

Central nervous system involvement in primary Sjögren's syndrome manifesting as multiple sclerosis

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ABSTRACT

إن أعراض الجهاز العصبي المركزي في المرضى الذين يعانون من متلازمة شوغرن الأولية هي نادرة. ويمكن أن تظهر على شكل غدية إضافية ويتطلب التشخيص التفريقي من التصلب المتعدد. بسبب مجموعة متنوعة من الأعراض، فأعراض شوغرن العصبية قد يصعب تشخيصها. هنا، يبين التقرير عن حالة امرأة تبلغ من العمر 75 عاماً والتي تم تشخيصها المبدي بالتصلب المتعدد في عام 2010م، ولكن الذين تم تشخيصهم لاحقاً مع متلازمة شوغرن الأولية تبين بعد مرور سنتين ظهور علامات عصبية شاذة. لذلك، ينبغي أن يُشخص متلازمة شوغرن الأولية في المرضى الذين يعانون من مظاهر العصبية السريرية وشعاعية شاذة.

Central nervous system symptoms in patients with primary Sjögren's syndrome are rare. They can present as extraglandular manifestations and require a differential diagnosis from multiple sclerosis. Due to a variety of presentations, Sjögren's syndrome with neurologic involvement may be difficult to diagnose. Here, we report a case of a 75-year-old woman who was first diagnosed with multiple sclerosis in 2010, but who was subsequently diagnosed with primary Sjögren's syndrome 2 years later after showing signs of atypical neurologic manifestations. Therefore, primary Sjögren's syndrome should be suspected in patients who present with atypical clinical and radiologic neurologic manifestations.

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Sjögren's syndrome (SS) is a chronic autoimmune disease of the exocrine glands characterized by focal lymphocytic infiltration and destruction of these glands. There is no consensus regarding the prevalence of CNS involvement in SS.^{1,2} The CNS manifestations in SS are diverse and span the entire neuroaxis. The diagnosis of SS requires a set of rigorous clinical and immunologic criteria, the most widely used being the European criteria of Vitali.³ Due to a complex array of symptoms, physicians should pay attention to atypical extraglandular symptoms in addition to the classic clinical triad: 1) xerophthalmia, 2) xerostomia, and 3) laboratory evidence suggesting a systemic autoimmune disease. Our objective in presenting this particular case is to report a patient who fulfilled Vitali's criteria for primary SS and presented atypical neurologic manifestations.

Case Report. A 75-year-old right-handed woman was first admitted in May 2010 with a history of numbness of limbs and sensory change from both lower extremities to both upper extremities progressively, with zonesthesia in waist and belly during the previous 2 years. She had no diplopia. Urination was normal. She suffered from diabetes. She visited a neurology clinical and was treated under the impression of myelitis, and she felt the symptoms lightened. However, in February 2011 the above-mentioned symptoms recurred, and she visited the neurology department of our hospital. She was diagnosed with multiple sclerosis (MS) following the neurologic examinations and auxiliary examination such as brain MRI, lumbar puncture, and so forth. Intravenous and oral Methylprednisolone therapy for 2 months improved her neurologic signs, whereas the MRI lesions remained stable. In July 2012, she felt paresthesia more seriously and swelling of the

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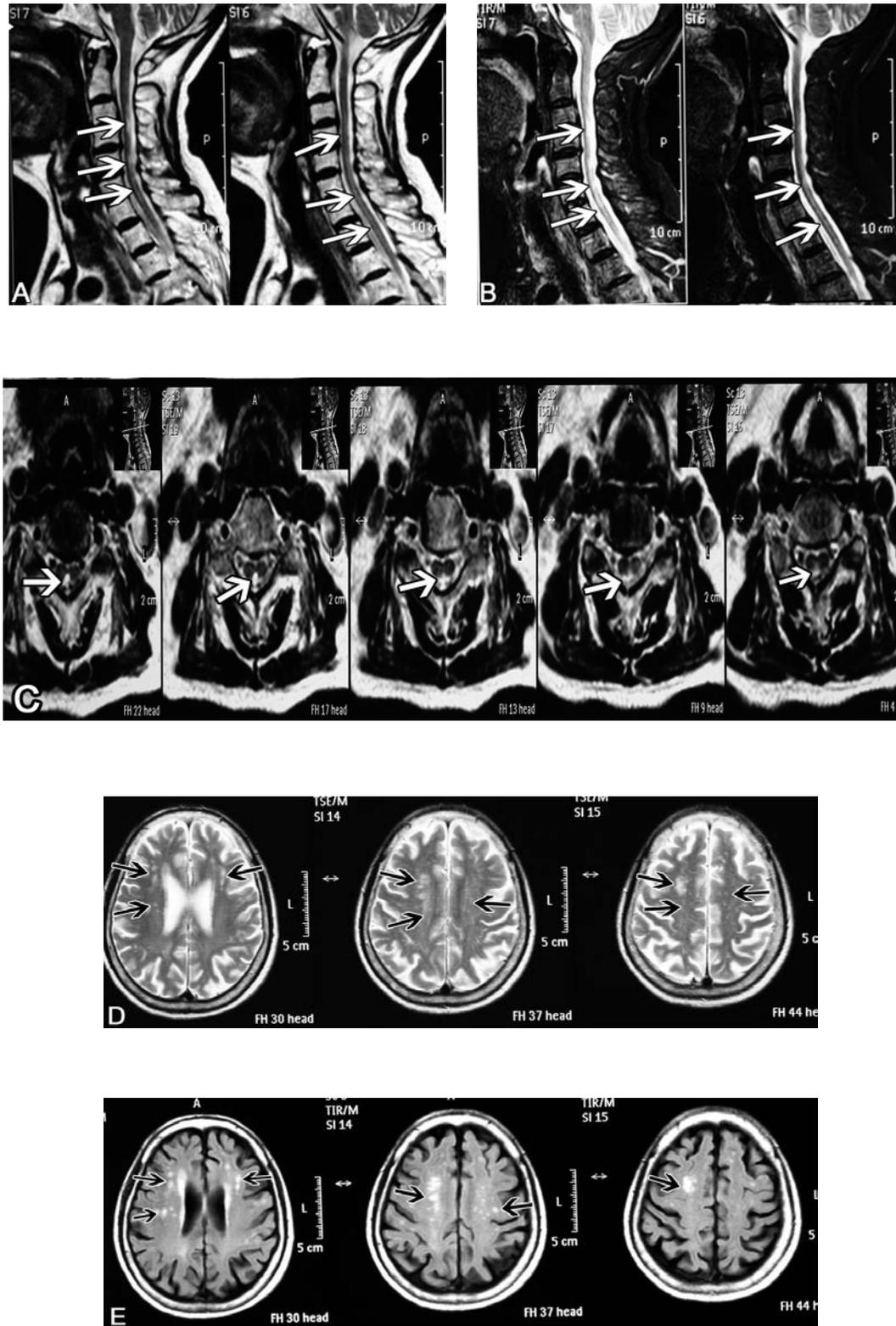


Figure 1 - Sagittal magnetic resonance T2-weighted A) and fat suppression B) images showing a strip of hyperintensity in the cervical cord (C3-C7). An axial T2-weighted C) image showing small hyperintensities in the cervical cord. Axial T2-weighted D) and FLAIR E) images showing several small hyperintensities in the white matter near both lateral ventricles in the brain.

parotid gland for 3 days. She had no dry eyes and dry mouth. On neurologic examination at that time, she showed spasticity of upper and lower extremities, more decreased muscle power, hyperesthesia on both lower extremities, and hyperreflexia on both upper and lower extremities. An MRI confirmed a strip of lesion in the cervical cord (C3-C7), and several small white matter lesions near both lateral ventricles. They showed T2-weighted hyperintensities (Figure 1). The CSF analysis revealed a pathologic IgG index (1.41) with only one band. Laboratory studies revealed the presence of antinuclear antibodies (1:100) and anti-SSA/Ro was positive; rheumatoid factor, total complement, and serum angiotensin convertase were normal. Oral and ocular sicca syndromes were suspected from history taking and confirmed by Schirmer test and labial salivary gland biopsies (Chisholm score greater than 4–Focus score >1) (Figure 2). This time she accepted intravenous and oral Methylprednisolone therapy for 2 months, followed by an immunosuppressive treatment (Plaquenil), which improved her neurologic signs again. After 6 months follow-up, she showed more improved muscle power and alleviated hyperesthesia in both lower extremities. She was also able to walk by herself again.

Discussion. Sjögren's syndrome is a chronic autoimmune disease of the exocrine glands that is characterized by focal lymphocytic infiltration and destruction of these glands. Diagnosis of primary SS is based on fulfillment of the criteria proposed by Vitali and coworkers in 1993.³ The patient in this case report presented with atypical clinical onset of the disease and unusual radiologic features, which are rarely described in the literature. She also had numbness of limbs that was associated with zonesthesia. The clinical presentation, MRI, and CSF analysis strongly suggested

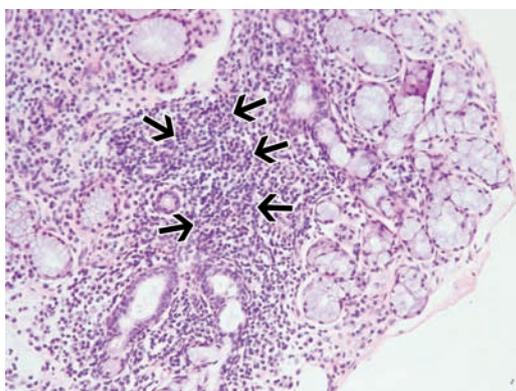


Figure 2 - Labial salivary glands densely infiltrated with small lymphocytes (hematoxylin and eosin staining; magnification 100x).

MS. However, the patient's age and the presence of sicca syndrome made MS unlikely. Approximately 10-33% of neurological forms of SS present as MS.⁴ A brain MRI is typically abnormal in more than 70% of primary SS patients with neurologic disease.⁵ In addition, most patients with focal CNS disease exhibit multiple T2-weighted hyperintensities in the subcortical and periventricular white matter as well as the spinal cord.² In brain MRIs, these lesions are consistent with micro-infarcts, but often cannot be distinguished from demyelinating lesions. In addition, hyperintensities are usually less than one cm and are often not enhanced with gadolinium.⁴ The patient in this study was positive for anti-SSA (Ro) antibodies. The frequency of anti-SSA/Ro or anti-SSB/La antibodies in primary SS patients has been found to be quite variable from study to study. Delalande et al⁴ detected anti-SSA antibodies in 48% of SS patients with CNS complications. Although most SS patients are positive for anti-Ro (SS-A)/anti-La (SS-B), ANAs, or anti-rheumatoid factor antibodies, the absence of antibodies does not exclude a diagnosis of SS.⁶

Sjögren's syndrome is one of the most common rheumatic diseases, but it is often under-recognized. The symptoms of SS may be subtle and are often insidious and dismissed as secondary to the normal aging process, depression, or neurosis. Sjögren's syndrome mimics other diseases, such as systemic lupus erythematosus, rheumatoid arthritis, chronic fatigue syndrome, and MS.⁶ However, the external stigmata characteristic of other rheumatic diseases are usually subtle or absent in SS.

The presence of unusual neurologic problems and a serologic profile of positivity for SS-A or SS-B auto-antibodies can complicate a diagnosis of SS.⁷ The CNS signs are multifocal and either progressive or relapsing, and often mimic MS in CSF profiles.⁸ The relationship between SS and MS is ambiguous, and SS may mimic MS both clinically and neuroradiologically.⁵ Therefore, we recommend that clinicians consider primary SS as a differential diagnosis of a patient presenting with a syndrome that resembles MS.

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