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LETTER TO THE EDITOR

Case report: hypertrophic pachymeningitis associated with Sjögren's syndrome

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Introduction

Sjögren syndrome (SS) is a systemic chronic autoimmune disorder characterized by lymphocytic infiltrates into the exocrine organs, particularly the parotid and lacrimal glands that results in typically distinct symptoms which manifest as xerophthalmia (dry eyes) and xerostomia (dry mouth). In addition, various organs could be involved with numerous extraglandular features, such as arthritis, Raynaud phenomenon, lymphoma, pulmonary disease, gastrointestinal disease, and neurological disease. Among the neurological diseases, sensory polyneuropathy is known to be the most common pattern, and mononeuropathy multiplex, polyradiculopathy, symptomatic dysautonomia, cranial neuropathy, myopathy, and central nervous system (CNS) involvement are less common [1].

The prevalence of CNS involvement in SS in a recent study was 67.5% [2]. However, a substantial variability in the reported prevalence exists because of the selection and referral bias [3]. Although the wide spectrum of CNS manifestations of SS have been reported, hypertrophic pachymeningitis (HP) in SS is rare and only a few cases have been reported [4, 5]. We describe a rare case of HP associated with SS.

Case report

A 77-year-old Asian housewife presented with binocular diplopia, headache, bilateral periorbital, and temporomandibular (TM) joint pain for 2 weeks. At first, the bilateral TM joint pain started insidiously 2 weeks prior to admission, then it was followed by a gradually deteriorating headache and periorbital pain. Two days prior to admission, she suddenly complained of binocular diplopia. Her past medical history included hypertension and type 2 diabetes mellitus. She was taking metformin, sitagliptin, and amlodipine. Her body temperature was 36.5 °C. Initial neurologic examination revealed a partial lateral gaze palsy in her right eye, indicating paralysis of the abducens cranial nerve (Fig. 1). Other neurologic examinations evaluating the other cranial nerve functions, muscle strength, sensory function, cerebellar function, and deep tendon reflexes were all normal. Funduscopic examination revealed normal discs, maculae, and retinal vasculature.

Initial gadolinium-enhanced, magnetic resonance images (MRI) of the brain revealed diffuse hypertrophic enhancement of the pachymeninges on the whole brain (Fig. 2a–c). Laboratory analysis revealed elevated C-reactive protein (CRP; 153.90 mg/L, normal range < 5 mg/L). Additional laboratory test investigating the potential cause of secondary HP showed that the anti SS-related antigen A (SSA; anti-Ro) antibody (Ab) was markedly elevated (> 600 U/mL, normal range < 8 U/mL).

Other laboratory studies to diagnose connective tissue diseases, vasculitis, and any other systemic diseases included tests such as the identification of triiodothyronine (T3), free thyroxine (T4), thyroid-stimulating hormone, anti-thyroid peroxidase antibodies, thyrotropin receptor antibodies, thyroglobulin antibodies, lupus anticoagulant, anti-neutrophil cytoplasmic antibodies (ANCAs), anti SS-related antigen B (anti La), human leukocyte antigens (HLA) B27, HLA B51, C3, C4, double-stranded DNA Ab, and antinuclear Ab. These tests were all unremarkable. The cerebrospinal fluid (CSF) study was conducted and the opening pressure was within normal range. Cell count and protein levels were normal. Based on the strong positive result of the anti-SSA Ab, we had a suspicion of her possibly having SS and recorded a detailed clinical history, asking questions again regarding sicca syndrome. She admitted that she had been struggling with an annoying dry eye and dry mouth symptoms for several years.

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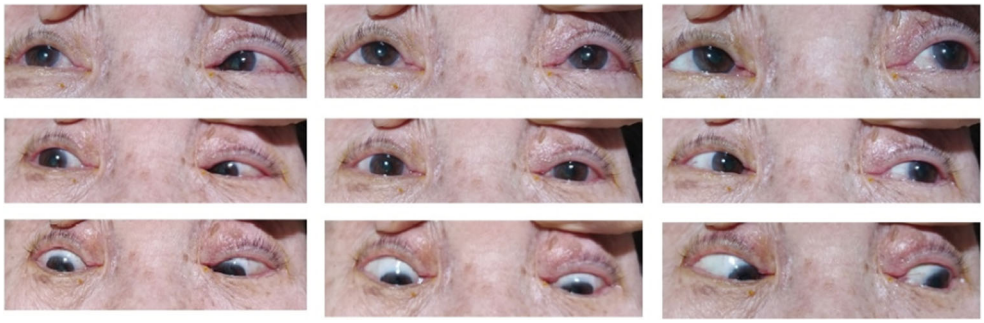

Fig. 1 Initial neurologic examination revealed partial lateral gaze palsy in her right eye indicating paralysis of abducens cranial nerve

On the salivary gland scintigraphy conducted with a Technetium-99m pertechnetate injection (Fig. 3), we obtained serial dynamic images of both salivary glands. Relative uptake ratios of salivary glands were decreased (2.28 in parotid glands and 3.28 in submandibular glands). After juice stimulation, the excretion of submandibular glands was decreased (right 15.3% and left 6.1%).

The minor salivary gland biopsy was performed under the inner surface of the lower lip, which revealed lymphocytic sialadenitis compatible with SS.

Intravenous methylprednisolone (1000 mg/day) was administered for 5 days, followed by the oral prednisolone (1 mg/kg) under the diagnosis of SS-related HP. During the steroid-pulse therapy, her headache and periorbital and TM joint pain dramatically subsided and her diplopia also gradually improved over the next few days. At day 5 after the initiation of steroid therapy, the level of serum CRP decreased to 6.38 mg/L from the initial 153.90 mg/L on the admission day (Fig. 4). A follow-up MRI performed 14 days after initial MRI study did not demonstrate HP findings anymore (Fig. 1d–f). The oral prednisolone was slowly and successfully tapered over several weeks without any recurrence.

Discussion

HP is a diffuse inflammatory disease that causes thickening of the dura mater. It can be divided into primary and secondary forms. The primary idiopathic form is when identifiable causes are not found [6], while the secondary form is considered when there is an identifiable cause. Various conditions have been reported to be associated with HP, including infection, malignancy, and autoimmune disease [7]. A Japanese study on pachymeningitis enrolled a cohort of 149 patients and the general HP etiology could be described as idiopathic (44%) and anti-neutrophil cytoplasmic antibody (ANCA)–related (34%) followed by IgG4/multifocal fibrosclerosis–related symptoms (8.8%) [5]. Rheumatoid arthritis, giant cell arteritis, sarcoidosis, mixed connective tissue disease, undifferentiated connective

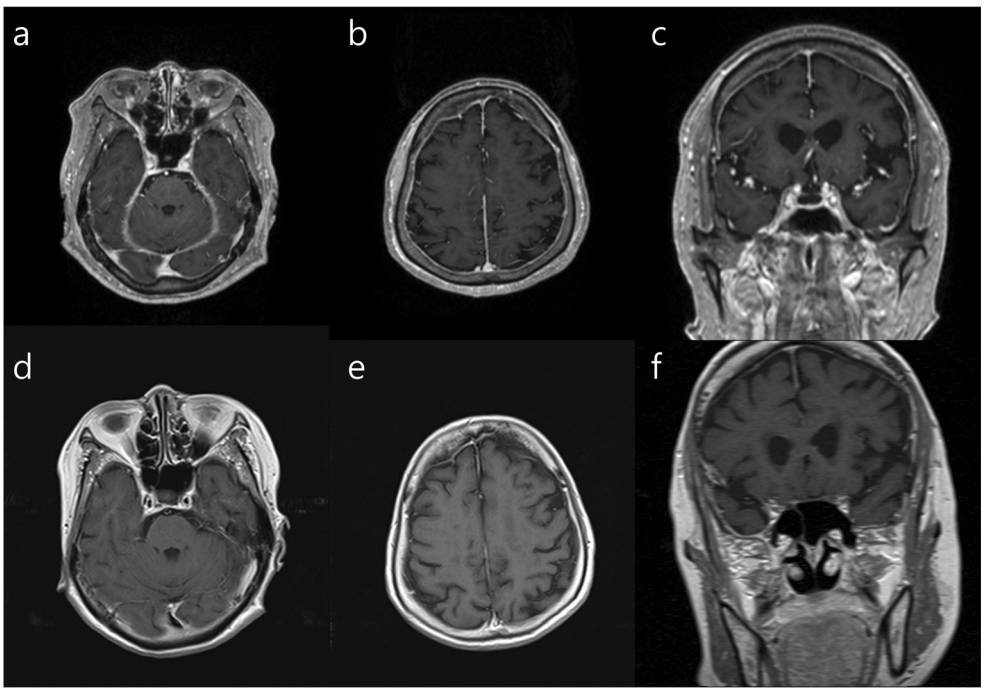

Fig. 2 Initial magnetic resonance imaging (MRI) of the brain with gadolinium enhancement revealed diffuse hypertrophic enhancement of pachymeninges on the whole brain (**a**–**c**). Follow-up MRI performed 14 days later with steroid therapy did not show the previously demonstrated hypertrophic pachymeningitis (HP) any longer (**d**–**f**)

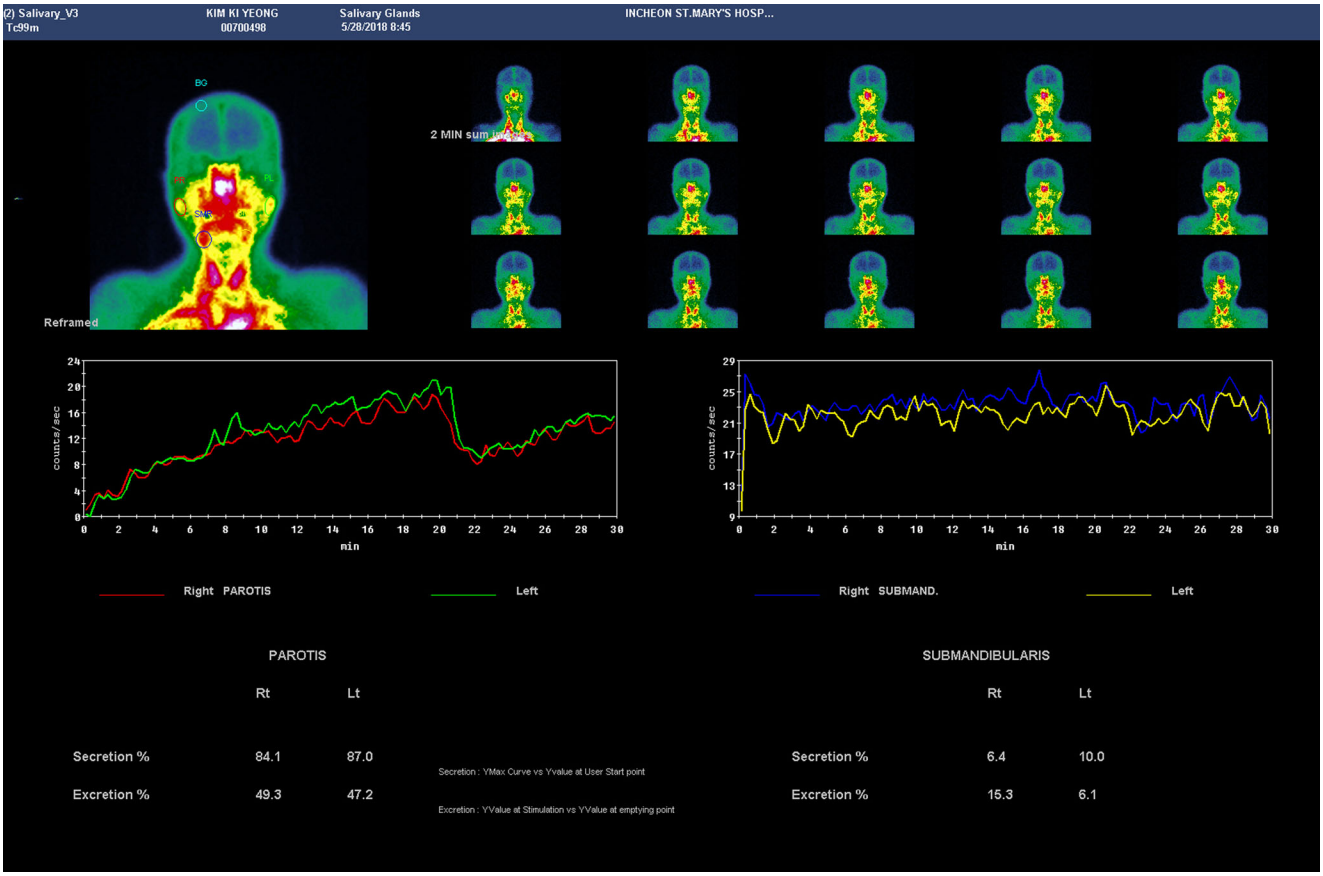

Fig. 3 On salivary gland scintigraphy with Technetium-99m pertechnetate injection, relative uptake ratios of salivary glands were decreased (2.28 in parotid glands and 3.28 in submandibular glands). After juice stimulation, the excretion of submandibular glands was decreased (right 15.3% and left 6.1%)

tissue disease, and relapsing polychondritis have also been reported to be associated with HP [8–10]. However, SS-related HP is very rare and only few cases have been reported [4, 11]. Among them, one study performed a surgical biopsy of the dura mater and histological evaluation demonstrated the inflammatory infiltration of small lymphocytes and plasma cells into the thickened dura which was compatible with the SS-related HP [11].

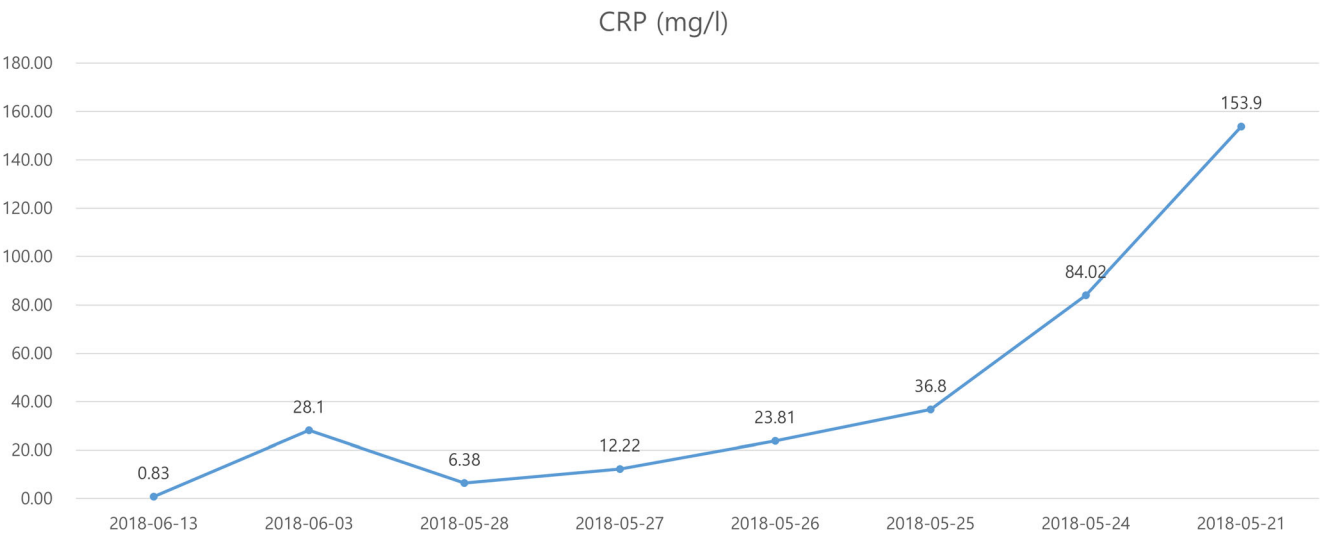

Fig. 4 The patient's serum level trajectory of C-reactive protein (CRP). Initial CRP level of 153.90 mg/L steeply decreased to 6.38 mg/L with 5 days of steroid therapy

In our case, HP was first identified and SS was diagnosed thereafter during the investigating the potential cause of secondary HP. Tailored clinical history taking performed later revealed that she had been suffering from typical sicca syndrome for several years. Her diagnosis as having SS was confirmed by tissue biopsy and histological evaluation. Our patients presented with binocular diplopia and demonstrated abducens cranial nerve palsy on neurologic examination. With respect to cranial nerve palsy, all previously reported cases with SS-related HP demonstrated no cranial nerve palsy [4, 11], whereas ANCA-related or IgG4-related HP was often accompanied with a cranial nerve palsy [5, 12]. Therefore, it is postulated that the clinical manifestations may differ between SS-related HP and ANCA, or IgG4-related HP, in that SS-related HP is not associated with cranial nerve palsy [4]. Interestingly, our patient demonstrated abducens cranial nerve palsy. Furthermore, given the fact that the idiopathic form of HP may or may not be accompanied with cranial nerve palsy [6, 13, 14], we think more studies need to be reported to assure the difference of clinical features regarding cranial nerve palsy between SS-related HP and ANCA or IgG4-related HP. We surmise that there is a possibility that whether the involvement of cranial nerve palsy in HS is present or not might be merely dependent on the extension degree of the inflammation regardless of the etiologies of the secondary form or even of the idiopathic form.

Our patient was dramatically responsive to steroid pulse therapy, followed by oral prednisolone. The optimal dosage of corticosteroids in the treatment of SS-related HP has not been determined. In one study, oral prednisolone 40 mg/day (0.8 mg/kg) with rapid tapering and without steroid pulse therapy was sufficient to ameliorate the symptoms and signs of HP [4].

In conclusion, we described a patient with SS-related HP. The manifestation with HP in SS is very rare. Therefore, we should keep vigilant in the consideration of SS as one of the differential diagnosis of HS. Unlike the previously reported cases with SS-related HP, our patient demonstrated the cranial nerve palsy. Corticosteroid therapy should be initiated promptly upon diagnosis of SS-related HP.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Chai J, Logigian EL (2010) Neurological manifestations of primary Sjogren's syndrome. Curr Opin Neurol 23(5):509–513. https://doi.org/10.1097/WCO.0b013e32833de6ab
2. Morreale M, Marchione P, Giacomini P, Pontecorvo S, Marianetti M, Vento C, Tinelli E, Francia A (2014) Neurological involvement in primary Sjogren syndrome: a focus on central nervous system. PLoS One 9(1):e84605. https://doi.org/10.1371/journal.pone.0084605
3. Soliotis FC, Mavragani CP, Moutsopoulos HM (2004) Central nervous system involvement in Sjögren's syndrome. Ann Rheum Dis 63(6):616–620. https://doi.org/10.1136/ard.2003.019497
4. Nakano Y, Yamamoto M, Komatsu K, Yagita M, Fujita M (2018) Hypertrophic pachymeningitis in Sjogren's syndrome. Intern Med 57(3):413–415. https://doi.org/10.2169/internalmedicine.9406-17
5. Yonekawa T, Murai H, Utsuki S, Matsushita T, Masaki K, Isobe N, Yamasaki R, Yoshida M, Kusunoki S, Sakata K, Fujii K, Kira J (2014) A nationwide survey of hypertrophic pachymeningitis in Japan. J Neurol Neurosurg Psychiatry 85(7):732–739. https://doi.org/10.1136/jnnp-2013-306410
6. Rossi S, Giannini F, Cerase A, Bartalini S, Tripodi S, Volpi N, Vatti G, Passero S, Galluzzi P, Ulivelli M (2004) Uncommon findings in idiopathic hypertrophic cranial pachymeningitis. J Neurol 251(5):548–555. https://doi.org/10.1007/s00415-004-0362-y
7. Kupersmith MJ, Martin V, Heller G, Shah A, Mitnick HJ (2004) Idiopathic hypertrophic pachymeningitis. Neurology 62(5):686–694
8. Fujimoto M, Kira J, Murai H, Yoshimura T, Takizawa K, Goto I (1993) Hypertrophic cranial pachymeningitis associated with mixed connective tissue disease; a comparison with idiopathic and infectious pachymeningitis. Intern Med 32(6):510–512
9. Ushiyama S, Kinoshita T, Shimojima Y, Ohashi N, Kishida D, Miyazaki D, Nakamura K, Sekijima Y, Ikeda SI (2016) Hypertrophic pachymeningitis as an early manifestation of relapsing polychondritis: case report and review of the literature. Case Rep Neurol 8(3):211–217. https://doi.org/10.1159/000450850
10. Wallace ZS, Carruthers MN, Khosroshahi A, Carruthers R, Shinagare S, Stemmer-Rachamimov A, Deshpande V, Stone JH (2013) IgG4-related disease and hypertrophic pachymeningitis. Medicine (Baltimore) 92(4):206–216. https://doi.org/10.1097/MD.0b013e31829cce35
11. Li JY, Lai PH, Lam HC, Lu LY, Cheng HH, Lee JK, Lo YK (1999) Hypertrophic cranial pachymeningitis and lymphocytic hypophysitis in Sjogren's syndrome. Neurology 52(2):420–423
12. Li S, Tang H, Rong X, Huang X, Li Q (2015) Pachymeningitis as a manifestation of ANCA-associated vasculitis: a care report and literature review. Int J Clin Exp Med 8(4):6352–6359
13. Huang Y, Chen J, Gui L (2017) A case of idiopathic hypertrophic pachymeningitis presenting with chronic headache and multiple cranial nerve palsies: a case report. Medicine (Baltimore) 96(29):e7549. https://doi.org/10.1097/md.0000000000007549
14. Mamelak AN, Kelly WM, Davis RL, Rosenblum ML (1993) Idiopathic hypertrophic cranial pachymeningitis. Report of three cases. J Neurosurg 79(2):270–276. https://doi.org/10.3171/jns.1993.79.2.0270