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Idiopathic hypertrophic pachymeningitis – case report and literature review

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Abstract

Idiopathic hypertrophic pachymeningitis (IHPM) is a rare pathological state, with still unclear aetiopathogenesis. We present a case of a 63-year-old woman with cranial variety of that disease. The manifestations of the disease included headaches, paresis of VI, IX, X nerves and cerebellar ataxia. The disease was diagnosed with magnetic resonance imaging (MRI) and histopathological assessment of the pachymeninx biopsy specimen. The MRI revealed significant thickening of the cranial base pachymeninx, compressing the pons and medulla oblongata. MRI examinations could be misinterpreted as extensive meningioma of the skull base. Dura mater biopsy revealed however inflammation with abundant lymphocytic infiltrations. Clinical improvement was obtained after the application of corticosteroids. We noted the subsidence of all symptoms of the disease, as well as radiological improvement, manifested through substantial regression of the described changes in the pachymeninx. The patient has been presented in the context of 65 cases of idiopathic hypertrophic pachymeningitis, described in the literature of English-speaking countries in the last five years.

Recently, the importance of the autoimmunogenic background of IHPM has been underlined. In that respect IHPM has become an interdisciplinary problem. Its diagnosis and treatment requires not only radiologists, neurologists, pathomorphologists and neurosurgeons, but also specialists in internal medicine, including immunologists, allergologists and rheumatologists as well - in other words, physicians that rarely take part in the processes of diagnosing and treating intracranial pathologies.

Key words: *idiopathic pachymeningitis*

Introduction

Idiopathic hypertrophic pachymeningitis (IHPM) is a rare, chronic inflammatory process, with unclear aetiology. Compression of anatomic structures by the meninx, thickened with inflammatory infiltrations, is the main cause of various symptoms of the disease. Inflammatory lesions may be located in the cerebral or spinal dura mater or less frequently in both locations simultaneously [1-3].

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Thickening of the dura mater is encountered in numerous pathological states, with diverse aetiologies: infectious ones such as syphilis, tuberculosis, sarcoidosis, mycosis; neoplastic ones such as meningioma, carcinosis of meninges, lymphoma, melanoma; collagenoses, storage diseases, after prolonged dialyses, and prolonged administration of medicines directly to the cerebrospinal fluid [4].

In that context, the diagnosis of IHPM consists of excluding those disease entities whose treatment is of causal type, which is of particular importance in the case of infectious and neoplastic diseases.

MRI is the examination of choice in preliminary diagnostics of IHPM. Histopathological examination of a biopsy specimen of the dura mater would finally confirm the diagnosis [1].

There are no described cases of idiopathic hypertrophic pachymeningitis in the Polish literature so far. The aim of this paper is to present the aetiology, diagnostics and treatment of IHPM in the light of contemporary specialist literature and to illustrate a patient suffering from IHPM.

Case description

A 63-year-old woman was admitted to the Department of Neurosurgery of the Silesian Medical Academy in Katowice on March 16, 2003, due to a three-year history of intense headaches and double vision. The CT examination performed two years earlier revealed no deviations from the norm. The MRI, performed in 2002, indicated thickening of the dura mater of the base of the skull in the clivus area, as well as over the right cerebral hemisphere (Fig. 1, 2). The MRI examination of the cervical spine, performed in 2003, revealed advanced spondylosis. On admission to the Department of Neurosurgery the patient was conscious, in full logical contact. Neurological examination revealed right abducent nerve paresis, with convergent squint of the right eyeball. Unsteady gait and dysphasia of dysarthria type were observed. The absence of pharyngeal and palatine reflexes indicated paresis of the glosso-pharyngeal and vagus nerves. No dysphagia was observed. There were no significant pathological changes detected in the basic laboratory tests except for elevated erythrocyte sedimentation rate (28/61).

The next MRI of the head was performed on March 19, 2003, which revealed planar pathological infiltrations on the cranial base, up to 5mm thick. The lesions extended from the posterior clinoid processes, through the clivus all the way to half the height of corpus C1. The described pathological structure revealed an isointense signal in T1-weighted images, and a slightly decreased one in T2-weighted images, and underwent significant contrast enhancement. It also caused slight deformation of the pons and medulla oblongata. Significant intensification of signals was noted in the calvarial meninges, in particular in the right fronto-temporal-parietal area as well. In the MRI examination, the radiologist stated a pathological infiltration, which might suggest meningioma "*en plaque*". On March 26, 2003, the

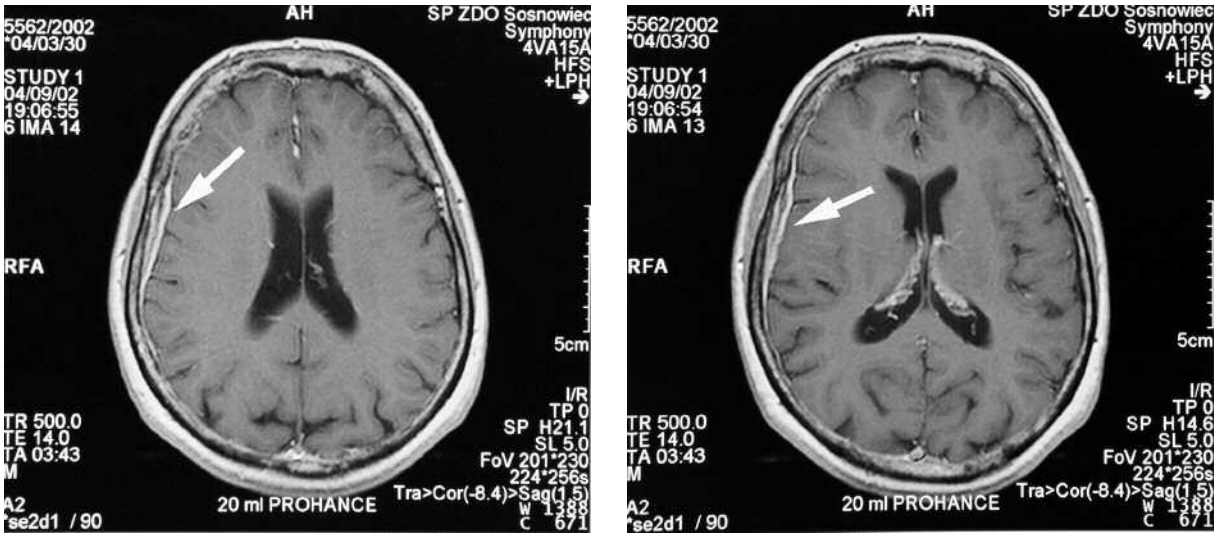


Fig. 1A-B. T1-weighted MRI axial images with contrast enhancement on admission

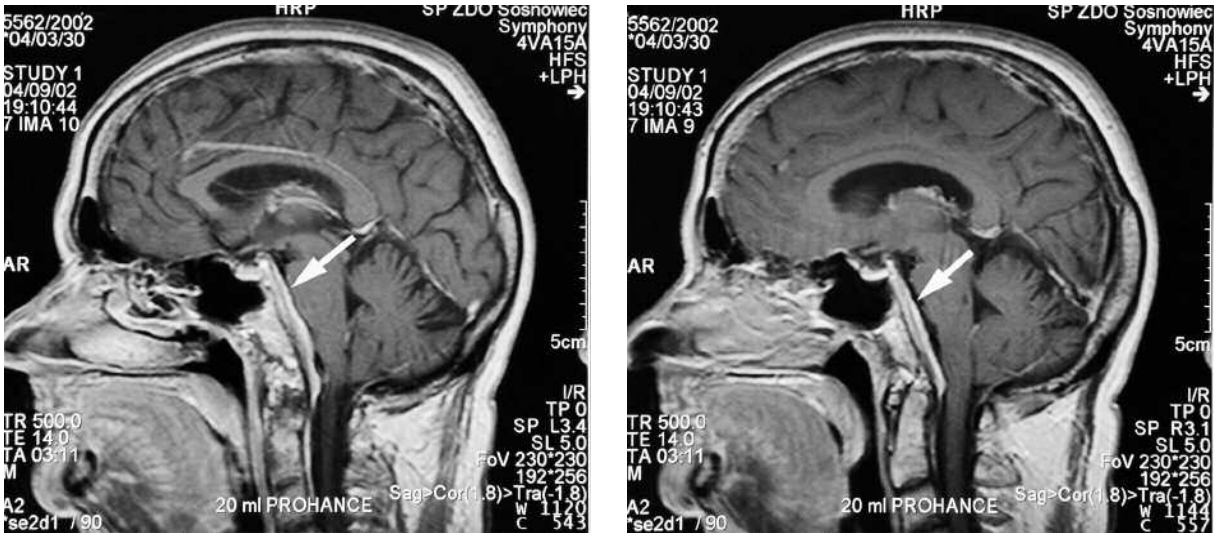


Fig. 2A-B. T1-weighted MRI sagittal images with contrast enhancement on admission

patient underwent a minor craniotomy in the right parieto-temporal area. A dura mater specimen was taken for histopathological examination. The procedure revealed the meninx to be thickened to 3 mm and covered with a coarse coating from the inside. The patient tolerated the biopsy well. The histopathological examination of the dura biopsy specimen revealed fibrous connective tissue with focal hyalinization, necrosis and calcification and extremely abundant, lymphocytic inflammatory infiltration, with a tendency to form lymphatic follicles with proliferation centres. The immunohistochemical reactions ordered (basic "nodal" panel) revealed no features that would allow a lymphoma to be diagnosed. In the immunohistochemical test we found: leukocyte common antigen (LCA) – positive reaction; CD3 – focally positive reaction; CD20 – focally positive reaction; lambda and kappa chains – focally positive reaction. The appropriate immunostainings are presented in figures 3-6. A few days after the procedure, steroid treatment was initiated. Dexaven administered in doses of 12 mg/24 h parenterally continued for 7 days was the initial treatment. Next, Dexamethasone was administered orally, in doses of

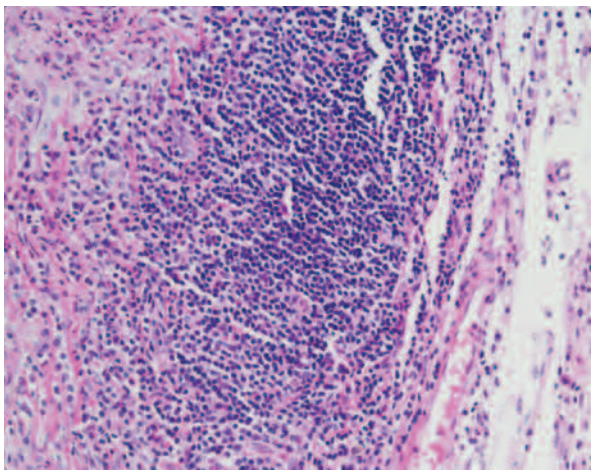


Fig. 3. Histopathological examination (HEx200). In the picture lymphatic follicles with proliferation centres are visible

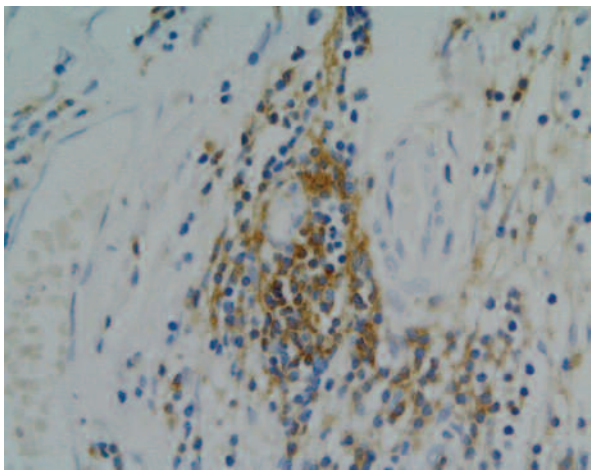


Fig. 4. Histopathological examination – immunostaining (CD20x300)

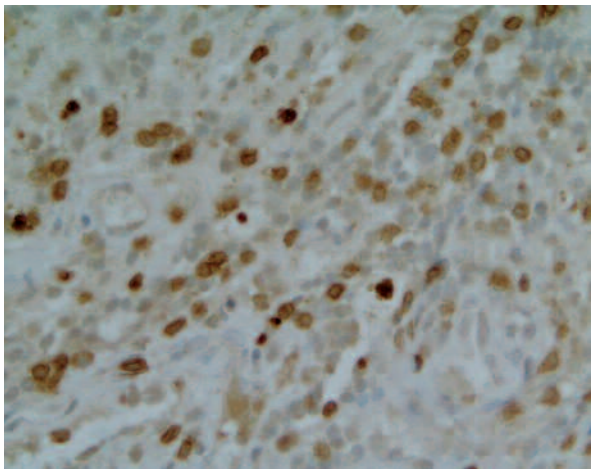


Fig. 5. Histopathological examination – immunostaining (CD3x400)

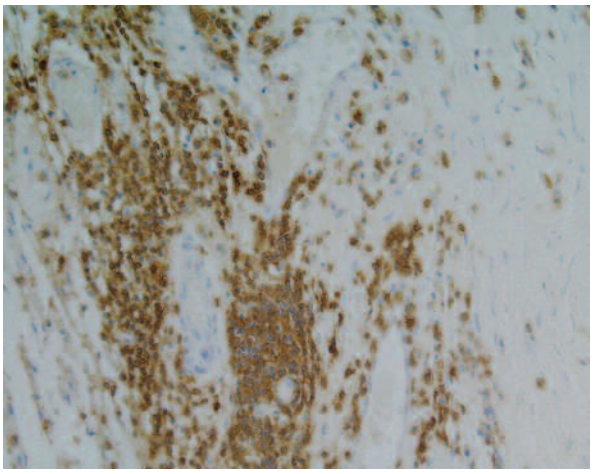
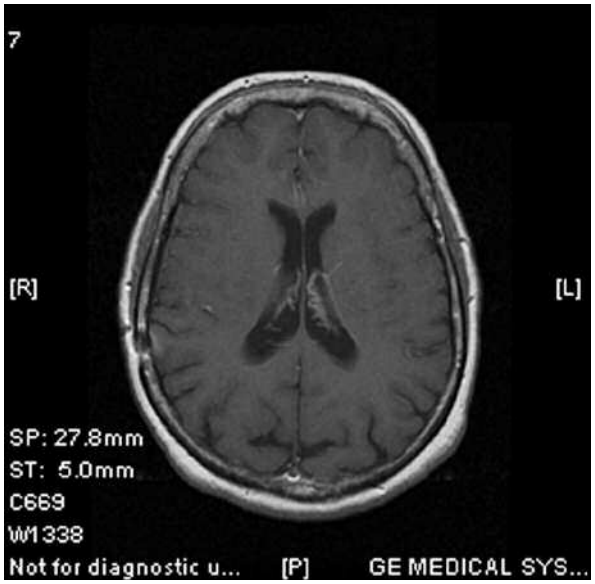


Fig. 6. Histopathological examination – immunostaining (LCAx400)

6mg/24h. The patient was discharged from the department on the seventh day after the procedure. The neurological manifestations continued after discharge, although the patient reported subsidence of headaches. Seven weeks later, the paresis of the right abducent nerve subsided, as did the disturbances in the form of hypokinetic dysartria. Administration of corticosteroids was discontinued after two months of treatment. The patient underwent a check-up MRI of the head on November 19, 2003, which revealed a clear regression of the lesions noted in the examinations carried out before the procedure and initiation of steroid therapy. The patient's clinical improvement has continued after the treatment. There are no observed headaches and no neurological deficits at present. The follow-up period has been continued for 3 years now. Actual MRI examinations are presented in figures 7 and 8.

Discussion

Idiopathic hypertrophic pachymeningitis (IHPM) is a rare disease with diverse manifestations, and assumed autoimmunological aetiopathogenesis.



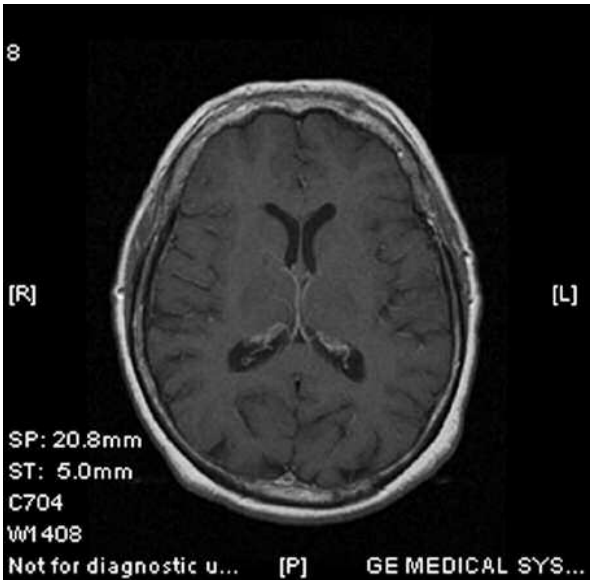


Fig. 7A-B. Current control T1-weighted MRI axial images with contrast enhancement

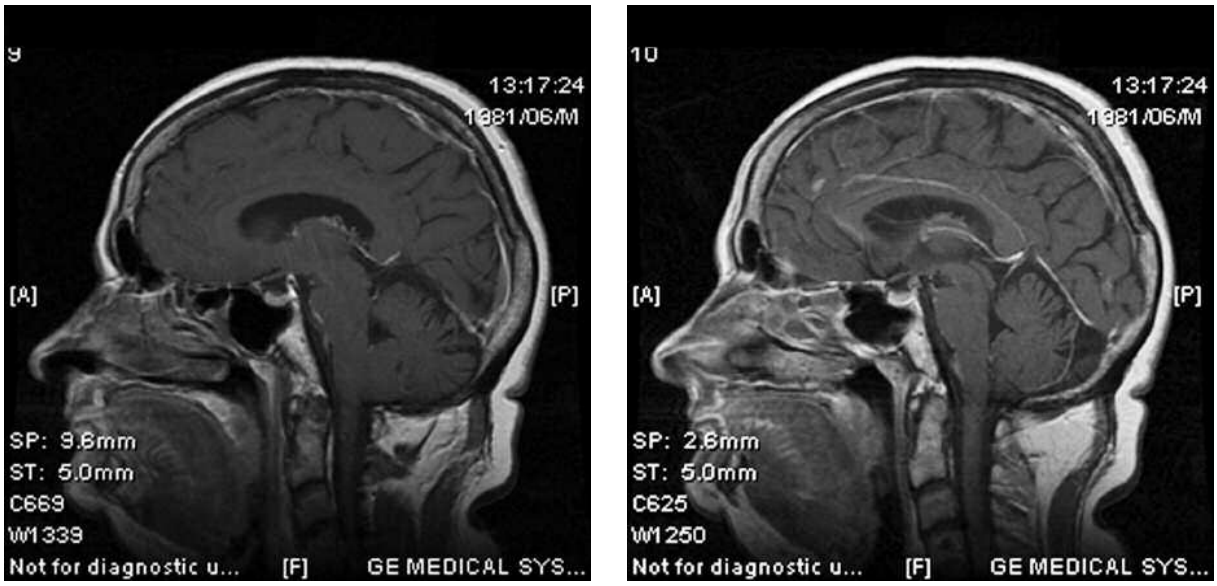


Fig. 8A-B. Current control T1-weighted MRI sagittal images with contrast enhancement

Charcot and Joffrey were the first to describe the medullar version of hypertrophic pachymeningitis, in 1869 [5]. In 1949, Naffziger and Stern reported for the first time the cranial variant of IHPM [6]. Until 1997, Parney gathered 33 documented cases of IHPM [7]. It is becoming obvious that its introduction to radiological diagnoses in MRI tomography has contributed to more frequent detection of the disease. The English-language literature has reported 65 cases of IHPM in the last five years. These matches were found in the Pubmed database. Clinical manifestations of IHPM depend upon the location of inflammatory lesions and compression of adjacent nervous structures. Location of pathological lesions in the vertebral canal is manifested by radiculopathies, limb paresis, as well as sphincter muscle functioning disturbances [8]. Neurological symptoms of the intercranial variation of IHPM depend upon the location of the inflammatory process, which is most frequently located at the skull base. Thickening of the dura mater in the area of the anterior fossa skull base, cavernous sinuses area, the optic canal, and superior orbital fissure, is frequently connected with the occurrence of pain behind the eyeball, deteriorated vision, and disturbances affecting the mobility of eyeballs. These symptoms are often manifested in the form of Tolosa-Hunt syndrome (THS) [9,10]. THS is also known as painful ophthalmoplegia and sometimes is considered to be a local, peri-cavernous form of IHPM. When the inflammatory lesions are located in the cerebellar tentorium, and at the posterior cranial fossa base, mainly in the clivus and foramen magnum area, lesions of cranial nerves VI to XII are observed, along with cerebellar ataxia features [1,2,4,12,13].

Lesions of VI, IX, X cranial nerves and of the cerebellum in our patient corresponded to the presence of inflammatory processes at the skull base, which most abundantly affected the dura mater of the clivus and the foramen magnum area.

Mikawa et al. subdivided IHPM into two groups: first those with inflammatory signs including fever, increased erythrocyte sedimentation rate, leukocytosis, and increased CRP (group P); and second those without inflammatory signs (group N). They analysed and suggested that group P had worse prognosis than group N [11,15]. Our patient belongs to group N. No inflammatory symptoms were noted.

In the 65 cases of IHPM described in the last five years, the most frequently encountered symptoms were headaches (91%) and lesions of cranial nerves (77%); less frequent ones comprised cerebellar ataxia (11%), epileptic seizures (8%), diabetes insipidus (5%), hypopituitarism (2%), and psychotic manifestations (2%) [1,2,4,14,16,17].

As mentioned before, at the time of MR imaging technique, the detectability of diseases involving thickening of the dura increased substantially. The diagnosis of IHPM must, however, exclude first those

disease entities which are subject to causal treatment, especially those in which immunosuppressive treatment is not effective or even contraindicated.

MRI examination of the dura mater in idiopathic hypertrophic pachymeningitis revealed an iso-intense or hypo-intense signal in T1-dependent time, and a hypo-intense one in T2-dependent time, in relation to the brain and spinal cord signal. After Gadolinium administration the lesion underwent significant post-contrast intensification. There are two forms of lesions distinguished in IHPM in MRI – planar and tumour-like. In the latter, inflammatory infiltrations take the form of nodules, which may suggest the presence of multiple meningiomas [18].

Bearing in mind the causes of lesions leading to the images described above, it is indispensable to carry out histopathological examination of a section of the pathologically changed dura mater, in order to confirm the diagnosis of IHPM. Most often, such examination reveals the focus of a chronic inflammation, with the presence of lymphocytes, plasma cells, histiocytes, and less frequently granulocytes [1,2,4,9,16]. An important piece of information resulting from the histopathological examination should be the exclusion of the presence of neoplastic and specific changes.

From the analysis of the literature it turns out that the most frequently instituted treatment for IHPM was steroid therapy. In 65 presented cases within the last five years, 54 patients (that is 83%) were treated with steroids. Azathioprine was administered to 10 patients, while methotrexate and cyclophosphamide were administered respectively to 5 and 2 patients. Often, the treatment consisted of polypharmacotherapy combining the above medicines. In one presented case, lymphocytopheresis was applied with good result, while in another one the therapy consisted only of anti-epileptic drugs administration [19-22]. Surgical intervention, besides taking a biopsy specimen for diagnosis, in three cases comprised suboccipital decompression, and in a further four cases multi-layer laminectomies in the cervical and thoracic section of the spine. In the other cases one procedure of optic nerve decompression in its canal was performed, one procedure of decompression craniectomy and treatment of hydrocephalus by means of implantation of a ventriculo-peritoneal shunt in one patient [2-4,8,12,18,23,24]. In the case of our patient, treatment with corticosteroids was administered, which resulted in complete withdrawal of neurological symptoms, as well as regression of lesions revealed by head MR imaging examination. Despite provisional diagnosis of skull base meningioma based mainly on neuroradiological findings, the biopsy revealed an inflammatory process. It should be kept in mind in such rare cases to avoid extensive neurosurgical procedure with all feasible adverse effects.

Clinical improvement after pharmacotherapy was noted in 49 patients in the group of 65 patients referred to above. In 21 patients, the attempted withdrawal of medication resulted in recurrence of disease symptoms. Among the patients who underwent control MRI examination of the head, 44 were found to have an improvement observed in radiological examinations, 5 had the images unchanged, and 6 revealed deteriorated images. The whole clinical observation period of our patient comprised 5 years, with two years after IHPM diagnosis. In the literature the clinical observation periods of the disease course are often several years long. Complete recoveries of IHPM are rather rare. The disease is most often progressive, with remissions, and requires prolonged treatment. Deaths of patients with IHPM are most often caused by obturation of large sinuses of the dura by inflammatory infiltrations, as well as compression of the latter upon the structures of the hypothalamus and brain stem [1,2,24].

The cause of IHPM remains unclear. Recently, the importance of the autoimmunological background of diseases has been underlined. IHPM may coexist with rheumatoid arthritis, Wegener's granuloma, lupus erythematodes, temporal arteritis, assorted diseases of connective tissue, or Hashimoto's disease. The co-occurrence of IHPM with diseases in which an important role is attributed to autoimmunological mechanisms, consisting of production of antibodies and T-lymphocytes reacting with their own antibodies, may confirm the hypothesis. An important role in the improper immunological reaction may be played by genetic factors. The use of immunosuppressive medicines in the treatment of IHPM supports the theory of immunological aetiopathogenesis of that disease entity [1,2,4,10,23,25]. In that respect IHPM has become an interdisciplinary problem. Its diagnosis and treatment requires not only radiologists, neurologists, pathomorphologists and neurosurgeons, but also specialists in internal medicine,

including immunologists, allergologists and rheumatologists as well – in other words, physicians that rarely take part in the processes of diagnosing and treating intracranial pathologies.

Conclusion

IHPM is a rare, chronic inflammatory process, with probably immunological aetiology. The most frequently encountered neurological manifestations include headaches and cranial nerves paresis. The diagnosis of IHPM is based upon MRI examination and histopathological assessment of dura mater biopsy specimen. The treatment of choice for this increasingly often diagnosed disease is the administration of immunosuppressive substances, with steroids as the main ones.

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