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Recurrent aseptic meningitis: a new CSF complication of Sjogren's syndrome

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Sirs: Sjögren's syndrome (SjS) is one of the major autoimmune disorders and is characterized by dry eyes and a dry mouth. A wide variety of extraglandular manifestations has been reported in SjS. Aseptic meningitis is a well-known manifestation of SjS; however, little is known about its pathomechanism [1, 3]. We detected a unique autoantibody in the serum and cerebrospinal fluid (CSF) of an SjS patient with recurrent aseptic meningitis.

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A 19-year-old female was readmitted to our hospital after the third recurrence of aseptic meningitis. Nine months and five months before this admission, she had experienced the same symptoms, i.e., headache, nausea, and fever. She was diagnosed with aseptic meningitis because of the presence of mononuclear pleocytosis in the CSF. The symptoms subsided spontaneously within a few days.

On examination, there were no subjective symptoms of sicca syndrome, and Schirmer's test was negative. Neurological examination revealed no abnormalities, except stiffness of the neck. Laboratory tests revealed elevated amylase (268 IU/dl) and serum IgG (2920 mg/dl) concentrations; positive rheumatoid factor (2+); accelerated erythrocyte sedimentation rate (30 mm/h); and positive serum antinuclear antibody (ANA) as well as the anti-SS-A and anti-SS-B antibodies at titers of 1:2560, 1:256, and 1:8, respectively. The CSF contained 153 mg/dl protein and 85 mm^3 of cells (81% mononuclear cells); the anti-SS-A and anti-SS-B antibodies were absent. These findings led us to suspect SjS. A sialogram revealed the destruction of the sialoducts, and a salivary gland biopsy revealed abundant lymphocytic infiltration. The patient was diagnosed with SjS and recurrent aseptic meningitis, and she was treated with 50 mg of daily oral prednisolone. Based on the results of the physical and serological examinations, we inferred that the overlapping of other systemic autoimmune diseases with SjS is unlikely. The clinical symptoms resolved immediately without subsequent recurrence.

The patient's serum and CSF were analyzed by using western blotting (WB) and immunohistochemistry as reported previously [4]. WB of bovine tissue samples showed that the CSF reacted with two bands with apparent molecular weights of 56 kD and 44 kD in the cerebral cortex, meningeal tissue, and liver (Fig. 1a). Immunohistochemical analysis by the avidin-biotin-peroxidase method using rat cerebral slices showed that the CSF labeled the nuclei of the neurons and meningeal cells (Fig. 1b). We detected an identical autoantibody in the patient's serum (data not shown).

Mauch et al. reported that approximately 70% SjS patients had neurological complications; of these, one-sixth had aseptic meningitis [3]. Alexander et al reported that from a group of 25 consecutive SjS patients with CNS involvements, 5 (20%) had recurrent aseptic meningitis or meningoencephalitis [1]. Although aseptic meningitis is common in SjS, recurrent aseptic meningitis without other CNS involvements is rare, and its pathoetiology has not been elucidated thus far.

Some autoantibodies may be related to the pathogenesis of the CNS involvement in SjS, for example, the possible association of the anti-SS-A antibody with cerebral angiitis [2]. However, the relationship between these autoantibodies and CNS involvement remains unknown. We demonstrated the presence of an autoantibody in the patient's CSF and serum; this autoantibody recognizes 56- and 44-kD nuclear antigens of the CNS neurons, meningeal cells, and cells of other systemic organs. The presence of this autoantibody in the patient's CSF may imply its causative association with recurrent aseptic meningitis in SjS. We already reported some other autoantibodies in SjS patients with CNS involvements, but this is the first report

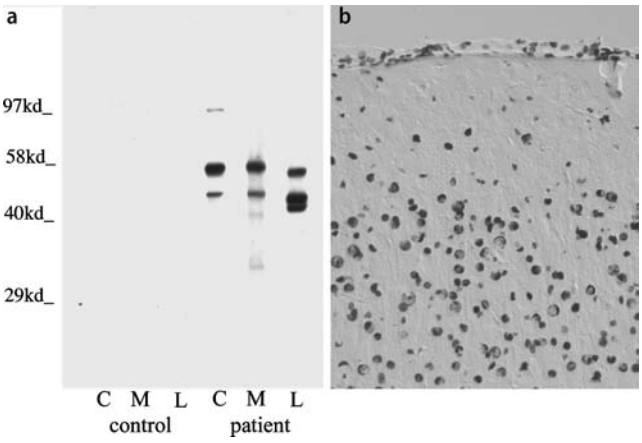

Fig. 1 **a** Western blot analysis of bovine tissues probed with patient's CSF. Two 56- and 44-kD positive bands were detected in the lanes containing bovine cerebral cortex (C), meningeal tissue (M), and liver (L) antigens. **b** Rat cerebral cortex probed with patient's CSF (1:1000). Nuclei of large cells of similar sizes (mostly neurons) were immunolabeled by the patient's CSF, as were those of meningeal cells

on an autoantibody associated with recurrent aseptic meningitis in SjS [4, 5]. Detailed characterization of the antigens is necessary to clarify the associated pathomechanism.

In conclusion, SjS, even in its clinically latent form, should be included in the differential diagnosis of recurrent aseptic meningitis.

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