Optic neuritis as an initial presentation of primary Sjögren syndrome
A case report and literature review

Jia-Yue Sun, MDa, Zheng Liu, PhDb, Peng Zhao, MDb, Tao Liu, MDa,*

Abstract

Background: Primary Sjögren syndrome (pSS) is a progressive autoimmune disease that primarily affects exocrine glands. The clinical presentation of pSS may vary from an asymptomatic condition to severe skin symptom, resulting in a difficult and challenging diagnosis and treatment.

Methods and results: Here, we report a 47-year-old Chinese woman who lost vision in the right eye for 7 days. She had been misdiagnosed with primary optic neuritis for 3 months. After 3 months, the results of immunohistochemistry, salivary gland scintigraphy, and antibody tests proved the diagnosis of pSS. After an IV methylprednisolone treatment for 3 days (1.0 g/d), her final visual and perimeter outcome were satisfactory. A review of the relevant English literature based on PubMed encompassing dates up to July 2016 has been discussed.

Conclusion: Our finding and the literature review suggest that an early treatment may be beneficial but long-term disease may cause permanent irreparable damage.

Abbreviations: ANA = antinuclear antibody, anti-SSA = anti-Sjögren-syndrome-related antigen A, anti-SSB = anti-Sjögren syndrome type B, MRI = magnetic resonance imaging, OCT = optical coherence tomography, ON = optic neuritis, pSS = primary Sjögren syndrome, SGB = salivary gland biopsy, SGS = salivary gland scintigraphy, VEP = visual evoked potential.

Keywords: case report, methylprednisolone, optic neuritis, primary Sjögren syndrome

1. Introduction

Primary Sjögren syndrome (pSS) is a chronic and progressive autoimmune disease that mainly affects the exocrine glands.1 It is clinically characterized by dry eyes (keratitis sicca or keratoconjunctivitis sicca) and dry mouth (xerostomia).2,3 The pathognomonic histological finding in biopsies is the infiltration of salivary glands by mononuclear lymphoid cells, replacing the glandular epithelium.4 Optic neuritis (ON) can be the initial presentation of pSS, but is uncommon. The damage to the optic nerves produces swelling and inflammation that cause pain and loss of vision in pSS patients.5 Since the initial clinical presentation of pSS is varied, such symptoms are easily attributable to other causes, thus a correct diagnosis is often delayed. In this study, we present a pSS patient who has been misdiagnosed as primary ON for 3 months.

2. Case report

A 47-year-old woman presented with a sudden vision loss in her right eye for 7 days. No other symptom was present. She had no previous history of ON, pSS, or other autoimmune diseases. On first admission to hospital, her visual acuity was 0.15 on right eye and 1.0 on left eye. The bulb conjunctiva of the right eye was slightly congested. The fundoscopic examination of both eyes was within normal limits. Her both eyes had a temporal visual field defect, and right eye had a central visual field defect (Fig. 1A-F). Visual evoked potential (VEP) showed that a prolonged P100 latency (120.5 milliseconds) was in the right eye and the difference of P100 amplitude between the left and right eye was significant (Fig. 2A). The examination results of optical coherence tomography (OCT), fundus fluorescein angiography, craniocebral computed tomography, and magnetic resonance imaging (MRI) were all normal. After examination by an ophthalmologist in our hospital, a clinical diagnosis of primary ON was made. She received a local ophthalmic treatment, but refused a glucocorticoid treatment plan. Informed consent was obtained from the patient. All procedures performed in this study involving human participants were in accordance with the ethical standards of the Xi’an Jiaotong University committee and the Helsinki declaration of 1975, as revised in 2000. Three months later, on her second admission to our hospital, she developed dryness of mouth and eye. Serological investigations revealed raised levels of the following autoimmune antibodies: anti-Sjögren-syndrome-related antigen A (anti-SSA), anti-Sjögren syndrome type B (anti-SSB), and antinuclear (ANA)
The result of her Schirmer test was 10 mm in the right eye, 5 mm in the left eye. The result of tear film breakup time was 5 seconds in the right eye, 4 seconds in the left eye. A salivary gland scintigraphy (SGS) and labial salivary gland biopsy (SGB) were used to confirm the diagnosis of pSS (Figs. 3 and 4). SGS showed that uptake of $^{99m}$Tc-pertechnetate increased gradually during the first 20 minutes. About 0.5 mL of citric acid was applied at 20 minutes to stimulate secretion. The quantity of $^{99m}$Tc-pertechnetate decreased slightly and increased again 3 to 5 minutes later. Based on these findings, the patient was diagnosed as pSS. She has received IV methylprednisolone treatment for 3 days (1.0 g/d) and oral administration of leflunomide (20 mg/d) for 25 days. After the glucocorticoid therapy, her visual acuity was 0.8 in the right eye, 1.0 in the left eye. There was a significant improvement in the symptom and the result of VEP and perimetry in her both eyes (Fig. 2B). In addition, her Schirmer test was 12 mm in the right eye, 9 mm in the left. Tear break-up time was 9 seconds in the right eye, 7 seconds in the left eye. No signs of relapse were noted during the 1-year follow-up visits.

3. Literature review

A review of the relevant English literature based on a PubMed search encompassing dates up to July 2016 is discussed. Only the cases with description of clinical manifestations and ON as clinical presentation were used. The keywords used were primary Sjögren’s syndrome and optic neuritis.

The preliminary literature search identified 26 articles. After screening titles and abstracts, 17 articles were rejected because they were not case studies. After the full-text examination, 7
studies were selected. Table 1 lists reported cases in reverse chronological order. Among the 7 selected studies, 6 were published between 2000 and 2015, and 1 was published in 1998. All 7 patients in these reports were female. One report was from Singapore, 1 from Romania, 2 from Japan, 1 from Turkey, 1 from United States, and 1 from Mexico. Four cases have been misdiagnosed as primary ON at the initial admission to hospital. Two cases had the history of SS.

4. Discussion

pSS is a systemic autoimmune disease that mainly affects the exocrine glands and usually presents as persistent dryness of the mouth and eyes due to functional impairment of the salivary and lacrimal glands. The difference of ON caused by pSS and caused by other certain conditions is important for reasons of treatment. This diagnostic differentiation was facilitated by positive tests for xerophthalmia and findings of positive minor SGB. High titers of anti-SSA and anti-SSB antibodies provided additional help in the differential diagnosis. In this study, our patients presented initially with the signs and symptoms of ON, and showed no dryness of the mucosal surfaces. The patients were diagnosed as pSS by the further laboratory tests after 3 months. First, positive results for the serum anti-SSA and anti-SSB antibodies suggested our patient had an autoimmune disease. Some previous studies have demonstrated that the anti-SSA and anti-SSB antibodies were positive in most pSS patients. Second, SGB can provide additional hints in the assessment of doubtful cases. The SGB is highly specific for the diagnosis of pSS and play a crucial role in avoiding misdiagnoses. Taking together, positive serum anti-SSA antibody, anti-SSB antibody tests, and SGB could make a definitive diagnosis of pSS.

On literature search, we found only a few previous reports of pSS-associated ON. The pSS-associated ON was predominantly seen in middle-aged women. When the vision starts to decrease, the patients may not have other symptoms. Therefore it can be easily overlooked or misinterpreted. This constituted a diagnostic and therapeutic challenge. The consequences of misdiagnosis of pSS-associated ON are multifold. Firstly, it may delay the proper treatment and cause unexpected complication and vision loss. Secondly, misdiagnosis may lead to mistreatment and cause adverse effects. In the previous reports, 5 of 7 cases have been misdiagnosed as primary ON or other eye diseases. Two other cases have made the correct initial diagnosis since they had the medical history of SS. It suggest that a SS history can often provide the most important information in diagnosis of pSS.

Figure 3. Findings of our pSS patient with severe salivary functional damage. (A) Regions of interest on the static scintigraphy after the injection of $^{99m}$TcO-4 and schematic presentation of a time-activity curve; (B) compressed dynamic scintigrams 0 to 30 minutes after the injection of $^{99m}$TcO-4.

Figure 4. (A) and (B) Hematoxylin and eosin staining of labial salivary gland biopsy (H & E × 200). Black arrows in each image indicate histopathological changes (moderate lymphocytic infiltration of labial salivary gland tissue). The labial salivary gland focus score is 1.5.
Treatment of pSS also is challenging, especially when the patients had no sicca symptoms. To date, there is no standard treatment for pSS-associated ON. In these 7 cases, methylprednisolone is the most frequent choice of treatment. Other options include the oral prednisolone, cyclophosphamide, or plasmapheresis. In Table 1, 3 patients’ vision have improved after methylprednisolone treatment, but 1 suffered a respiratory arrest. These 2 patients’ vision improved after receiving a high-dose methylprednisolone treatment in the first 5 days. However, 2 cases reports have shown no benefits of methylprednisolone treatment. For example, Tan et al[6] reported a case of a 56-year-old female who received combination therapy with IV methylprednisolone (1 mg/kg body weight/d) and plasmapheresis for severe pSS, but the patient’s vision was not recovered. The reason for this may be the fact that the patient had SS for 12 years. The Schirmer test (<5 mm in both eyes) and MRI (swelling, edema, and enhancement of the orbital segment of the right optic nerve with marked enhancement and stranding in the intracanal fat) demonstrated she had severe optic nerve damage. Another case also has 10 years history of SS.[10] These suggest that history of SS and optic nerve damage may lead to permanent vision impairment. In addition, treatment to stop inflammation of pSS-associated ON may be sufficiently early to prevent significant permanent damage and save the patient’s eyesight. However, these conclusion need to be further investigated in a large number of cases.

In conclusion, a detailed medical history, antibodies test, and SGB are indispensable in the diagnosis of pSS. Moreover, in order to develop the appropriate management plan and subsequent prophylaxis in patient with ON caused by pSS, it is fundamental to differentiate between pSS-associated ON and primary ON. Last, based on our case report and the review of literatures, we conclude that the use of high-dose methylprednisolone therapy in the first several days of admission is a promising treatment option for pSS-associated ON.

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