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Reversible cortical lesions in primary Sjögren's syndrome presenting
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Abstract

We report a 50-year-old woman with primary Sjögren's syndrome (SjS) who initially showed forgetfulness, and later developed disturbance of consciousness. In addition to aseptic meningoencephalitis revealed by cerebrospinal fluid examination and magnetic resonance imaging (MRI), the presence of serum anti-SS-A and anti-SS-B antibodies and inflammatory findings in lip biopsy indicated primary SjS. Fluid attenuated inversion recovery (FLAIR) of MRI revealed well defined small, high signal intensity areas in the cortex involving the the subcortical white matter. Corticosteroid therapy resulted in rapid and nearly complete resolution of the cortical lesions with marked improvement of the clinical manifestations. Memory disturbance is a rare initial manifestation in meningoencephalitis associated with SjS. Our patient with SjS showed inflammatory cortical lesions on MRI, which were reversed by corticosteroid therapy.

Key words

Sjögren's syndrome; Meningoencephalitis; Initial manifestation; MRI;

Forgetfulness (memory disturbance)

1. Introduction

Central nervous system complications have been reported in up to 25% of patients with Sjögren's syndrome (SjS) [1]; meningitis is common in SjS patients [2]. There have been previous reports of SjS patients showing meningoencephalitis without characteristic symptoms of xerosis [6]. As meningoencephalitis in primary SjS is treatable, understanding of its clinical features is important in the differential diagnosis of meningoencephalitis. There have been no previous reports of detailed magnetic resonance imaging (MRI) findings of such cases. Here, we report a case of primary SjS presenting with aseptic meningoencephalitis showing reversible cortical lesions on MRI.

2. Case report

The patient was a 50-year-old Japanese woman. She had no history of cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, hyperlipidemia, heavy drinking, or drug use. Her family history was not contributory. Two weeks before admission to our hospital, she complained of forgetfulness, which was followed by a low-grade fever. When she visited a local hospital, clinical examinations and brain computed tomography (CT) revealed

no abnormalities. On the day before admission, she developed psychosis. Mononuclear pleocytosis (63 cells/mm²) was noted in the cerebrospinal fluid (CSF). Technetium-99m ethyl cysteinate dimer (^{99m}Tc-ECD) brain single photon emission computed tomography (SPECT) perfusion imaging for cerebral blood flow revealed regions of decreased uptake in the parietal lobes. Brain MRI, and magnetic resonance angiography (MRA) were normal.

On the day of admission (day 1), the patient's body temperature was 36.7°C. She had no xerophthalmia, xerostomia, uveitis, mucocutaneous lesions, eruption, arthritis or Raynaud's phenomenon. Neurological examinations revealed disturbance of consciousness (Glasgow coma scale = 12; E4-V2-M6) with delirium, mutism, ocular bobbing, and urinary retention, but no nuchal stiffness. During the first day, her consciousness disturbance showed rapid deterioration with a fever of 38°C. On day 5, she fell into a coma showing roving eye movement, decorticate posture of the upper limbs, positive Babinski signs, and loss of deep tendon reflexes in the lower limbs.

Initial laboratory evaluation included an increase in erythrocyte sedimentation rate (ESR) (33.2 mm in 1h), negative C-reactive protein (CRP) (0.3 mg/dl), positive antinuclear (101.4 titer), anti-SS-A (135.3) and anti-SS-B (28.9) antibodies, positive

rheumatoid factor, and polyclonal elevation of serum immunoglobulins.

Anti-double-stranded DNA antibodies, plasma complement, and thyroid function were negative or normal. Lumbar puncture revealed mononuclear pleocytosis (43 cells/mm²) with mildly elevated protein (56 mg/dl) and normal glucose levels (46 mg/dl). Further analysis of the cerebrospinal fluid (CSF) indicated an increase in IgG index (0.832), and normal or negative results for the following tests: IL-6, gram stain, Ziehl-Neelsen stain, India ink preparation, and cultures for bacteria, tubercle bacillus mycobacteria, and fungi. Paired serologic tests for viruses, including herpes simplex, herpes zoster, Epstein-Barr, mumps, rubella, and cytomegalovirus, and cryptococcal latex agglutination test gave negative results.

On day 5, fluid attenuated inversion recovery (FLAIR) and T2-weighted MR images demonstrated abnormal high signal areas in the cortical and subcortical white matter, including the right occipital cortex and left insular cortices with no gadolinium-enhancement (Fig. 1A). Electroencephalogram (EEG) on day 6 revealed diffusely abnormal slow activities, especially in the occipital lobes. Biopsy of the minor salivary gland from the lip revealed a mildly atrophic gland surrounded by focal infiltration of lymphoplasmacytic cells (focus score 1). Salivary gland scintigraphy showed delayed uptake and reduced concentration of technetium-99m-O₄⁻

($^{99m}\text{TcO}_4^-$) indicating salivary gland dysfunction. Schirmer's test revealed a significant decrease in lachrymal secretion, which indicated subclinical xerophthalmia.

After establishment of a diagnosis of primary SjS with aseptic meningoencephalitis based on the positive results of serological tests and lip biopsy, the patient was treated with pulsed therapy with intravenous methylprednisolone at 1 g/day for three days four times, followed by oral administration of prednisolone at 60 mg/day with gradual tapering of the dose. Corticosteroid therapy resulted in marked improvement of both consciousness and CSF findings. The abnormal MRI findings disappeared on day 40 (Fig. 1B). The EEG and SPECT findings were normalized within 2 months. She was discharged from our hospital on foot with mild memory disturbance, dysarthria, and ataxic movement two months after admission. There has been no recurrence of meningoencephalitis or other manifestations of SjS during the following four years.

3. Discussion

We described a patient with primary SjS who initially developed subacute aseptic meningoencephalitis. Although the patient was free of sicca symptoms, the

significant decrease in salivary and lachrymal secretion, inflammatory cell infiltration, and the presence of anti-SS-A and anti-SS-B antibodies satisfied the diagnostic criteria for definite SjS [10]. Subacute progression of memory disturbance and disturbance of consciousness were the initial symptoms of aseptic meningoencephalitis associated with primary SjS in this patient.

Among SjS patients with aseptic meningoencephalitis [2, 3, 4, 5, 6], there have been a few rare cases in which the patient presented with meningoencephalitis as the initial manifestation [6]; in such cases, including our patient, memory impairment and disturbance of consciousness are common neuropsychiatry symptoms. The present patient showed characteristic brain MRI findings of well defined multiple focal lesions involving the occipital and limbic cortex, which disappeared after corticosteroid therapy.

In SjS patients with neuropsychiatry manifestations, focal brain lesions on MRI have been reported to be located predominantly within the periventricular or subcortical white matter [7, 9], except in one case in which the lesions were confined to the limbic cortex [6]. In our patient, the remarkable response of the cortical lesions involving the white matter to steroid therapy indicated inflammatory pathogenesis of the lesions. There have been a few pathological studies of

meningoencephalitis associated with SjS [3, 8]. Necrotizing vasculitis involving numerous small arteries and arterioles was found diffusely in the cerebral cortex of one case at necropsy [8]. Another case showed microinfarcts and focal laminar necrosis, but no evidence of active or healed vasculitis or parenchymal infiltration of inflammatory cells [3]. Although no neuropathological study was performed in our patient, the lack of enhancement by gadolinium-ethylene-diamine-tetraacetic acid (Gd-EDTA) on MRI suggested minimal injury of vascular endothelial cells even if small vessels were involved by meningocortical inflammation.

Finally, we emphasize that evidence of SjS should be investigated in cases of aseptic meningoencephalitis even when sicca symptoms are absent, as in our patient who showed isolated occurrence of meningoencephalitis without other manifestations of SjS for, at least, four years. Furthermore, MRI findings are useful to demonstrate the inflammatory cortical lesions in SjS, which are reversible in response to corticosteroid therapy.

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Legends for figures

Figure 1. Fluid attenuated inversion recovery MR images before (A, TR 10,002 ms, TE 175 ms) and 5 weeks after the initiation of corticosteroid therapy (B, TR 10,002 ms, TE 157 ms). High signal intensity areas were found in the right occipital cortex and left insular cortex involving the subcortical white matter (A). After five weeks of therapy, the high signal intensity areas were no longer observed (B).

Fig. 1.