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Atypical case of primary sjögren's syndrome with psychiatric disorder

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Abstract

Primary Sjögren's Syndrome (PSS) is a systemic autoimmune disorder characterized by chronic inflammation of exocrine glands. Neurological manifestations are sometimes found in patients with PSS, and both the Central Nervous System (CNS) and Peripheral Nervous System (PNS) can be involved. Psychiatric disorder is a rare manifestation caused by PSS. Herein, we report a 67-year-old woman admitted from the department of neurology for further investigations of progressive psychiatric abnormalities. High titers (1:320) of Antinuclear Antibodies (ANA) and antibodies against SSA and Rheumatoid Factor (RF) were detected. Rheumatology review revealed a history of Sicca symptoms and her Schirmer's test was positive. This lead to the diagnosis of CNS complications associated with PSS. She had an excellent response to intravenous methylprednisolone followed by oral prednisolone and intravenous immunoglobulin infusions. This case highlights that CNS involvement can precede the diagnosis of PSS. For a patient with psychiatric disorder, attention should be paid to screening for accompanying PSS, especially in female patients.

Keywords: Primary Sjögren syndrome; Autoimmune disease; Neurological involvement; Central nervous system; Psychiatric disorder.

Background

Primary Sjögren Syndrome (PSS) is an autoimmune disease characterized by a chronic lymphocytic and plasmacellular infiltration of the lachrymal and salivary glands. PSS is associated with nervous system involvement, including both Peripheral Nervous System (PNS) and Central Nervous System (CNS) (Mori et al., 2005). CNS manifestations can be focal (acute transverse or progressive myelopathy, multiple sclerosis-like symptoms, sensory deficits, optic neuropathy) or diffuse (cognitive dysfunction, subacute aseptic meningitis, encephalopathy, psychiatric symptoms, chorea, and seizures). Here, we report a patient with PSS who also suffered psychiatric symptoms. We then discuss and review the literature on CNS involvement in PSS.

Case presentation

We present a case of a 67-year-old woman referred to neurology clinic with a 2-week history of unsteadiness and progressive psychiatric symptoms (authorized consent for publication from patient). She presented with severe physical asthenia, fatigue, irascibility, depression, insomnia and agitation, she was recalcitrant, verbally aggressive with the family and the medical staff. Meanwhile, she had a fever. The Rheumatology review revealed a history of Sicca symptoms for a few years and fatigue for a few months. She denied any arthralgia, skin rashes, mouth ulcers, hair loss or any other systemic symptoms. The Schirmer's test was positive; the biopsy of the salivary gland was refused by the patient.

Blood analysis showed that eosinophilic granulocyte, serum electrolytes, calcium, thyroid hormone, and creatine kinase were all normal. High-sensitivity C reactive protein level was 38.7 mg/L (normal <3 mg/L). Erythrocyte Sedimentation Rate (ESR) was 121 mm/h (normal <20 mm/h). Serum complement C3 and C4, immunoglobulin G, cryoglobulins, anti-phospholipid, anti-aquaporin 4 (anti-AQP4), anti-SSB, NMDAR, GABABR, LGI1, and antineutrophil cytoplasmic antibodies were negative. High titers (1:320) of Antinuclear Antibodies (ANA) and anti-SSA antibodies and Rheumatoid Factor (RF) were detected. However, results were negative for autoantibodies against dsDNA, Sm, and Scl-70, and antibodies against human immunodeficiency virus. Results were negative for the other paraneoplastic syndrome-associated antibodies, including anti-Hu, anti-Yo, anti-Ri, and anti-AMPA. Her Cerebrospinal Fluid (CSF) analysis was abnormal with increased level of proteins. Oligonucleotide bands were not detected.

Cranial MRI scan showed multiple small high-intensity lesions in the periventricular white matter on T2-weighted and Fluid-Attenuated Inversion Recovery (FLAIR), without gadolinium enhancement. Electroencephalogram (EEG) was performed. Slow wave were observed.

The ophthalmological exam showed a cornea without brightness, with erosions, a lachrymal secretory failure (positive Schirmer's test, both eyes 5 mm, and remained positive after the stimulation with 5% ammonium chloride vapors emitted 20 cm from the nose). The oral exam exhibited dry mucus, dental decays, filiform papillae atrophy, and decrease of the parotid glands salivary flux.

Psychiatric examination revealed a depressive anxious disorder. Endocrine examination eliminated thyroid disease as a possible cause of the physical asthenia. Neurological examination removed other neurological diseases, hereditary or achieved neuropathies.

Differential diagnosis should include other causes of psychiatric disorder including vasculitic causes, infection, other autoimmune diseases, and paraneoplastic syndromes. Antineutrophil cytoplasmic antibodies and autoimmune encephalitis associated antibodies are negative. Additionally other autoimmune antibodies are also negative, her CSF analysis was abnormal with a higher level of proteins, but CSF testing did not found bacteria, fungi and virus. Clinical assessment did not found any evidence of underlying malignancy. She also had negative onconeural antibodies testing including anti-HU, anti-YO, anti-RI. Consequently, these causes were also excluded in the case of our patient.

Our patient was treated with three doses of 1 g intravenous methylprednisolone followed by oral prednisolone and had two cycles of intravenous immunoglobulin infusions. The patient had an excellent response to the treatment, with significant improvement in her psychiatric abnormalities. Her CSF analysis returned to normal. After 1-year follow-up she remained in remission.

Discussion

PSS is associated with systemic involvement, including the nervous system. A variety of neurological complications has been reported in PSS patients, and both the CNS and PNS are associated with PSS [1,2]. Our patient showed typical PSS symptoms such as dry eyes and dry mouth, positive ANA and anti-SSA antibodies (with high titer over 1:320). There was no evidence of other autoimmune diseases. Therefore, the diagnosis of PSS was unquestionable. In addition, she displayed characterized features of psychiatric abnormalities, including irascibility, depression, insomnia, and she was recalcitrant, verbally aggressive with the family and the medical staff. The patient had an excellent response to immunosuppressive treatment, with significant improvement in her psychiatric symptoms. In our patient, the diagnosis of PSS was based on the 2012 American College of Rheumatology criteria. She had Sicca symptoms, strongly positive Schirmer's test, and positive ANA and anti-SSA antibodies. Hence, salivary gland biopsy was not considered to be essential.

CNS involvement in PSS includes focal and diffuse disorders (presenting encephalopathy, cognitive dysfunction, dementia, psychiatric abnormalities, seizures and aseptic meningoencephalitis). However, psychiatric abnormality is a rare form of CNS involvement in PSS. Malinow et al. reported a significant psychiatric impairment in about half of the examined patients [3]. Moreover, Belin et al. found neuropsychiatric impairment fails to correlate with structural damage and seems to be associated with SPECT abnormalities, but not MRI imaging results [4]. In clinical practice, CNS involvement frequently preceded the diagnosis of PSS [5]. Mori et al. reported 93% of patients were diagnosed with PSS after neurological symptoms appeared [2]. Furthermore, Teixeira et al. observed the absence of Sicca symptoms in 46% of patients at the onset of neurological symptoms in patients of CNS involvement [6].The diversity and complexity of CNS involvement in PSS could explain why this disease is frequently misdiagnosed, being in these a diagnostic challenge and emphasizing the need of systematically screening for PSS in patients with neurological symptoms.

Our patients had white matter MRI lesions. MRI abnormalities frequently showed white matter lesions in the subcortical and periventricular areas in the patient of CNS-PSS [7]. But these lesions represent an unspecific finding. In some patients, this actually leads to misdiagnosis with MS, which shows characteristic lesions similar to PSS [8]. Sometimes, these lesions precedes diagnosis with PSS [9]. These lesions have been detected in 80% of patients with PSS and in 50% of patients with a diffuse pattern [5,10]. For patients with memory deficit or cognitive dysfunction, these lesions are always observed [11,12]. When the results are uncertain, SPECT is recommended to assess regional Cerebral Blood Flow as an alternative to MRI.

Up to now, the confirmed pathophysiological mechanisms responsible for CNS involvement in PSS are still unclear. The pathophysiological mechanism may be different according to neuropathy type. Three pathophysiological mechanisms may explain the CNS involvement. The first mechanism is the direct infiltration of the CNS by mononuclear cells [13]. The second mechanism is the vascular involvement [14]. The third underlying mechanism is the ischemia secondary to small vessel vasculitis [2].

There is no consensus about the specific treatment of CNS involvement in PSS. Generally, immunosuppressive therapy is the

principal treatment (such as corticosteroids or cytotoxic drugs). However, multiple studies offered alternatives, dependent on the neuropathological type. Therefore, all therapy must be individualized. Our patient had significant functional improvement with intravenous methylprednisolone followed by pulses of intravenous immunoglobulin infusions.

Concluding remarks

In conclusion, CNS involvements are common in PSS and often as the first manifestation of PSS. The accurate prevalence of these manifestations is difficult to assess due to the heterogeneity of the diseases. The pathophysiological mechanisms responsible for most forms of CNS involvement in PSS remain unknown, but vascular, ischemia, and immunological mechanisms have been described. For our patient, psychiatric disorder was considered a rare and special manifestation of central neuropathy resulting from PSS. Thus, for a patient with psychiatric disorder, more attention should be paid to screening for accompanying PSS, especially in female patients with neurological symptoms without other evident cause. It will help us correctly diagnose and effectively treat.

Key points

- CNS involvement can be the first symptoms of PSS. Psychiatric disorder can be a rare CNS involvement of PSS.
- As such PSS or other connective tissue diseases should be considered in patients presenting with psychiatric abnormalities.
- Appropriate immunosuppressive therapy can improve symptoms and function in these patients.

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