

[ CASE REPORT ]

## Hypertrophic Pachymeningitis in Sjögren's Syndrome

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### Abstract:

Although central nervous system manifestations seem common in primary Sjögren's syndrome, hypertrophic pachymeningitis is rare. We herein describe a case of Sjögren's syndrome that was associated with hypertrophic pachymeningitis. Sjögren's syndrome should be considered as a cause of hypertrophic pachymeningitis.

**Key words:** hypertrophic pachymeningitis, Sjögren's syndrome, central nervous system manifestations

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### Introduction

Hypertrophic pachymeningitis (HP) is a rare disease characterized by localized or diffuse thickening of the dura mater. Headache and fever are common symptoms and the compression of blood vessels or nerves may cause cranial nerve palsy, ataxia, and ophthalmic complications (1). HP may occur in association with underlying diseases such as infection, malignancy, and autoimmune disease (1). In the case of autoimmune disease, anti-neutrophil cytoplasmic antibody (ANCA)-related (microscopic polyangiitis and granulomatosis with polyangiitis) HP is the most common cause, followed by IgG4/multifocal fibrosclerosis-related HP (1, 2). Furthermore, associations with rheumatoid arthritis, giant cell arteritis, sarcoidosis, mixed connective tissue disease, undifferentiated connective tissue disease, and relapsing polychondritis, have been reported (3-6). However, HP in Sjögren's syndrome (SS) is rare (2). We herein describe a case of HP associated with SS.

### Case Report

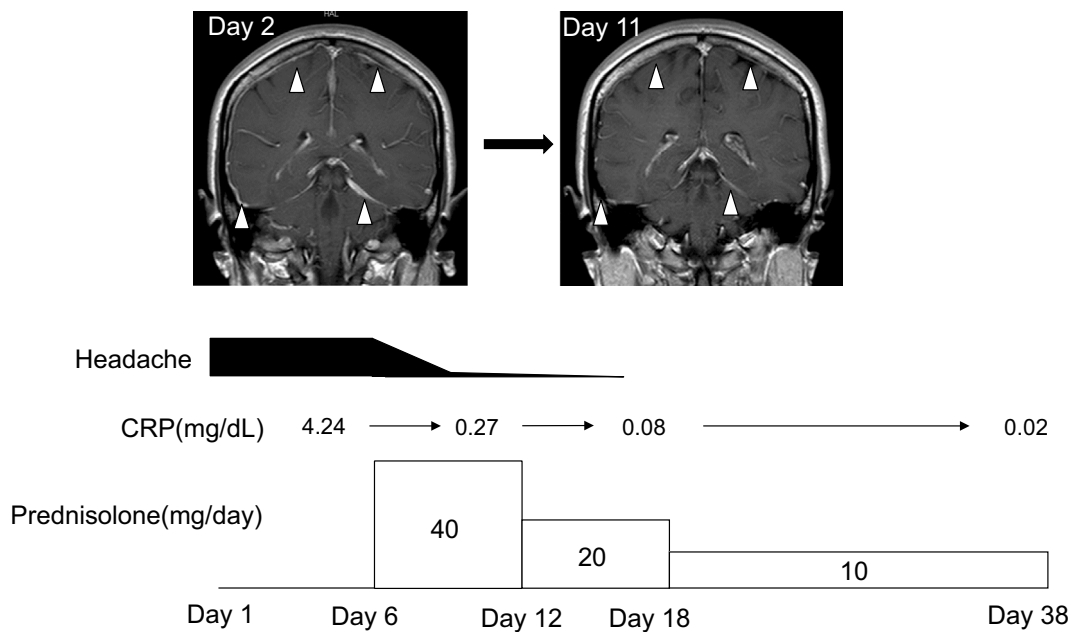
A 32-year-old woman was admitted with a 1-week history of fever, fatigue, and headache. She had a 6-month history of recurrent cervical lymphadenopathy. On admission to our hospital, there was no rash, arthritis, vision loss, or hearing loss. She did not complain of dry eye, dry mouth, cough,

phlegm, dyspnea, or chest pain. A physical examination showed bilateral cervical lymphadenopathy. The results of lung, cardiovascular, and abdominal examinations were normal. Otitis media, sinusitis, meningeal signs and cranial nerve involvement were absent. Her body temperature was 38.5°C. A laboratory analysis revealed following findings: white blood cells, 7,100/μL; hemoglobin, 13.4 g/dL; C-reactive protein (CRP), 7.64 mg/dL; blood glucose, 88 mg/dL; urea nitrogen, 6.6 mg/dL; and creatinine, 0.48 mg/dL. A urinalysis showed no proteinuria and hematuria. An analysis of her cerebrospinal fluid (CSF) revealed the following: polynuclear cells, 2/μL; mononuclear cells, 5/μL; glucose, 50 mg/dL; protein, 44.1 mg/dL; IgG, 11.1 mg/dL (0.8-5.0 mg/dL); and IgG index, 1.03 (<0.70). CSF cultures were negative for bacteria, *Mycobacterium tuberculosis*, and fungi. A cytological examination of the CSF showed no evidence of malignancy. Thus, the cause of headache was not specified at the time and a brain gadolinium-enhanced MRI study was performed. MRI revealed a thickened, abnormally enhanced dura mater (Figure) and the patient was diagnosed with HP. Next, we tried to identify an underlying disease of HP. Additional laboratory data included the following: IgG, 2,602 mg/dL; IgG4, 24.5 mg/dL; anti-nuclear antibodies, 11,280 (speckled); anti-SS-A antibodies, 1,256; anti-SS-B antibodies, 1:128; and anti-neuronal cell antibodies, 178 U/mL (<18 U/mL). The patient was negative for antibodies to double-stranded DNA, cardiolipin, ribonucleoprotein, RNA-polymerase III, PR3-ANCA, myeloperoxidase (MPO)-

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**Figure.** The patient's clinical course. A gadolinium-enhanced MRI study revealed a thickened, abnormally enhanced dura mater (day 2). Oral prednisolone [40 mg/day (0.8mg/kg)] was started on day 6. Follow-up MRI revealed a decrease in the thickness of dura mater (day 11). The dose of prednisolone was rapidly tapered to 10 mg/day within 2 weeks. The dura mater (arrowheads).

ANCA, and N-methyl-D-aspartate receptor NR2 subunit (NR2). The CSF was positive anti-neuronal antibodies [2.97 U/mL (<0.27 U/mL)] and anti-NR2 antibodies [0.16 U/mL (<0.1 U/mL)]. Thus, it was suspected that the patient had SS. Next, an ophthalmological examination was performed. Schirmer's test yielded a positive result (right, 2 mm/5 min; left, 4 mm/5 min). A fluorescein eye stain test was also positive. The salivary gland involvement was evaluated. A chewing gum test was positive (6.1 mL/10 min). Salivary gland scintigraphy showed no abnormalities. We did not perform a salivary gland biopsy or sialography. Taken together, the patient fulfilled the 1999 revised criteria of the Japanese Ministry of Health and Welfare for SS (positive results on Schirmer's test and a fluorescein staining test, and anti-SS-A antibody and anti-SS-B antibody positivity) (7). Based on these findings, the patient was diagnosed with SS-related HP, and treatment with oral prednisolone [40 mg/day (0.8 mg/kg)]; a prompt response was observed. Her fever and cervical lymphadenopathy disappeared 1 day after the initiation of prednisolone therapy. Her headache disappeared 10 days later. Her CRP level decreased to 0.27 mg/dL 5 days later. Follow-up MRI after 5 days revealed a decrease in the thickness of the dura (Figure). The dose of prednisolone was rapidly tapered to 10 mg/day within 2 weeks. Her clinical course is shown in Figure.

## Discussion

Central nervous system (CNS) manifestations seem common in primary SS; the reported prevalence varies (3.6% to 84%) (8-12). However, HP was not observed, even in five large studies, which included a total of 1,114 patients with

SS. Yonekawa et al. studied the underlying causes of pachymeningitis in Japan. A total of 149 patients with HP were enrolled in this nationwide survey (2). Among them, ANCA-related HP was found in 54 patients (34.0%). IgG4/multifocal fibrosclerosis-related HP was found in 14 patients (8.8%). Seventy cases (44%) were classified as idiopathic. Only two cases of SS-related HP were found. However, the details of the two cases were not described in that study. To our knowledge, only one case involving a patient with SS who developed HP has been described in detail in the past 30 years (13). In this case, the patient was diagnosed with SS 2 years prior to developing headache, dizziness, and fatigue. The patient did not show any visual field defects, visual loss, cranial nerve palsy, or ataxia. The patient underwent not only CSF and brain MRI studies, but also a surgical biopsy of the dura mater. A histological specimen showed the inflammatory infiltration of small lymphocytes and plasma cells into the thickened dura. Based on these findings, the patient was diagnosed with SS-related HP. The patient was treated with steroid pulse therapy followed by oral prednisolone (0.5 mg/kg/day); the dose was gradually tapered. After four courses of steroid pulse therapy, brain MRI showed a reduction in the thickness of the dura, and her clinical symptoms resolved. Interestingly, our patient had no visual or hearing impairments or cranial nerve palsy, similarly to the reported case. It has been reported that ANCA-related and IgG4-related HP often involve cranial nerve palsy, otological symptoms, or visual impairment (2, 14). The clinical features may differ between SS-related HP and ANCA/IgG4-related HP.

Importantly, SS was identified after the diagnosis of HP in our case. The patient lacked common symptoms, such as

rash, arthritis, dry mouth and dry eye; however, she had a 6-month history of recurrent cervical lymphadenopathy, which is retrospectively thought to have been related to SS. When the differential diagnosis of HP was considered, SS should be considered as a possible cause of HP.

Interestingly, anti-neuronal and anti-NR2 antibodies were detected in our case. These antibodies are reported to be associated with CNS involvement in systemic lupus erythematosus (SLE) (15, 16). However, they are not specific to SLE and are also detected in other rheumatic diseases, such as SS, ANCA-related vasculitis and rheumatoid arthritis (17-21). Several of the neurological complications in SS, including CNS involvement, are associated with anti-neuronal antibodies (17, 18) and memory dysfunction and/or hippocampal atrophy are associated with anti-NR2 antibodies (20, 21). Thus, the CNS involvement in SS may include HP. However, it is unclear whether these antibodies are associated with HP and the relationship between HP and these antibodies remain to be studied.

The optimal treatment of HP in SS remains unclear. In the treatment for ANCA-related, IgG4-related, or idiopathic HP, high-dose corticosteroids, including steroid pulse therapy, are the first line therapy and immunosuppressants are often added (2, 13). In the one reported case of HP in SS, the patient was treated with four courses of steroid pulse therapy and moderate-dose corticosteroids with gradual tapering (12). On the other hand, in our case, the patient was successfully treated with moderate-dose corticosteroids with rapid tapering and without steroid pulse therapy. Moderate-dose corticosteroids may be sufficient for the treatment of HP in SS, but further studies are needed to determine the optimal treatment.

In conclusion, we described the case of a patient with HP associated with primary SS. HP may occur in association with underlying diseases such as infection, malignancy, and autoimmune disease. However, most cases are classified as idiopathic HP, and lack an identifiable cause. SS should be considered as one cause of HP.

Informed consent was obtained from the patient described in the present study.

**The authors state that they have no Conflict of Interest (COI).**

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