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Letter to the Editor

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Letter to the Editor (Case report)

Area postrema syndrome secondary to primary Sjogren's syndrome

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Rheumatology key message

- Intractable nausea, vomiting or hiccups may signal APS in pSS, warranting autoimmune and MRI diagnostics.

Dear Editor, As area postrema syndrome (APS) secondary to primary Sjogren's syndrome (pSS) is a rare occurrence, we report here a case of a female patient with APS secondary to pSS.

A 35-year-old female had been hospitalized for a few days in July 2020 in the Department of Gastroenterology for the treatment of intermittent nausea, vomiting and persistent hiccups. She underwent gastroscopy, which revealed gastroesophageal reflux disease. She initially received antiemetic drugs and omeprazole, but showed a poor response. Several weeks later, she presented with severe dry cough and was hospitalized in the Department of Pneumology. The results of bronchofiberoscopy and bronchodilation test were normal. She was administered an antitussive agent, but this approach failed. She then developed optic neuritis. Antinuclear antibody (ANA) was positive, and extractable nuclear antigen (ENA) was positive for anti-U1RNP, anti-SSA and anti-Ro-52 antibodies. Results for antineutrophilic cytoplasmic antibody (ANCA) and anti-dsDNA were negative. Serum IgG level was 23.70 g/l (normal: 6–18 g/l). A bilateral Schirmer's test showed normal values. Lip biopsy demonstrated focal collections of lymphocytes (>4 foci/4 mm2 (Fig. 1B)) in keeping with the diagnosis of pSS. During her disease process, she experienced neither dry mouth nor dry eyes.

Additional examinations were conducted. Encephalic MRI was normal; however, cervical medullary MRI showed a hypersignal lesion in the T2 sequence at the C2 level (Fig. 1A). Cytochemical and microbial assessments showed normal cerebrospinal fluid. However, serum anti-aquaporin-4 (AQP4) antibody test was positive (titre: 1:32) (Fig. 1C). On the basis of these findings, she was diagnosed to have neuromyelitis optica spectrum disorder (NMOSD). She declined to undergo plasma exchange and was treated with 500 mg/day intravenous methylprednisolone and 20 g/day intravenous immunoglobin for 3 days. She was then administered 40 mg/day methylprednisolone continuously and 0.4 g cyclophosphamide once every 2 weeks. She is being followed up to monitor her response to the treatment.

Primary Sjogren's syndrome is an autoimmune disease that affects multiple systems, including the nervous system. NMOSD is a rare relapsing disease of the central nervous system (CNS), which is associated with pSS. Because NMOSD rarely coexists with pSS, the morbidity of NMOSD in pSS remains unknown [1]. Approximately 75% of patients with NMOSD often have an antibody that targets AQP4, the primary CNS water channel protein [2]. Area postrema (AP) is one of the AQP4-enriched areas that controls emetic reflex and houses chemosensitive neurons that mediate the process of hiccups [3]. NMOSD lesions in the AP lead to episodes of intractable nausea, vomiting or hiccups (INVH), particularly when the lesion is located in the dorsal medulla; this condition is known as AP syndrome (APS). APS is considered as a critical clinical criterion for NMOSD. A retrospective study showed a high prevalence of isolated APS in AQP4-IgG-seropositive patients with NMOSD, and nausea was more commonly observed in APS [4]; however, reports on the occurrence of APS secondary to pSS are rare.

Interestingly, our patient had dry cough. It is known that cough-related signals are conveyed to the caudal nucleus tractus solitarii (cNTS) that projects to the brainstem respiratory network. The latter is reconfigured to generate the cough motor pattern [5]. The study showed that electrical stimulation to the cNTS induced a cough-like response [6]. Because the cNTS is located near the AP, inflammatory lesions in the AP may potentially cause an intractable cough.

The mainstay of acute treatment of NMOSD secondary to a connective tissue disease is high-dose intravenous steroids, plasma exchange, cyclophosphamide, immunoglobulin and rituximab. The main long-term immunosuppressant therapies

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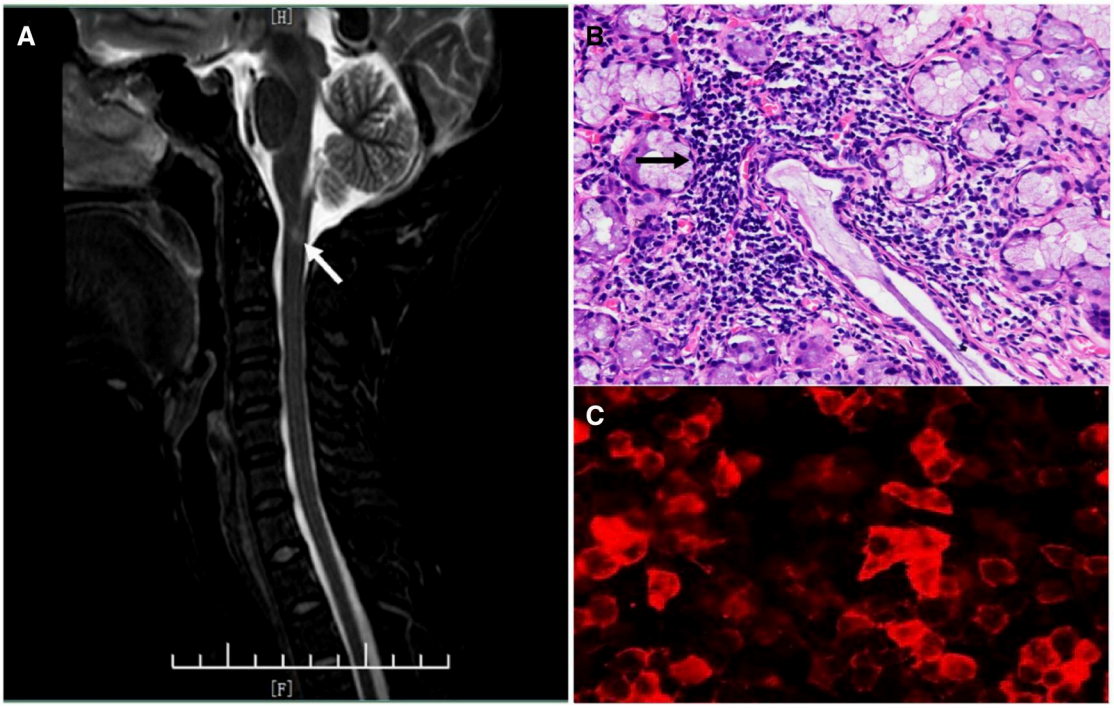

Figure 1. Imaging and biopsy results of the patient with NMOSD secondary to pSS. (A) Cervical medullary MRI showed a hypersignal lesion in the T2 sequence at the C2 level (highlighted by an arrow). (B) Lip biopsy showed focal collection of lymphocytes (highlighted by an arrow). (C) Serum anti-aquaporin-4 (AQP4) antibody test was positive by using cytometric bead array

used as preventive therapeutic strategies were rituximab, mycophenolate mofetil and azathioprine. Moreover, some new biologics such as eculizumab, inebilizumab and satralizumab have been approved for the treatment of NMOSD [1].

As APS secondary to pSS is a rare incidence, we suggest that patients presenting with INVH and without infection, metabolic disturbance or drug use should undergo autoimmune antibody test and brain MRI to exclude the presence of autoimmune diseases.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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