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Idiopathic hypertrophic cranial pachymeningitis successfully treated with dexamethasone – a case report

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ABSTRACT

Introduction: Idiopathic hypertrophic cranial pachymeningitis (IHCP) is a rare pathological entity which is diagnosed after the exclusion of secondary reasons. Most frequently, IHCP is related to rheumatological diseases such as rheumatic arthritis, sarcoidosis, anti-neutrophil cytoplasmic antibody-associated vasculitis, and IgG4-related disorders. The inflammatory process concerns dura mater and manifests with symptoms of cranial nerve damage or compression.

Case description: A 59-year-old Caucasian man presented with transitional episodes of tinnitus and an unspecific headache. Imaging studies (magnetic resonance imaging – MRI) demonstrated a thickened dura mater. Lymphoma was suspected due to an abnormal flow cytometric analysis of a cerebrospinal fluid (CSF) sample. Hematological diagnostics including bone marrow biopsy, whole body computed tomography (CT) and digestion tract examination were performed leading to the exclusion of hematological malignancy. The patient underwent surgery, and a specimen from the lesion was obtained. On this basis, intracranial idiopathic hypertrophic pachymeningitis was diagnosed. First line treatment strategy was introduced with corticosteroids with a gradual dose reduction. After the 48-month follow-up, we observed an alleviation of symptoms with a gradual significant decrease in the thickening of dura matter with almost complete resolution.

Conclusions: Idiopathic hypertrophic pachymeningitis should be considered in the differential diagnosis of a thickened dura mater. Administration of steroids appears reasonable as a first line treatment of IHCP.

Keywords: idiopathic hypertrophic pachymeningitis; lymphoma; dexamethasone; IHCP.

INTRODUCTION

Idiopathic hypertrophic cranial pachymeningitis (IHCP) is an uncommon disease of unknown pathogenesis. The postulated mechanism for the development of this condition is the inflammatory process which leads to a thickening of the dura mater and then to ischemia and neuropathy of the cranial nerves [1]. This pathological entity is characterized by symptoms of cranial nerve damage or compression, with clinical features of pain or dysfunction of organs that are innervated by these nerves. The most commonly reported symptoms are facial pain, visual impairment, ptosis, headache, tinnitus or symptoms resulting from dural sinus thrombosis or mass effect [2]. Since inflammation plays a role in the process, immunosuppressive drugs such as steroids are an effective treatment. However, the beneficial effects of these are usually transient [1]. Early diagnosis and treatment are crucial to prevent irreversible neurological damage [3].

A thickened dura mater is the most common symptom of IHCP. Other conditions leading to a thickening of the dura mater are sarcoidosis, Wegener's granulomatosis, Sjogren's syndrome, rheumatoid arthritis, tuberculosis, syphilis, Lyme disease and IgG4-related disease [1]. The distinction between IHCP and other causes of symptoms still remains a diagnostic challenge. During the diagnostic process, a profound physical examination, imaging studies including brain magnetic resonance imaging (MRI), immunological tests (e.g. IgG, antinuclear antibodies), and cerebrospinal fluid (CSF) examination play a main role [2]. In many cases, surgical biopsy and histopathological examination leads to the final diagnosis. A thickened dura mater raises the suspicion that a neoplastic process is occurring. Thus, it is important to differentiate IHCP from neoplastic invasion. In this case, lymphoma infiltration of the central nervous system (CNS) was also suspected based on brain imaging. Hematological diagnostics were performed on the patient because of this suspicion. The case reported herein illustrates the process of the differential diagnosis of IHCP and its effective treatment with glucocorticoids.

CASE REPORT

A 59-year-old Caucasian man experienced the first symptoms in December 2015. He suffered from transitional episodes of tinnitus which went from one side to the other and lasted 2 weeks. The tinnitus was accompanied by an unspecified headache. During a brain MRI, a thickened dura mater was found (Fig. 1) and because of this, the patient was diagnosed in the Department of Neurology in June 2016. He complained about a feeling of fullness in the head and periodically occurring tinnitus. His past medical history included cardiovascular burden such as arterial hypertension, abdominal aortic aneurysm, ischemic heart disease, and arrhythmias. In 2008, the patient experienced a transient loss of consciousness and for this reason, an MRI of the head was performed revealing normal findings.

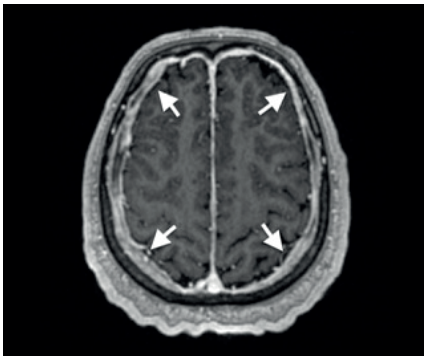

FIGURE 1. Gadolinium-enhanced axial T1-weighted image shows an infiltrative thickening involving the whole dura mater (arrows) as homogeneous enhancement

At the beginning of 2016, a neoplastic process was suspected – firstly, of a meningeal infiltration by a lymphoma. The patient had lost 14 kg. However, he was on a special diet for weight loss. He denied night sweats and itching. Neurological examination revealed no neurological focal deficits. Laboratory work revealed a mild thrombocytopenia. A brain MRI showed a thickened dura mater with attenuated homogeneous enhancement after the administration of contrast. A flow cytometric analysis of a CSF sample revealed the presence of about 1% monoclonal lymphocytes B and about 60% reactive T lymphocytes with the predominance of CD4+ cells. Carcinomatous cells were not detected. On this basis, a lymphoma was suggested. X-rays were normal. A lumbar puncture was performed and a CSF sample was analyzed. Slightly increased protein levels were found. Lyme borreliosis was excluded during the diagnostic process. In September 2016, the patient was diagnosed in the internal medicine ward. An upper gastrointestinal endoscopy revealed gastritis. A colonoscopy showed polyps which were then removed. An abdominal computed tomography (CT) showed an abdominal aortic aneurysm. A chest CT revealed normal findings. Finally, the investigation for a neoplasia or systemic disease was negative.

Then in November 2016, the patient was admitted to the Department of Hematology for diagnostics due to a suspicion of B-cell lymphoma. Hematological diagnostics included bone marrow biopsy, flow cytometry of a bone marrow sample and repeat CSF flow cytometry. As a result of these tests, lymphoma infiltration was excluded. A preliminary suspicion of hypertrophic cranial pachymeningitis was raised. As such, the patient was referred to the Neurosurgery Department where samples of the dura mater were obtained for histopathology and a meningeal biopsy was performed by frontotemporal craniotomy (Fig. 2). Hypertrophy of the inner part of the dura mater was found. It was remarkably thickened by a proliferation of dense fibrous tissue, filled with numerous blood vessels of various calibers (Fig. 3) and not very abundant in mononuclear inflammatory infiltrates mainly around some vessels (lymphocytes, plasmocytes). This might correspond to IHCP associated with, for example, intracranial negative pressure. Eventually, a final diagnosis of IHCP was established. During the stay, the patient received dexamethasone intravenously twice and he continued the oral dexamethasone treatment at home at a reduced dose. In July 2017, the patient was hospitalized at the Department of Hematology in order to perform control tests and determine the next step. On admission, the patient was in good general condition, he did not report any complaints except slight tinnitus, sweating and moderate pain in the lower limbs after prolonged walking. A physical examination was conducted and no significant discrepancies were found. In his blood count, slight features of thrombocytopenia (platelets 114 G/L) were found. A control MRI examination of the brain showed a generalized thickening (up to 2.5 mm) of the dura mater, with an intensive enhancement of the dura mater after administration of a contrast, as before. Compared to the previous study, the thickness of the dura matter was considerably reduced. Due to the reduction in dura matter, Dexaven 40 mg iv was administered as a single dose. The patient was discharged from the clinic in good general condition. He continued his treatment of Dexaven 40 mg intravenously once a month in the Day Ward of the Hematology Clinic.

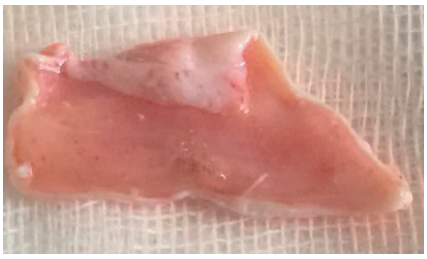

FIGURE 2. Photo of the resected part of dura mater from the right frontotemporal region. The inner surface of the dura covered by gray dense fibrous tissue is exposed. The dura itself is significantly thickened

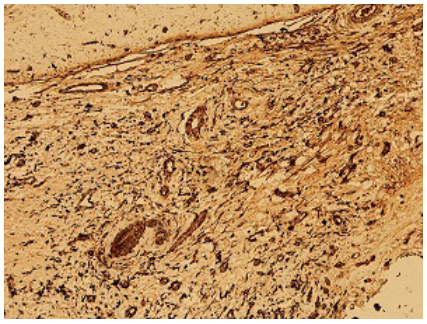

FIGURE 3. Vimentin immunohistochemical stain (DAB, 200X). It was remarkably thickened by proliferation of dense fibrous tissue, filled with numerous blood vessels of various calibers

The patient was followed up in the outpatient clinic. After the introduction of an intravenous dexamethasone 40 mg dose once a month, a gradual reduction of remittent tinnitus was observed. The MRI obtained after several months of treatment showed a mild decrease in thickness and a regression of the dura mater enhancement. Re-examination of the brain in an MRI scan after 24 months showed a reduction in the thickness of the dura mater from 2.5 mm to 1.5 mm, along with a reduction in the intensity of the contrast enhancement. In February 2018, the administration of dexamethasone was switched from intravenous to oral therapy. An MRI of the brain after 36 months showed a reduction in the thickness of the dura mater from 2.5 mm to 1.5 mm, along with a reduction in the intensity of the contrast enhancement. The last examination of the brain with an MRI scan showed further reduction in the thickness of the dura mater, along with a reduction in the intensity of the contrast enhancement (Fig. 4). Only a trace thickness of dura matter was found. Currently, 48 months after the introduction of 20 mg of oral dexamethasone once a month, the patient is doing well and his corticotherapy is tapered.

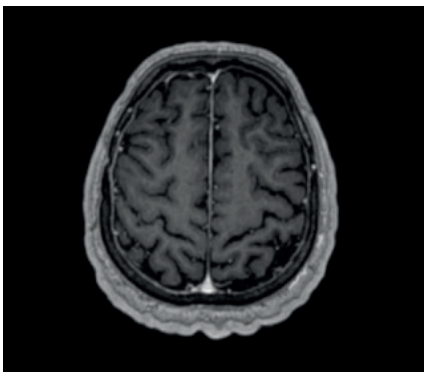

FIGURE 4. Follow-up examination gadolinium-enhanced axial T1-weighted image at the same cross-section level depicted an almost complete resolution of the thickened and enhanced dura matter

DISCUSSION

We presented a case of a patient diagnosed with IHCP as confirmed by MRI and a histopathological analysis of a biopsy. There are several case reports in the literature of this rare disease [4, 5, 6, 7, 8, 9] and the clinical presentation of IHCP is heterogeneous. The symptoms of IHCP are often nonspecific and the most common symptoms include headache, nausea and vomiting. In the course of the disease, other manifestations and corresponding symptoms such as serous otitis and retro-orbital pain with a later development of vision loss and hearing impairment occur which are connected with cranial nerve involvement. An involvement of nerve VIII is most common, but other nerves such as V, VII, IX, X, XII can also be involved [10]. It is worth mentioning that ICHP is not always accompanied by clinical symptoms and the disease may also remain latent in further observation [1]. In the reported patient, the symptoms included transitional episodes of tinnitus which went from one side of the head to the other and lasted 2 weeks as well as a nonspecific headache. However, IHCP has a variety of clinical masks. Since the most common symptoms concern the nerves, the first diagnostic process carried out is for neurological disorders [6, 7, 9]. In the present case, disturbances in peripheral blood morphology and the presence of suspected cells in CSF led to a suspicion of lymphoma. This resulted in a number of examinations including hematological diagnostics conducted to look for other locations of possible neoplasm.

This rare entity is divided into idiopathic and secondary type and can occur in cases of lymphoplasmacyte-rich meningioma, histiocytosis, infectious diseases, and autoimmune diseases such as granulomatosis with polyangiitis (GPA), rheumatoid arthritis, and Sjogren syndrome. In the case of a diagnosis of IHCP, comprehensive screening towards secondary causes is necessary, and cannot be omitted during diagnostics because only about 30% of cases are idiopathic [3]. It has been suggested that the pathophysiology of idiopathic HP is a nonspecific chronic non chemokine inflammatory process – also regarded as autoimmune [11, 12]. However, the pathogenesis of this rare entity remains unresolved.

In previously reported cases, many changes such as dural thickening, dural mass, sinus thrombosis, and venous congestion with white matter changes were found in brain imaging [7]. A linear thickening of the falx and tentorium is the most common finding. Focal nodular thickening that simulates a dural mass is also very common. Among others are effusion, sinus abnormality, cavernous sinus involvement, white matter edema, and hydrocephalus [3]. In our patient, a generalized thickening of the dura matter was found in MRI with a significant enhancing of dura after contrast administration. This was the only finding through brain imaging.

A number of therapeutic strategies have been employed in the treatment of IHCP [1, 3, 13, 14]. However, appropriate treatment is still unknown. Immunosuppressive therapy such as steroids or methotrexate is effective therapy, but the outcome is usually transient. There is an agreement that corticotherapy should be the first therapeutic option. Corticosteroid therapy has been shown to be effective in alleviating symptoms and in arresting the clinical progression of IHCP. However, it has been also described as leading to partial clinical improvement with relapse after dose tapering [7]. Other accepted drugs are rituximab, cyclophosphamide and azathioprine. In a national French study, immunosuppressive treatment was initiated and consisted of steroids in 73% of cases. Other drugs included in treatment were cyclophosphamide, azathioprine, methotrexate, ciclosporin, interferon, and rituximab. In the case of our patient, after confirmed diagnosis, dexamethasone was administered intravenously once a month. As a result, clinical improvement was observed, and the intravenous treatment was converted to oral dexamethasone with dose tapering. In the abovementioned French retrospective study involving the observation of 60 patients, the authors reported the characteristics and treatment of patients with pachymeningitis. This is the largest cohort of patients described in the literature. On the basis of the study, it has been concluded that early diagnosis and treatment are crucial in preventing neurological damage [3].

The limitation of our case report is the relatively short period of observation.

CONCLUSIONS

To sum up, ICHP is a rare disease with a diverse clinical presentation. The diagnosis should be based on an MRI or CT scan of the brain as well as a biopsy of the dura mater with histopathological examination. To date, there are no clear guidelines for the treatment of the disease and all reports refer to a series of cases. Glucocorticoids should be considered as a first line treatment. Here, we present a patient with a neurological manifestation of the disease, treated with glucocorticoids with a good clinical effect as opposed to cases previously described in the literature where in the majority of patients, the course of the disease was unfavorable [1, 3, 7]. Most patients experience recurrent symptoms and a relapse of the disease. Fortunately, the treatment with glucocorticoids was effective and safe in the presented patient. We observed an alleviation of symptoms with a gradual significant decrease in the thickening of dura matter with almost complete resolution.

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