CLINICAL CASE

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HYPERTROPHIC PACHYMENINGITIS AS A RARE CAUSE OF HEADACHES: A CLINICAL CASE

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The article presents a description of the clinical case of a 62-year-old woman who had been suffering from headaches for 5 months. MRI of the brain revealed pachymeningeal enhancement, especially in frontal-parietal regions, and tentorium cerebellum. Based on the clinical picture and neuroimaging data, the patient was diagnosed with idiopathic hypertrophic pachymeningitis. Corticosteroid therapy resulted in regression of pain and reduction of MRI changes. The article also discusses the difficulties of differential diagnostics of hypertrophic pachymeningitis with other diseases, which can be imitated by clinical picture and changes on MRI images.

Keywords: hypertrophic pachymeningitis, dura mater, headache, meningeal signs.

Introduction. Hypertrophic pachymeningitis (HPM) is a rare disease resulting from localized or diffuse thickening of the dura mater of the brain and/or spinal cord [9]. The most frequent manifestations of HPM are headaches, cranial neuropathies, and less frequently focal symptoms [5].

According to pathogenesis, HPM can be primary and secondary. Secondary forms of HPM develop in infectious and non-infectious diseases. Infectious causes include tuberculosis, fungal infections, Lyme disease, syphilis; and noninfectious HPM can develop in systemic inflammatory diseases such as granulomatosis, rheumatoid arthritis, systemic lupus erythematosus, sarcoidosis, IgG4-associated diseases, and neoplastic processes. Primary (idiopathic) HPM is diagnosed in the absence of causative factors [9, 12].

The prevalence of HPM is unknown, and scientific data on the disease are based on single clinical observations.

The aim of the study is to describe our own clinical case of a patient diagnosed with HPM on the basis of clinical and neuroimaging data and to discuss the difficulties of differential diagnosis of this disease.

Clinical part. A 62-year-old woman, accountant, living in a rural area, was hospitalized in the neurological department with complaints of constant severe headaches in the occipital region, right temporal region of compressive, aching, pulsating character (VAS = 5-6 points), non-systemic dizziness, unsteadiness when walking, interrupted sleep and increased fatigability.

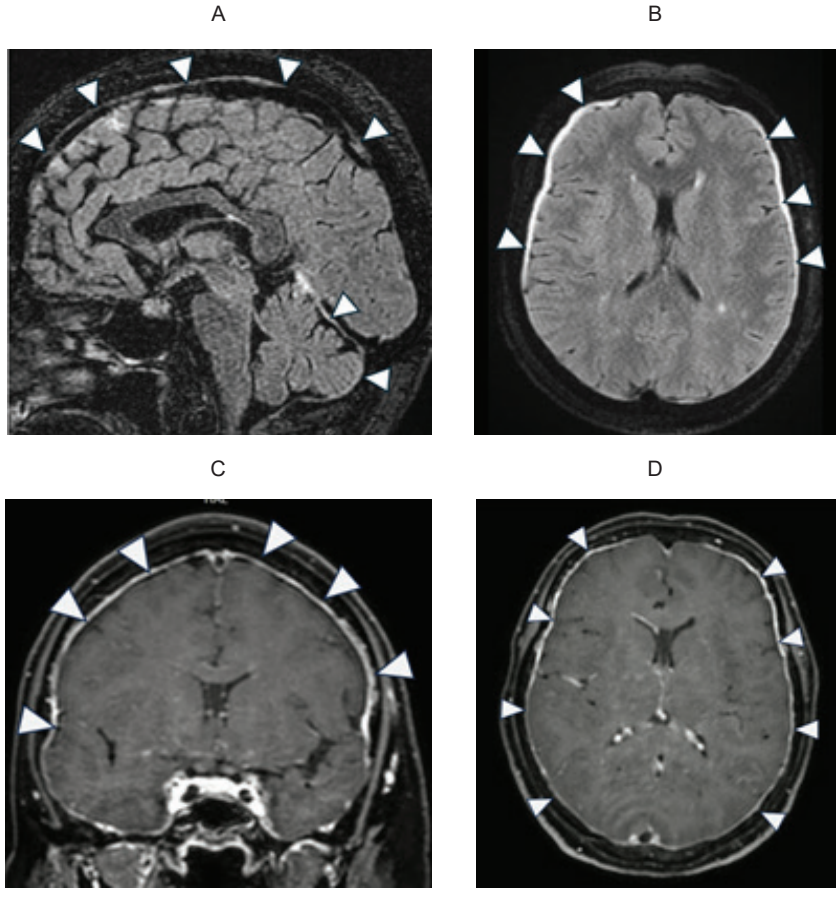

Fig. 1. Brain MRI of the patient (2 months after the onset): A (sagittal), B (axial) – FLAIR images showing higher signal from the dura mater and the tentorium of cerebellum; C, D – post-contrast pachymeningeal enhancement. Arrows indicate the corresponding changes in FLAIR images an increase in the signal from the dura mater is determined, mainly in the fronto-parietal regions, and the tentorium of the cerebellum; C, D – contrast enhancement reveals a uniform accumulation of contrast in the meninges and tentorium of the cerebellum. Arrows indicate the corresponding changes.

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5 months ago, she first felt soreness and stiffness in her neck area, which she attributed to high blood pressure. A few days later she developed severe headaches of compressive character, mainly in the occipital region (VAS = 7-8 points). The woman had not practically suffered from headaches before; she rarely experienced pressing headaches, which were quickly relieved; she attributed them to increased blood pressure, sleep disorders or stress. The real headaches were constant, intensified by turning, head tilting, pushing, not accompanied by nausea, vomiting, but the patient noted photo- and phonophobia. The patient also had disturbed sleep and developed increased fatigue, and her work capacity decreased sharply.

The patient did not receive treatment. After 2 months, she underwent a contrast-enhanced magnetic resonance imaging (MRI) of the brain, which revealed pachymeningeal enhancement (Fig. 1).

Despite the MRI results, the patient consulted a neurologist only one month later, but the clinical manifestations and head MRI changes were associated with vascular encephalopathy. Neurometabolic therapy was prescribed, which did not lead to improvement.

She also underwent an ultrasound examination of the carotid and vertebral arteries, which revealed stenosis of the left common carotid artery up to 32%. She also independently visited an ophthalmologist and was diagnosed with hypertensive retinal angiopathy, myopia, presbyopia.

Due to persisting headaches in the 5th month from the moment of the disease she was referred to the vascular center. After exclusion of stroke, the patient was transferred to the neurological department.

Chronic diseases: hypertension; chronic heart failure; stenotic atherosclerosis of carotid arteries.

Constant intake of medications: amlodipine 5 mg/day, azilsartan medoxomil 20 mg/day.

On objective examination: condition of average severity. The skin is of normal color. Peripheral lymph nodes are not enlarged, painless. Respiration in the lungs is vesicular, no rales. Cardiac tones rhythmic, muffled. Blood pressure 130 / 80 mm Hg, heart rate - 88 beats per min. The abdomen is soft, painless. Urination is regular.

In the neurological status at the time of admission to the department, no focal symptoms were detected, mild rigidity of occipital muscles, Kernig's symptom 60. On the MoCA scale - 28 / 30 points (normal), HADS-D (depression) - 5 points (normal), HADS-A (anxiety) - 7 points (normal).

Laboratory blood tests without inflammatory changes, the biochemical blood test showed signs of dyslipidemia (increase in total cholesterol to 6.66 mmol/L, triglycerides to 2.98 mmol/L, with normal values of LDL and HDL).

MRI of the brain with contrast-enhanced gadolinium revealed previously detected signs of dura mater thickening; it was recommended to differentiate intracranial hypotension, hypertrophic pachymeningitis and neurosarcoidosis.

General and biochemical analyses of cerebrospinal fluid did not reveal pathology.

After lumbar puncture, the patient subjectively noted a short-term improvement, but headaches resumed the next day.

To exclude sarcoidosis and other systemic diseases, a computed tomography (CT) scan of the chest organs was performed, which was normal, and a blood test for C-reactive protein, ASLO, and rheumatoid factor was performed; all parameters were within reference values.

Based on the presence of general cerebral, meningeal symptoms, absence of evidence of infectious and systemic lesions (e.g., fever, cough, lymph node enlargement, normal cerebrospinal fluid and inflammatory markers), taking into account pachymeningeal enhancement, the patient was diagnosed with idiopathic hypertrophic pachymeningitis.

Treatment with prednisolone 90 mg/day for 5 days with subsequent dose reduction was carried out.

Starting from the 2nd day of steroid therapy a significant improvement of the condition in the form of meningeal and general cerebral symptoms was noted.

The control MRI of the brain (20th day of hospitalization) showed a significant decrease in the previously detected pachymeningeal enhancement and reduction of paramagnetic accumulation (Fig. 2).

For oncologic search we analyzed specific markers (alpha-fetoprotein, CA 15-3, CA-125, CA 19-9), ultrasound examination of abdominal and pelvic organs. The results were negative.

The patient was discharged in satisfactory condition with recommendations to gradually reduce the dose of prednisolone until complete withdrawal.

The patient was followed for one year, there was no recurrence of general cerebral and meningeal symptoms, she continues to work professionally.

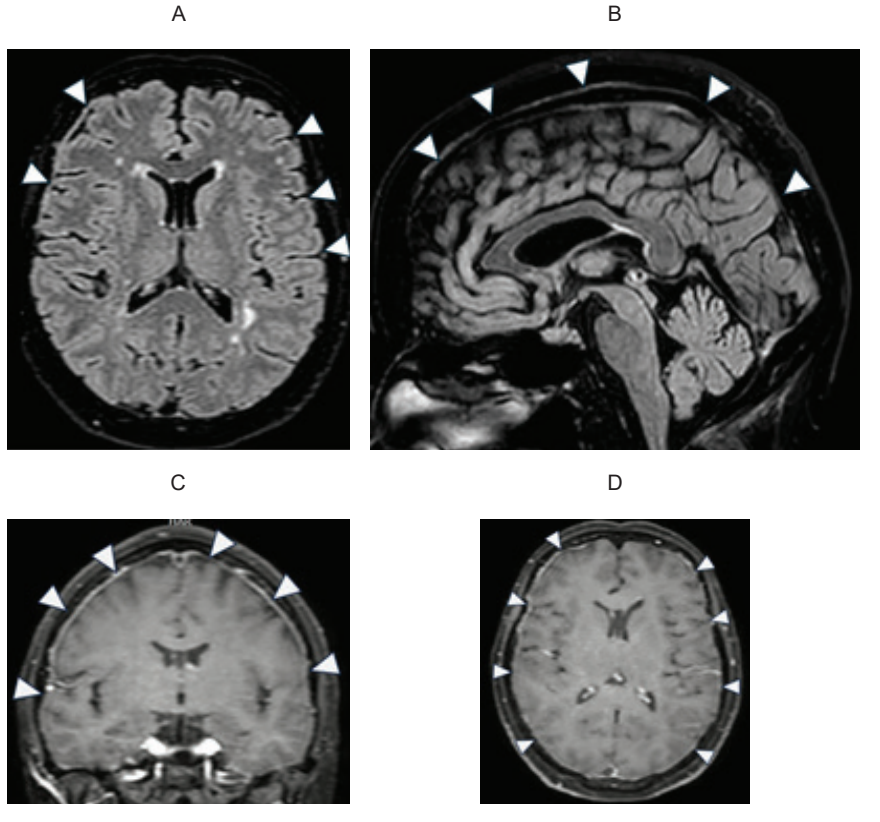

Fig. 2. MRI of the brain after steroid therapy: FLAIR images show a decrease in previously identified pachymeningeal enhancement in axial (A) and sagittal (B) sections; paramagnetic accumulation was reduced in coronal (C) and axial (D) sections

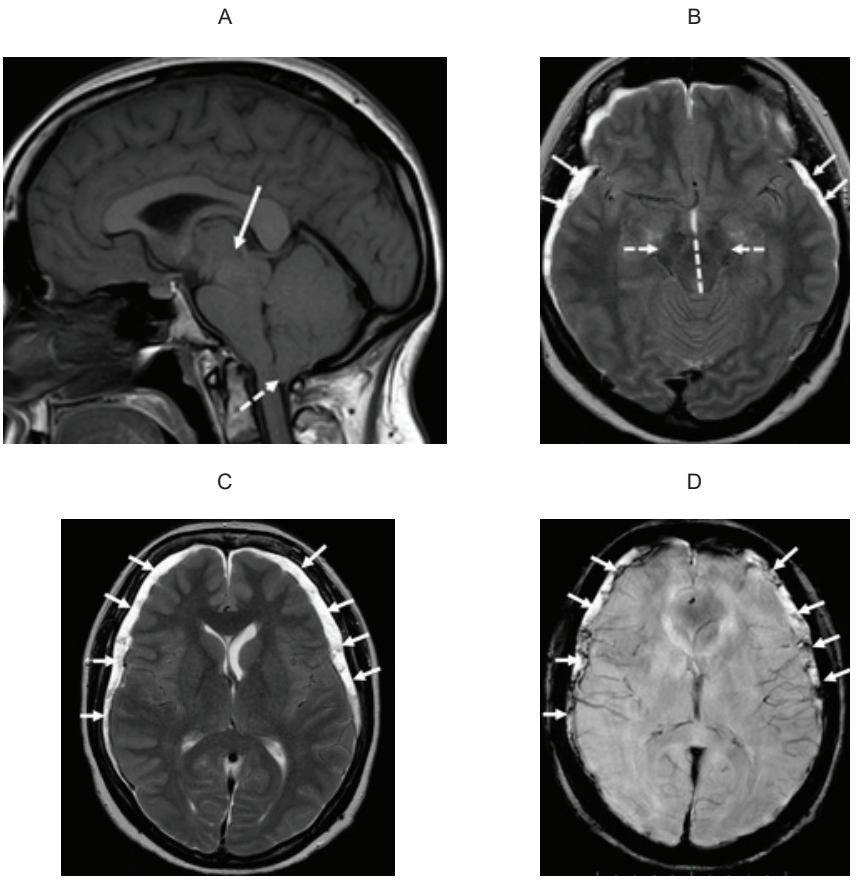

Fig. 3. Barin MRI in intracranial hypotension (own observation): A – caudal displacement of the cerebellum (dashed arrow), stem structures and midbrain, with narrowing of the basal cisterns of the brain, deformation of the pons and cerebral peduncles (solid arrow) on T1-weighted sagittal images; B – subdural hygromas (solid arrows), "flattening" of the midbrain on the lateral sides with an increase in its anteroposterior size (dashed arrows) on T2-weighted axial images; C (T2 images), D (SWI mode) – subdural effusions with a slight accumulation of hemosiderin, which indicates previous subdural hemorrhages; significant narrowing (slit-like shape) of the lateral ventricles on axial images

Discussion. We present a clinical observation of a patient with a rare disease - idiopathic HPM. The patient had "red flags" from the moment of disease debut, which reduce the likelihood of primary headache (primarily migraine and tension headache) and require further evaluation, namely: 1) development of unusual headache after age 50; 2) absence of remissions; 3) meningeal signs; 4) signs of intracranial hypertension (increased headache on pushing) [3]. Neuroimaging performed independently revealed specific signs that required specialized care, but the patient continued to work and turned to a specialist late. The initial examination by the neurologist also missed "red flags" and changes on MRI of the head. These circumstances were the reason for the patient's late hospitalization.

According to a study of HPM in India, 52% of patient cases have primary (idiopathic) form and 48% have secondary form (immune mediated, infectious and neoplastic). The most common cause of secondary HPM was IgG4-associated forms (25%), with sarcoidosis, tuberculosis and fungal infection accounting for 3 cases each (18.75%). Headache occurred in all patients and cranial neuropathies were identified in 73% of cases. Focal symptoms indicated the secondary nature of HPM. MRI showed localized pachymeningeal enhancement in 97% of cases and diffuse enhancement in only one patient (with fungal osteomyelitis of the skull base). Treatment was with glucocorticosteroids, except for cases of fungal etiology. In severe cases, intravenous immunoglobulins, rituximab, cyclophosphamide and azathiaprine were administered [12]

Of particular interest in recent years is IgG4-associated HPM, which, according to some researchers, was previously diagnosed as idiopathic (primary) HPM [6, 10, 13]. Clinically, IgG4-associated HPM does not differ practically from idiopathic HPM: headaches (67%) and signs of cranial nerve damage (33%) are the most common. However, approximately half of patients with IgG4-associated HPM may have systemic manifestations: weight loss, thyroid dysfunction, autoimmune pancreatitis, interstitial pneumonia, and salivary gland enlargement. MRI of the brain reveals pachymeningeal enhancement. Serum IgG4 antibody levels correlate with systemic manifestations of the disease. Antibodies to IgG4, mild protein and cell (lymphocyte) elevation are detected in the cerebrospinal fluid. "The gold standard" for diagnosis is a biopsy of the dura mater, which reveals whirling fibrotic inflammatory reactions. There is no consensus in treatment, but glucocorticosteroids are used, and if they are ineffective, cytostatics (methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide) may be used; the use of anti-B-cell therapy with rituximab is promising [11]. Unfortunately, in the Russian Federation, it is not possible to conduct research on IgG4, and probably IgG4-associated forms are hidden under cases of idiopathic HPM. At the same time, there is currently no convincing evidence that the treatment of these two forms is fundamentally different.

In the literature there are descriptions of HPM in combination with Tolosa-Hunt syndrome (HTS). Ivanov V.V. and colleagues reported a successful surgical intervention with decompression of the orbital structures and optic nerve in a 39-year-old patient with HTS and suspected volumetric process of the right orbit, who complained of acute decrease of vision in the right eye and burning pain in the right eye. Intraoperative biopsy made it possible to establish the diagnosis of HPM [2]. No cranial neuropathies were detected in the patient we presented.

There are also rare causes of HPM. For example, a 13-year-old girl who had been bothered by headaches, facial and withdrawal nerve neuropathies for 8 months was found to have contrast enhancement of the dura mater on brain MRI. Subsequently, antibodies to GFAP were detected, characteristic of autoimmune glial fibrillary acidic protein astrocytopathy, a rare inflammatory disease of the nervous system that manifests with steroid-sensitive encephalitis, myelitis, and meningitis. Administration of steroid therapy improved the girl's condition [7]. Mendelevich E.G. and colleagues reported on the development of HPM in a 44-year-old patient in whom the disease debuted with narrowing of the eye slit and only 2 years after the development of ocular symptoms headaches developed, followed by optic atrophy with complete

blindness in the left eye, transient deafness in the left ear, and hypersomnia. According to MRI of the brain and laboratory tests (proteinuria, microhematuria), HPM was diagnosed, probably as part of Wegener's granulomatosis. The patient was treated with corticosteroids (prednisolone 40 mg/day) with positive effect [4].

In 2020, guidelines for idiopathic HPM were issued, the most frequent clinical manifestations are headaches and cranial nerve dysfunction, the cerebrospinal fluid may show increased protein levels and lymphocytic pleocytosis, and MRI with contrast-enhanced gadolinium is the priority method of diagnosis. The pain syndrome is mimicked by chronic daily headache or chronic migraine with typical features (nausea, vomiting), less commonly by SUNA [8].

A similar neuroimaging picture to HPM can be observed in intracranial hypotension. At the same time, intracranial hypotension is also characterized by swelling of venous sinuses, prolapse of cerebellar tonsils into the greater occipital foramen, increased pituitary size, decreased mammillopontine distance, and pontomesencephalic angle, as well as a number of other changes [1, 14]. No such changes were detected in our patient, which reduces the possibility of intracranial hypotension. Figure 3 shows MRI of the brain of our other patient with intracranial hypotension.

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