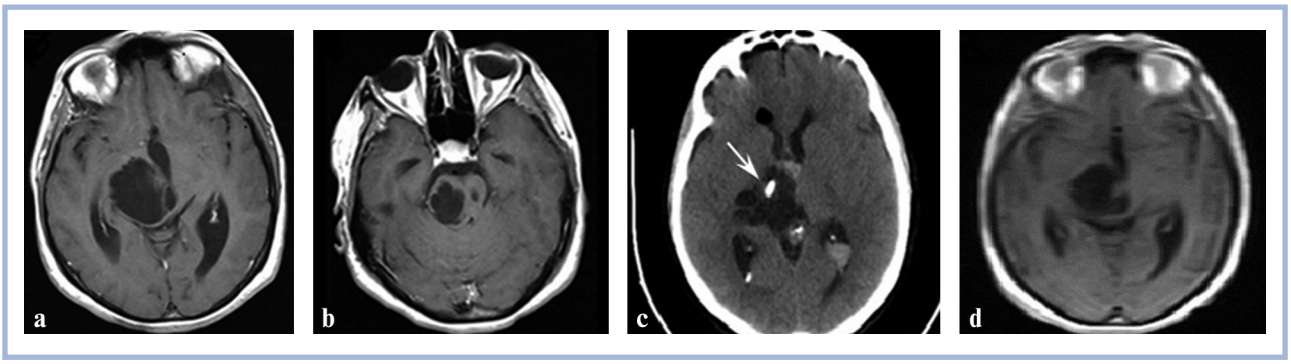


Fig. 1. **Enlarged perivascular spaces of thalamus and brainstem on the right.**
a, b — T2WI Ax (a) and T1WI+contr. Ax (b) — polycystic lesion not accumulating contrast agent; c — CT after surgery, catheter in the cyst of the right thalamus (arrow); d — T1WI Ax in 3 months after surgery, shrinkage of the cyst of the right thalamus.

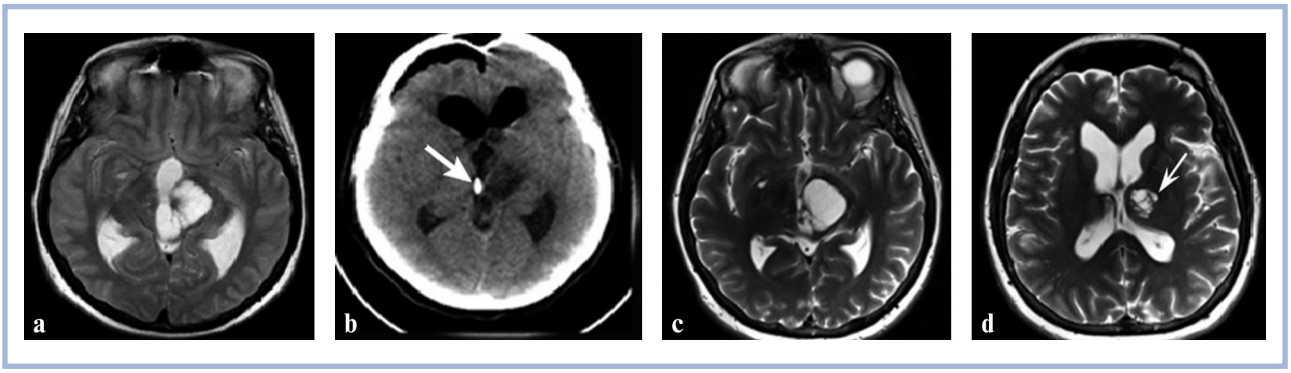


Fig. 2. **Enlarged periventricular spaces of thalamus and midbrain on the left.**
a — T2-FLAIR Ax before surgery: thalamic cyst on the left with dilated ventricles; b — CT on the first day after surgery: shrinkage of the cyst of the left thalamus, stent in cerebral aqueduct (arrow); c, d — T2WI Ax in 6 months after surgery: enlargement of cystic cavity of the left thalamus with restoration of normal dimensions of brain ventricles (c); appearance of new cystic cavities (arrow) (d).

Among 57 primary manuscripts, we excluded non-English-language reports and articles not related to our issue. A total of 30 studies were analyzed. Systematic review was not performed due to small number of studies, as well as small and heterogeneous patient groups.

We analyzed 5 with dilated perivascular spaces between 2009 and 2024. All patients were female aged 35—64 years (median 45 years). Each patient underwent a thorough preoperative clinical and radiological examination. Mean follow-up period was five years (range 1—14).

Results

In four cases, preliminary clinical diagnosis of dilated perivascular spaces was straightforward and based on MRI data (conglomerate of cysts in the midbrain, thalamus and ponto-mesencephalic junction not accumulating contrast agent). Signal from cystic contents corresponded to CSF intensity. In DWI mode, diffusion was not limited. Brain matter surrounding the cysts had normal signal intensity **(Fig. 1 a, b, Fig. 2 a, b)**.

In one case, MRI picture was atypical. Disjointed cysts in the right half of the pons, middle cerebellar peduncle and lateral cistern caused deformation and enlargement of the brainstem. This required differential diagnosis of possible cystic neoplasms.

In most patients, symptoms developed slowly. Thus, mean duration of disease in our series was 34 months (range 2—156). Only in one case, symptoms (weakness in the right limb and numbness in the right half of the body) occurred quickly. Thus, stroke was suspected.

Upon admission, moderate symptoms of damage to conduction pathways and extrapyramidal system prevailed. If the process was localized in the pons, symptoms of damage to cranial nerve nuclei of pontine tegmentum prevailed. Mean KS before surgery was 80 points **(Table)**.

Surgical intervention consisted of microsurgical perforation of cysts. In four cases, surgery was performed through anterior interhemispheric transcallosal approach. Microsurgical cystoventriculostomy was performed. In 2 cases, cystoventriculostomy was combined with drainage of large cysts into ventricular system through silicone catheters. Two patients required insertion of silicone stent into cerebral aqueduct for occlusive hydrocephalus.

The patient with dilated PVS of the pons and middle cerebellar peduncle underwent cyst perforation and biopsy of their wall via median suboccipital craniotomy. Histo-

Patients with dilated perivascular spaces between 2009 and 2024

No.	Anamnesis	Symptoms Karnofsky score	Surgery	After surgery	Follow-up
1	4 months	Paresis V, VI, VII, ataxia KS 80	Cyst perforation+biopsy	Deterioration. Progression of VI, VII nerve paresis and ataxia. Sensitivity disorders, KS 70	Deterioration KS 60
2	8 months	Hemiparesis 4 score, hemihypesthesia, ataxia KS 70	Drainage of thalamic cyst	No changes KS 70	No changes KS 70
3	2 months	Kinetic tremor KS 80	Drainage of thalamus and midbrain cysts	Multidirectional. Regression of tremor; III nerve paresis, KS 70	No changes KS 70
4	156 months	ICP, kinetic tremor KS 80	Cyst perforation t+aqueduct stenting	Multidirectional. Regression of tremor, ICH VI nerve paresis, memory disorders, KS 70	Deterioration KS 70
5	2 months	ICP, ataxia KS 80	Cyst perforation t+aqueduct stenting	Multidirectional. Regression of ICH III nerve paresis, KS 60	No changes KS 60

logical analysis revealed glial and ependymal cells, as well as areas resembling astrocytoma. Considering morphological data, we scheduled distant gamma therapy after surgery (total focal dose 60 Gy). Combined treatment worsened clinical status in early and late postoperative period. The patient developed facial nerve insufficiency, horizontal eye movement disorder, sensitivity disorders, mnestic disorders and aggravated brainstem vestibular disorders.

In one case of perforation and drainage of the largest thalamic cyst, there were no neurological in immediate and late period. In three cases, neurological changes in early postoperative period were multidirectional due to regression of intracranial hypertension and kinetic tremor together with new paresis of the oculomotor nerve (n=2), abducens nerve (n=1) and fixation amnesia (n=1). Although oculomotor nerve insufficiency decreased in delayed period, these disorders did not disappear. This complicated self-care. Mnestic disorders that appeared after surgery worsened even in late postoperative period. In addition, kinetic tremor returned to preoperative level in this patient. Mean KS in late postoperative period was 70 points **(Table)**.

According to MRI data, drainage of large cysts decreased their size in delayed postoperative period (n=2). The volume of cysts without drainage was the same **(Fig. 1 c, d)**. The volume of cysts did not decrease after cystoventriculostomy without drainage (n=2). In addition, new dilated PVS appeared **(Fig. 2 c, d)**. Dimensions of ventricular system did not change in two patients after cerebral aqueduct stenting. There were no clinical signs of intracranial hypertension. Dimensions and number of cysts remained the same after combined treatment in a patient with dilated pontine PVS.

Discussion

In 1843, Durand-Fardel M. first mentioned perivascular spaces in brain and spinal cord parenchyma [6]. Detailed research of PVS began with the work of R. Virchow in 1851 and C.F. Robin in 1859.

Presumably, these spaces may be important for CNS metabolism as a part of lymphatic system. Despite their importance, these structures remain poorly understood. Biochemical composition of PVS content, communication with subarachnoid space, as well as causes and mechanisms of their possible enlargement are still unclear [3, 9].

Currently, there are several theories explaining PVS enlargement: segmental necrotic angiitis increasing vascular wall permeability; brain matter atrophy and spiral elongation of the vessels; impaired drainage of interstitial fluid; leakage of interstitial fluid into pial space around arterioles [10—17].

PVS enlargement leads to neurological symptoms in 55—60% of cases. Clinical manifestations are determined exclusively by localization of the process. There are 3 types of dilated PVS depending on topography: the first type along the lenticulostrial arteries; the second type along the arteries of the corona radiata passing from the cerebral cortex into the depths of the white matter; the third type in the midbrain and ponto-mesencephalic region around the penetrating branches of the collicular and accessory collicular arteries [4, 7].

The last type of dilated spaces is most often the cause of neurological symptoms. Midbrain cysts not only cause cerebral aqueduct compression and symptoms of intracranial hypertension [3, 15], but also contribute to focal symptoms due to effect on extrapyramidal system and conduction pathways [8, 18, 19]. All our patients had the third type of dilated PVS.

Typical MR pattern of cystic clusters not accumulating contrast agent with intensity of signal from content similar to CSF is key for diagnosis of dilated PVS [20, 21]. However, differential diagnosis with neuroepithelial cysts, neurocysticercosis, lacunar stroke, periventricular leukomalacia and mucopolysaccharidosis is necessary.

In one case, MRI pattern was less typical for dilated PVS. Incorrect interpretation of radiological and histological data led to erroneous radiotherapy that worsened clinical status.

To date, there is no unified treatment strategy, but surgical intervention is recommended only in symptomatic patients. The main surgical methods are cerebrospinal fluid shunting, microsurgical and endoscopic cystoventriculostomy and cysternostomy. Although the effectiveness of the latter is not confirmed, endoscopic interven-

tion is preferable to microsurgical due to less invasiveness with possible simultaneous various procedures, including triventriculostomy, cystoventriculostomy and, if necessary, biopsy [1—3, 5, 22, 23].

Microsurgical intervention was performed in our patients. In one case, it was necessary due to localization of cysts within the pons. In two cases, cyst wall excision was accompanied by their drainage into ventricular system. Insertion of silicone stent into aqueduct was performed in 2 cases.

Results of microsurgical drainage of dilated PVS demonstrated insufficient effectiveness of this method. Cyst shrinkage did not significantly improve clinical status of patients. In addition, four patients developed additional neurological symptoms after surgery. These disorders persisted in delayed postoperative period.

In two cases, clinical status improved after aqueduct stenting due to ICP decrease. However, postoperative oculomotor disorders worsened self-care capabilities.

Importantly, cyst shrinkage after drainage did not decrease total volume and number of dilated PVSs. This pattern is described in the literature and indicates that cavities in dilated PVS are isolated and have no connection with each other. Drainage of one or even several cavities does not lead to shrinkage of others [1—3, 5, 21, 23, 24].

The causes of new neurological symptoms after cyst perforation are still unclear. Perhaps, the walls of dilated PVS, unlike arachnoid and ependymal cysts, initially represent the brain substance. The last one becomes thinner due to slow enlargement of cavities, but continues to play a functional role. Its intraoperative damage leads to new neurological symptoms.

Conclusion

To date, the causes and mechanisms of PVS enlargement are still unclear. This complicates effective approaches to treatment. Cerebrospinal fluid shunting is recommended for intracranial hypertension. Microsurgical cystoventriculostomy can lead to temporary regression of baseline focal symptoms. At the same time, this procedure may be followed by new persistent symptoms.

Author contribution:
Concept and design of the study — Veselkov A.A., Maryashev S.A., Gavryushin A.V.
Collection and analysis of data — Veselkov A.A., Bekhtereva T.L.
Writing the text — Veselkov A.A., Gavryushin A.V.
Editing — Konovalov A.N., Gavryushin A.V., Pitskhelauri D.I., Maryashev S.A., Veselkov A.A.

The authors declare no conflicts of interest.

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COMMENT

The authors analyzed own results of surgical treatment of a rare disease. They rightly conclude no clear approaches to surgical treatment of this pathology. The causes of PVS enlargement are unclear, and modern data on pathophysiological mechanisms are not fully studied. Similar analyses are rare in the literature. The difficulties of diagnosis and treatment are obvious. A new report allows us to take a fresh look at this rare problem and develop new patterns of process, as well as options for surgical interventions. The manuscript is obviously interesting for neurologists, neurosurgeons and radiologists.

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