Rhombencephalitis as an Initial Manifestation of Primary Sjögren’s Syndrome: A Case Report and Review of the Literatures

San-Feng Chen, Ming-Jang Chiu, Jen-Jen Su

Abstract-

Purpose: We present a case report and a comprehensive review of the literature concerning aseptic meningoencephalitis and Sjögren’s syndrome (SS).

Case Report: We report a 44-year-old woman of primary SS with initial presentation of aseptic meningoencephalitis and a reversible magnetic resonance image (MRI) lesion in the medulla. The diagnosis of primary SS based on ocular dryness, lacrimal hyposecretion, secretory and excretory dysfunction from sialocintigraphy, and positive anti-SS-A antibodies. Corticosteroid and cyclophosphamide therapies reversed the neurological deficits and the MRI lesion.

Conclusion: Primary SS may have variable manifestations in the central nervous system which may precede the classic sicca symptoms. SS should be investigated in cases of aseptic meningoencephalitis even without clinical signs of xerostomia or xerophthalmia. MRI is useful in demonstrating brain lesions and in evaluating treatment efficacy of the SS.

Key Words: Sjögren’s syndrome, meningoencephalitis, anti-Sjögren’s syndrome A antibody, anti-Sjögren’s syndrome B antibody

INTRODUCTION

Sjögren’s syndrome (SS) is an autoimmune disease, which may be either primary or secondary to other connective tissue diseases. The pathology of SS is characterized by mononuclear cell infiltration and destruction of salivary and lacrimal glands, leading to xerostomia and xerophthalmia. Peripheral nervous system (PNS) involvement is a well-documented occurrence with a frequency of 10-20%. However, prevalence of the central nervous system (CNS) involvement is still a controversial issue, with a frequency ranging from 1.5% to 25%. Since meningoencephalitis in primary SS is treatable, it is important to understand its clinical features in order to make a differential diagnosis of meningoencephalitis. We report a patient with primary SS, who presented with aseptic meningoencephalitis and a reversible magnetic resonance image (MRI) lesion in
the medulla oblongata.

**CASE REPORT**

The 44-year-old woman suffered from progressive dizziness, nausea, and vomiting for 2 weeks before admission, she later developed an unsteady gait with deviation to the right side and occasional vertigo and diplopia. She also complained of numbness in the lower part of her face. Neurological examination revealed that the patient was in a state of clear consciousness. She displayed mild weakness with scores of manual muscle test (MMT) 4+/5 in bilateral lower limbs. She was normal in all modalities of sensory test including pinprick, light touch, temperature, and joint position sense. She had overt dysphagia, thus a nasogastric tube was inserted. Head magnetic resonance image (MRI) showed an abnormal high signal intensity (SI) at the left medulla oblongata without definite contrast medium enhancement (Figure 1A & B). Brain tumor was suspected. After admission, she developed progressive weakness and became bed-ridden on the 5th day of hospitalization. Her muscle power reduced to MMT 0/5 (right upper limb), 2/5 (right lower limb), 3/5 (left upper limb), and 2/5 (left lower limb). Generalized hyper-reflexia was found. Methylprednisolone, 40 mg, every 8 hours, was given by intravenous injection for clinical deterioration. However the clinical condition did not improve after steroid therapy.

Follow-up MRI identified an ill-defined lesion with a fluffy margin and mild mass effect in the left medulla oblongata with minimal peripheral enhancement. But there was no evident intrathecal lesion or focal SI change in the cervicothoracic cord. Inflammatory or demyelinating lesion was then considered (Figure 1C & D). Brain tumor was suspected. After admission, she developed progressive weakness and became bed-ridden on the 5th day of hospitalization. Her muscle power reduced to MMT 0/5 (right upper limb), 2/5 (right lower limb), 3/5 (left upper limb), and 2/5 (left lower limb). Generalized hyper-reflexia was found. Methylprednisolone, 40 mg, every 8 hours, was given by intravenous injection for clinical deterioration. However the clinical condition did not improve after steroid therapy.

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Visual evoked potential (VEP) study showed absence of goggle VEP from the left eye. The somatosensory evoked potential study showed a prolonged central conduction time from both median nerves compatible with a central lesion. A nerve conduction velocity (NCV) study showed markedly reduced compound muscle action potentials in nearly all sampled nerves, reduced sensory action potentials and mildly slowed sensory conduction velocity in some nerves. The F-wave study showed normal responses in the left tibial nerve, prolonged minimal latency in the right tibial nerve, and absence of F-waves in all other sampled nerves. The findings suggested a motor-predominant axonal polyradiculoneuropathy. The results of cerebrospinal fluid were unremarkable with normal cell count (L/N 3/0), normal level of protein (43 mg/dL) and no malignant cells.

The patient developed multi-lobar pneumonia. Chest X-ray showed patchy lesions and increased infiltration in the bilateral lung fields. Chest computed tomography scans showed patchy ground glass opacity in both lungs and consolidation in the right lung (Figure 2). Dyspnea progressed in the patient and she received intubation, ventilator support and finally tracheotomy. Follow-up chest x-ray did not show obvious improvement after antibiotic adjustment. Interstitial lung disease caused by the autoimmune process was highly considered. Therefore, we gave her steroid pulse therapy with intravenous methylprednisolone of 1000 mg per days for 5 days followed by oral steroid therapy. The dyspnea improved and the ventilator weaning program was then successful.

Because of the possible association between brain-stem encephalitis and interstitial lung disease, we started a series of autoimmune examination, which revealed normal anti-nuclear antibody, normal complement (3,4) but positive anti-Sjogren’s syndrome A (anti-SSA) antibody. The Schirmer test showed no tears after 5 min. Tc-99m sialoscintigraphy showed secretory and excretory dysfunction of bilateral salivary glands. Tracing back her history, the patient suffered from dry mouth and dry eyes for several years. The patient was then diagnosed with primary SS with aseptic meningoencephalitis, on the basis of the positive clinical and serological tests, Schirmer test, and sialoscintigraphy. For disease modification, the patient was treated with cyclophosphamide (500 mg) by intravenous infusion. The nasogastric tube and Foley catheter were both removed smoothly, and the
tracheotomy was closed later. Her muscle power almost fully restored after rehabilitation. The patient took one tablet of hydroxychloroquin twice a day after discharge with gradual tapering of oral steroid. During the regular follow-up at our outpatient clinic, there was no recurrence of meningoencephalitis or any other manifestation of SS in the following 2 years. Follow-up head MRI 2 years after the episode did not show any new lesion (Figure 1E & F).

DISCUSSION

Among the extra-glandular manifestations of primary SS, involvement of CNS has been described as non-existing to quite common depending on the diagnostic and inclusion criteria used by the study(7). CNS lesion of primary SS could be monofocal, multifocal or diffuse involvement with wide-spectrum clinical manifestations of neuropsychiatric and spinal cord symptoms. Its clinical course could be insidious onset, remitting course, or progression(4). Meningoencephalitis as the initial manifestation of patients with primary SS has been reported in few cases (Table). Acute rhombencephalitis with fever and bilateral hearing loss secondary to SS was reported in one patient(12). In Kurne at al’s series five SS patients presenting transverse myelopathy, two patients developed additional lesions in the brainstem and one had them in the cerebellum(13).

Cerebral vasculitis has been considered to be the pathologic mechanism of CNS manifestation of primary SS. Necrotizing vasculitis, involving numerous small arteries and arterioles, was observed in a patient with
primary SS at necropsy (16). Severe necrotic arterial vasculitis and thrombus formation was noted in another patient of chronic Sjögren’s cerebritis complicated by bilateral superior cerebellar artery occlusion and diffuse subarachnoid hemorrhage (17). On the other hand, Caselli et al reported five cases of steroid-responsive encephalopathy and proposed the term nonvasculitic autoimmune inflammatory meningoencephalitis (18), which was also described in patients with SS, systemic lupus erythematosus, and Hashimoto’s disease (19). Gerraty et al presented a fatal case of aseptic meningoencephalitis in an 18-year-old woman with primary

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**Table. Review of literature for primary Sjögren’s syndrome with CNS involvement. (NR: not recorded)**

<table>
<thead>
<tr>
<th>Author (et al)</th>
<th>Patient no</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Country</th>
<th>Year</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Rafai MA</td>
<td>5</td>
<td>F</td>
<td>43</td>
<td>4 chronic myelopathy, 1 aseptic meningoencephalitis</td>
<td>Confusional syndrome in the one with meningoencephalitis</td>
<td>Maroc</td>
<td>2009</td>
<td>29</td>
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<tr>
<td>Béjot Y</td>
<td>1</td>
<td>F</td>
<td>53</td>
<td>Bilateral optic neuropathy with aseptic meningitis</td>
<td>Rapidly progressive visual loss</td>
<td>France</td>
<td>2008</td>
<td>26</td>
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<tr>
<td>Kurne A</td>
<td>5</td>
<td>F</td>
<td>10-52</td>
<td>Transverse myelopathy, 2 cerebrum/brainstem lesion; 1 cerebrum/cerebellum lesion</td>
<td>NR (just MRI and diagnosis in figure)</td>
<td>Turkey</td>
<td>2008</td>
<td>13</td>
</tr>
<tr>
<td>Hoshina T</td>
<td>1</td>
<td>F</td>
<td>16</td>
<td>Meningoencephalitis, Cerebrothoracic myelitis 2 months later</td>
<td>Disturbed consciousness, urine retention, paresthesia</td>
<td>Japan</td>
<td>2008</td>
<td>30</td>
</tr>
<tr>
<td>Lin CC</td>
<td>`</td>
<td>F</td>
<td>59</td>
<td>Cervical cord atrophy</td>
<td>Neck/arms numbness</td>
<td>Taiwan</td>
<td>2008</td>
<td>36</td>
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<tr>
<td>Azeroual A</td>
<td>1</td>
<td>F</td>
<td>54</td>
<td>Cerebellar syndrome</td>
<td>NR (article in France)</td>
<td>Maroc</td>
<td>2007</td>
<td>11</td>
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<tr>
<td>Moutaukilef F</td>
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<td>F</td>
<td>25</td>
<td>Aseptic meningoencephalitis</td>
<td>Mental confusion</td>
<td>Maroc</td>
<td>2005</td>
<td>31</td>
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<td>Hirohata M</td>
<td>1</td>
<td>F</td>
<td>50</td>
<td>Aseptic meningoencephalitis</td>
<td>Disturbed consciousness</td>
<td>Japan</td>
<td>2005</td>
<td>14</td>
</tr>
<tr>
<td>Devos D</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>Acute rhombencephalitis associated with hearing loss</td>
<td>NR (article in France)</td>
<td>France</td>
<td>2002</td>
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<tr>
<td>Nishida H</td>
<td>1</td>
<td>F</td>
<td>64</td>
<td>Aseptic meningoencephalitis</td>
<td>Consciousness loss</td>
<td>Japan</td>
<td>1999</td>
<td>32</td>
</tr>
<tr>
<td>Miyachi T</td>
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<td>F</td>
<td>76</td>
<td>Aseptic meningoencephalitis</td>
<td>Disturbed consciousness</td>
<td>Japan</td>
<td>1997</td>
<td>33</td>
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<tr>
<td>Giordano MJ</td>
<td>1</td>
<td>F</td>
<td>55</td>
<td>Cerebritis complicated by bilateral superior cerebellar artery occlusion and diffuse subarachnoid hemorrhage.</td>
<td>Lethargy, dysarthria, dysphagia, diplopia, right hemiparesis</td>
<td>USA</td>
<td>1995</td>
<td>17</td>
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<tr>
<td>Gerraty RP</td>
<td>1</td>
<td>F</td>
<td>18</td>
<td>Aseptic meningoencephalitis</td>
<td>NR (no full text)</td>
<td>Australia</td>
<td>1993</td>
<td>15</td>
</tr>
<tr>
<td>Peña-Sagredo JL</td>
<td>3</td>
<td>1M</td>
<td>2F</td>
<td>1 focal meningoencephalitis, 2 previous diagnosed definite MS</td>
<td>NR (article in Spanish)</td>
<td>Spain</td>
<td>1993</td>
<td>34</td>
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<tr>
<td>Caselli RJ</td>
<td>1</td>
<td>F</td>
<td>56</td>
<td>Dementia</td>
<td>Cognitive change</td>
<td>USA</td>
<td>1993</td>
<td>2</td>
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<tr>
<td>Kawashima N</td>
<td>1</td>
<td>F</td>
<td>48</td>
<td>Subcortical dementia</td>
<td>Cognitive change</td>
<td>Japan</td>
<td>1993</td>
<td>10</td>
</tr>
<tr>
<td>Alexander EL</td>
<td>5</td>
<td>NR</td>
<td>NR</td>
<td>Aseptic meningoencephalitis, 4 recurrent</td>
<td>NR (no full text)</td>
<td>USA</td>
<td>1983</td>
<td>9</td>
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<tr>
<td>Alexander GE</td>
<td>5</td>
<td>NR</td>
<td>NR</td>
<td>5 aseptic meningoencephalitis, 1 recurrent, 3 myelopathy</td>
<td>NR (no full text)</td>
<td>USA</td>
<td>1981</td>
<td>8</td>
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</table>
SS, in whom there was no evidence of cerebral vasculitis at autopsy.

The NCV study of our patient showed motor-predominant axonal polyradiculopathy. This is rather unusual in patients with multiple sclerosis or clinical isolated vasculitis syndrome. The patient did not have any other CNS lesion in neuroimage follow-up. Multiple sclerosis was not favored after 2-year follow-up. Her autoimmune profile revealed only positive anti-SS-A antibody but no antibodies for systemic lupus erythematosus, rheumatoid arthritis, or other autoimmune diseases. Therefore neurological complications due to other autoimmune diseases were excluded from the diagnosis. In patients with neuromyelitis optica (NMO) / optospinal form of multiple sclerosis, autoantibodies involving SSA and ANA are occasionally detected. Neuropathological characteristics of NMO were as follows: 1) the involved sites adjacent to the third and fourth ventricles and in the posterior limb of the internal capsule, 2) unique configurations, such as the longitudinal course from the internal capsule to the midbrain, large cerebral or cerebellar lesions over 3 cm, and cavity-like formation. Our patient did not fulfill the neuropathological criteria of NMO. VEP study showed absence of goggle VEPs from the left eye of our patient. Optic neuropathy has been reported as the rare symptom of primary SS. The patient was diagnosed with primary SS according to the criteria of the European Community. We concluded that her neurological symptoms were due to SS. The clinical picture of SS often shows spontaneous remission, whenever overt neurological symptoms occur or the clinical course become progressive, high-dose corticosteroid and cytotoxic agent may be indicated. Our patient received plasma exchange for deteriorating muscle power, prednisolone pulse therapy for interstitial lung disease, followed by cyclophosphamide. She remained in stable condition and did not have any new neurological symptoms till the day of this report.

In conclusion, primary SS may have variable CNS manifestation and could precede the classic sicca symptoms. SS should be investigated in cases of aseptic meningoencephalitis even without clinical signs of xerostomia or xerophthalmia. Our patient showed an isolated occurrence of meningoencephalitis without any other manifestation of SS for at least 2 years. MRI is useful in demonstrating brain lesions and in evaluating treatment efficacy of SS.

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REFERENCES


