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CHRONIC HEADACHE REVEALING PRIMARY SJÖGREN'S SYNDROME: A CASE OF HYPERTROPHIC CRANIAL PACHYMENINGITIS

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ABSTRACT

Introduction: Hypertrophic cranial pachymeningitis is a rare fibro-inflammatory disorder of the dura mater, most often revealed by headache and cranial nerve palsies. Primary Sjögren's syndrome is an exceptional cause, and pachymeningitis is very rarely its presenting feature.
Case presentation: A 59-year-old woman with no relevant medical history was admitted for a recent worsening of her chronic headache, which had become more intense and refractory to analgesics. Neurological examination was normal. Brain magnetic resonance imaging showed diffuse dural thickening with intense gadolinium enhancement of the falx cerebri, the tentorium cerebelli and the clivus, extending into the cervical spinal canal, with ventricular enlargement. Cerebrospinal fluid analysis was normal, and the infectious, neoplastic, granulomatous and vasculitic work-up, including antineutrophil cytoplasmic antibodies and serum IgG4, was negative. Directed questioning revealed xerostomia and xerophthalmia. Minor salivary gland biopsy showed Chisholm–Mason grade IV sialadenitis, and anti-SSA and anti-SSB antibodies were positive, establishing the diagnosis of primary Sjögren's syndrome. Intravenous methylprednisolone pulses led to marked improvement of the headache, followed by tapered oral corticosteroids and azathioprine.
Conclusion: A change in the pattern of a chronic headache, or resistance to symptomatic treatment, warrants contrast-enhanced brain imaging. Although rare, primary Sjögren's syndrome should be systematically considered in the etiological work-up of pachymeningitis, as simple, minimally invasive tests may establish the diagnosis and avoid dural biopsy.

KEYWORDS

Headache, Hypertrophic pachymeningitis, Primary Sjögren's syndrome, Dura mater, Magnetic resonance imaging, Case report

MAIN ARTICLE

INTRODUCTION

Chronic headache is one of the leading reasons for neurological consultation. Although common and costly for society, it remains under-recognised, and any change in the pattern of a long-standing headache should prompt a search for a secondary cause.

In hypertrophic cranial pachymeningitis (HCP), an uncommon disorder, fibrosis and inflammation together cause hypertrophy of the dura mater, which typically presents with headache and cranial nerve palsies [1]. It may be idiopathic or secondary to infectious, neoplastic or systemic inflammatory diseases [1,2]. Among the central nervous system complications of primary Sjögren's syndrome (pSS), pachymeningitis is one of the least common, and only a few cases have been reported, some of which revealed the disease [3–8].

We report a case of HCP revealing pSS, in which a change in the pattern of a long-standing headache was the sole clinical feature.

CASE PRESENTATION

A 59-year-old woman with no relevant medical history was admitted to the Department of Neurology for the etiological assessment of a worsening chronic headache. Her long-standing headache had recently become more intense and resistant to usual analgesic treatment. General and neurological examinations were normal.

Brain magnetic resonance imaging (MRI) showed pachymeningitis involving the falx cerebri, the tentorium cerebelli and the clivus, with extension into the cervical spinal canal: the dura mater was thickened and strongly enhanced on T1-weighted sequences after gadolinium injection (Figures 1–3). An enlargement of the cerebral ventricles was also noted (Figure 2).

Cerebrospinal fluid (CSF) analysis was normal, with fewer than three leukocytes/mm^3, a protein level of 0.30 g/L and a glucose level of 0.60 g/L. The etiological work-up for infectious, neoplastic, granulomatous and vasculitic causes was negative, including serum IgG4 levels and antineutrophil cytoplasmic antibodies (ANCA) (Table 1).

Directed history-taking then revealed xerostomia and xerophthalmia. Minor salivary gland biopsy showed Chisholm–Mason grade IV lymphocytic sialadenitis, and anti-SSA (Ro) and anti-SSB (La) antibodies were positive. pSS was diagnosed according to the American-European Consensus Group criteria [9]; the patient also fulfilled the 2016 ACR/EULAR classification criteria [10].

The patient received intravenous methylprednisolone pulses (1 g/day for 5 days), with considerable improvement of her headache. Treatment was continued with oral corticosteroids at 60 mg/day, progressively tapered, and azathioprine was introduced as a steroid-sparing agent.

DISCUSSION

Histologically, HCP combines fibrosis and inflammation, both contributing to dural hypertrophy [1]. Clinically, headache and cranial nerve deficits dominate; in a French multicentre series of 60 patients, headache was present in 72% and cranial nerve palsy in 55% of cases [11]. In our patient, headache was the only symptom, and it was its change in character that led to the diagnosis.

Contrast-enhanced MRI is the key investigation, confirming the diagnosis and showing how intense and widespread the dural involvement is [2]. On T1-weighted images, the thickened dura is hypointense and enhances markedly after gadolinium injection. On T2-weighted images, the fibrotic dura also appears hypointense, occasionally bordered by a hyperintense margin that indicates ongoing inflammation [12]. The thickening can be diffuse, but it is usually most marked along the tentorium and the posterior falx, and may occasionally mimic a tumour [13]. Our patient displayed this typical distribution, with additional involvement of the clivus and the cervical spinal canal, as well as ventricular enlargement, which has also been described in association with HCP [14].

When no cause is found despite a complete work-up, pachymeningitis is labelled idiopathic [15]; otherwise, it is secondary to infectious or non-infectious conditions [1]. It may reveal systemic diseases including sarcoidosis, granulomatosis with polyangiitis [1], rheumatoid arthritis [16], mixed connective tissue disease [17] or undifferentiated connective tissue disease [18]. ANCA-associated vasculitis and IgG4-related disease are now recognised as major causes: in a Japanese nationwide survey, ANCA-related forms accounted for about 30% of cases [19], and IgG4-related disease is thought to underlie many cases once classified as idiopathic [20]. In our patient, ANCA were negative and serum IgG4 levels were normal, although a normal serum IgG4 level does not completely rule out IgG4-related disease in the absence of dural histology.

Neurological involvement in pSS is mostly peripheral, and central nervous system manifestations are polymorphic [21]. Pachymeningitis is one of the rarest: a literature review published in 2022 identified only nine reported cases worldwide [8]. Li et al. described pachymeningitis associated with lymphocytic hypophysitis that improved with corticosteroid pulse therapy [3]. Abouzaid et al. reported a 50-year-old woman presenting with intracranial

hypertension and third and seventh cranial nerve palsies, who improved with corticosteroids and cyclophosphamide [4]. Ashraf et al. described recurrent multiple cranial neuropathies with pachymeningitis and hypophysitis [5], and Abdelhedi and Khammassi reported a patient whose chronic headache had become more intense, together with sicca symptoms [6]. More recently reported patients also responded to corticosteroids [7,8]. Our observation is closest to that of Abdelhedi and Khammassi: there was no cranial nerve involvement, the only warning sign being the change in the headache pattern, and the dural involvement extended to the cervical spinal canal.

Dural biopsy is recommended when the work-up fails to identify a cause. Here, it was not performed because the work-up established pSS, with salivary gland histology and positive anti-SSA and anti-SSB antibodies, and because of the rapid response to corticosteroids. The absence of dural histology is nevertheless a limitation, and the causal relationship between pSS and pachymeningitis remains presumptive because so few cases have been published. Even so, the favourable outcome under corticosteroids and immunosuppressive drugs in the reported patients argues for it [3–8].

There is no standardised treatment for pachymeningitis [21]. Corticosteroids are the first-line treatment, but relapses during tapering are frequent; in the series of Kupersmith et al., methotrexate or azathioprine was added in four of 12 patients to reduce the corticosteroid dose [15]. In systemic pSS, EULAR advises keeping glucocorticoid exposure as low and as short as possible, and reserves synthetic immunosuppressants mainly for steroid sparing, without preferring any particular drug [22]. The regimen used in our patient, high-dose corticosteroids followed by azathioprine, is consistent with these principles: in the series of Choi et al., steroid-dependent patients were able to stop corticosteroids once long-term azathioprine had been added, with both clinical and imaging recovery [23]. Other reported agents include methotrexate [24], cyclophosphamide [4] and, in refractory cases, intraventricular cytarabine [25]. Radiological outcome varies between patients, although marked regression of dural thickening under treatment has been described [14,23].

CONCLUSION

This case shows that a chronic headache which stops responding to analgesics, or whose pattern changes without explanation, deserves further investigation. Rare as it is, pSS should be routinely sought in patients with pachymeningitis: a careful search for sicca symptoms, anti-SSA/SSB antibodies and minor salivary gland biopsy are simple, minimally invasive tests that may establish the diagnosis and avoid dural biopsy.

FIGURES:

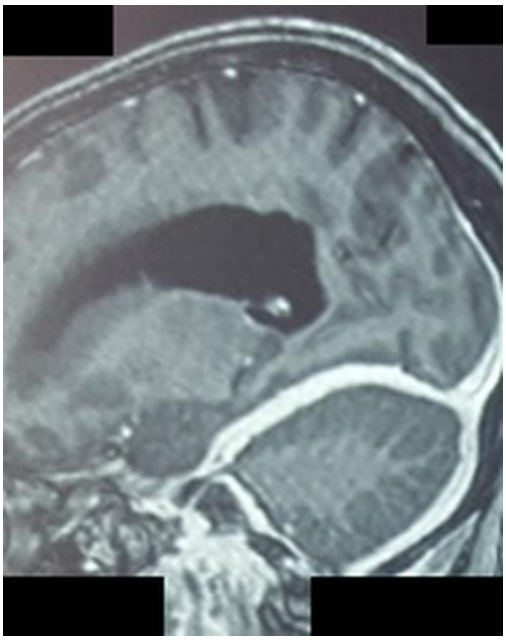


Figure 1: Brain MRI, sagittal T1-weighted sequence after gadolinium injection. Pachymeningitis of the tentorium cerebelli: thickening of the dura mater with contrast enhancement.

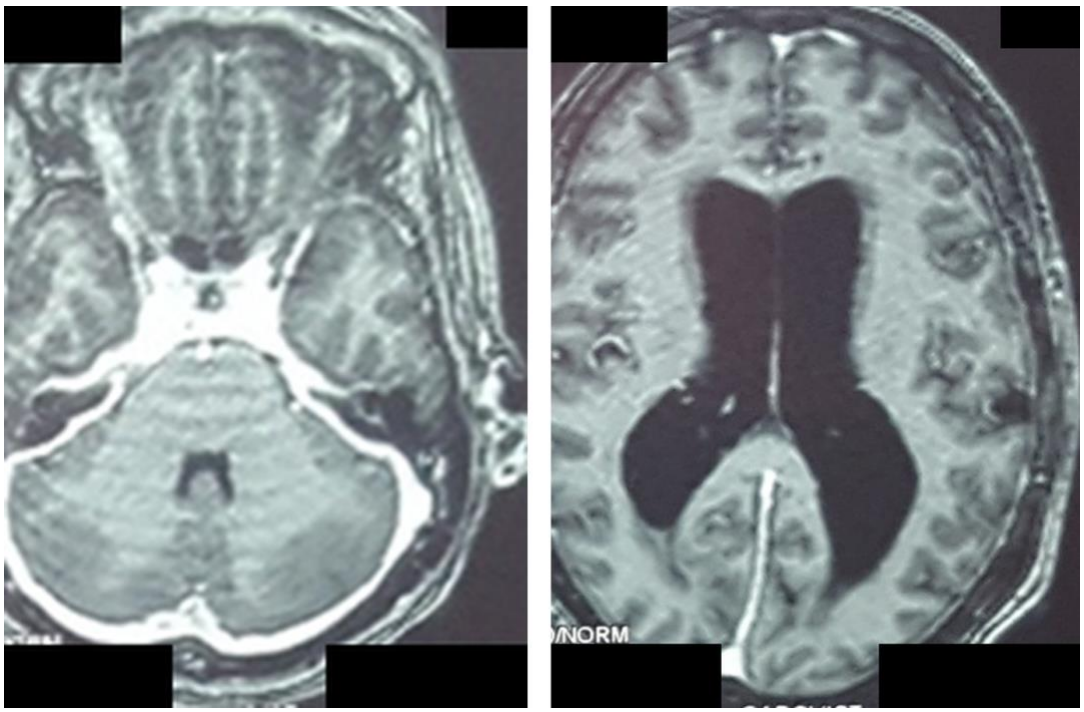


Figure 2: Brain MRI, axial T1-weighted sequences after gadolinium injection. Pachymeningitis of the tentorium cerebelli and the clivus (left), with enlargement of the lateral ventricles (right).

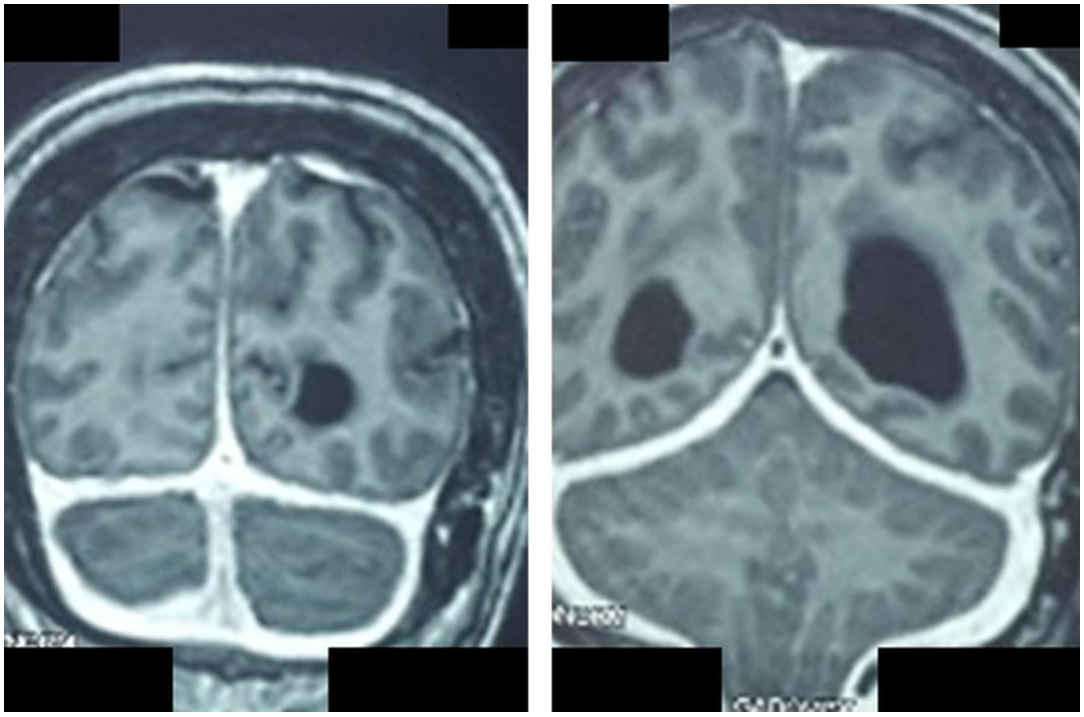


Figure 3: Brain MRI, coronal T1-weighted sequences after gadolinium injection. Pachymeningitis of the falx cerebri and the tentorium cerebelli: thickening of the dura mater with contrast enhancement.

TABLES :

Table 1 : Etiological work-up

Investigation	Result
CSF cytology	< 3 leukocytes/mm³; no tumour cells
CSF protein / glucose	0.30 g/L / 0.60 g/L
Protein immunoelectrophoresis (serum and CSF)	Normal
GeneXpert MTB/RIF (blood and CSF)	Negative
Serum IgG4	Normal
ANCA	Negative
Serology: syphilis, HIV, hepatitis B and C	Negative
Angiotensin-converting enzyme	Normal
Serum calcium and phosphate	Normal
HLA-B51	Negative
Chest X-ray / abdominal ultrasound	Normal
Anti-SSA (Ro) / anti-SSB (La) antibodies	Positive
Minor salivary gland biopsy	Chisholm–Mason grade IV sialadenitis

ANCA: antineutrophil cytoplasmic antibodies; CSF: cerebrospinal fluid; HIV: human immunodeficiency virus; HLA: human leukocyte antigen.

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Ethics approval: Not required for a single anonymised case report according to institutional policy.
Informed consent: Written informed consent was obtained from the patient for the publication of this case report and accompanying images.
Author contributions: O.C.R. managed the patient, collected the data, reviewed the literature and wrote the manuscript.

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