Primary biliary cirrhosis complicated by transverse myelitis in a patient without Sjögren’s syndrome

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ABSTRACT

Transverse myelitis is an acute inflammatory process, affecting one or more segments of the spinal cord. Its association with primary biliary cirrhosis has been documented in only four cases – all along with Sjögren’s syndrome. Herein, we report for the first time, a patient who developed recurrent acute transverse myelitis in association with primary biliary cirrhosis without any clinical or histological indication of Sjögren’s syndrome. A 42-year-old woman with primary biliary cirrhosis developed acute onset quadriplegia and urinary retention. Diagnostic evaluation excluded the presence of Sjögren’s syndrome, other autoimmune syndromes, infections and multiple sclerosis. Magnetic resonance imaging of the spinal cord disclosed signal intensity abnormalities from C1 to T2 after gadolinium enhancement. As diagnosis of acute transverse myelitis was prominent, the patient was treated with intravenous methylprednisolone. The patient had a fair outcome despite an early recurrence of the symptoms after treatment withdrawal.

KEY WORDS: Primary biliary cirrhosis, Transverse myelitis, Sjögren’s syndrome

Transverse myelitis (TM) is an acute or subacute focal inflammatory disorder of the spinal cord affecting motor, sensory and autonomic function.[1] Magnetic resonance imaging (MRI) and lumbar puncture usually show evidence of inflammatory process.[2] TM is an uncommon, well-described neurological manifestation of autoimmune diseases. Its association with primary biliary cirrhosis (PBC) has been documented in only four cases – all along with Sjögren’s syndrome (SS).[3] Herein, we report the first case of PBC-related TM without any clinical or histological indications of SS.

Case History

A 42-year-old Caucasian female was admitted to our hospital in December 2002 for severe myalgia, headache, neck stiffness and low grade fever over the last 5 days. Her medical history was significant for PBC since 2001, based upon the presence of anti-mitochondrial antibodies and a liver histology suggestive of PBC Stage II-III: mild chronic portal inflammation with bridging fibrosis, bile duct destruction, focal granulomas without necrosis and bile ductular proliferation. Her medication consisted of ursodeoxycholic acid, cholestyramine and vitamin D and K.

On admission, her blood pressure was 130/80 mmHg, pulse rate 96/min, and body temperature 37.1 °C. On the 7th day of her hospital stay the patient started complaining of low back pain and gradually aggravated weakness and numbness in both the lower extremities. Neurological evaluation revealed motor weakness of both upper and lower extremities with reduced tactile sensation being worse in the right arm and left leg, indicative of level C5 and below. A bilaterally positive Babinski sign was noted. No cognitive or cranial nerves disturbances were noted. During the following four days a gradually aggravated paralysis prevented her from moving the lower extremities. Simultaneously, she developed urinary retention necessitating urinary bladder catheterisation.

Laboratory work-up revealed normal hematocrit, white blood cell counts and platelets and an increased erythrocyte sedimentation rate (23 mm/hr). Subsequent ELISA-based serological tests showed the presence of anti-nuclear factor (titre 1/160), anti-mitochondrial (titre 1/320) and anti-Ro (SS-A) (titre 5.6 U/ml, normal <2 U/ml) antibodies. Antibodies to ds-DNA, ribonucleoproteins, La (SS-B), smooth muscle, cardiolipin, lupus anticoagulant and rheumatoid factor were not found. Analysis of the cerebrospinal fluid revealed a clear colour, lymphocytic pleocytosis (110 white blood cells per cubic millilitre, with a differential of 96% lymphocytes), protein 0.56 g/l and glucose 73 mg/dl. Real-time polymerase chain reaction amplification of the IS6110 of the Mycobacterium tuberculosis complex yielded a negative result. Oligonucleotide bands were negative for multiple sclerosis.

According to SS criteria,[4] Schirmer’s test was normal (15 mm), salivary flow measurement assured enough production of saliva (over 0.5 ml in 5 minutes), slit lamp examination revealed no pathological findings and lip biopsy showed normal salivary glands.
An MRI examination of the brain and spinal cord, obtained on the 10th day of her hospital stay, was suggestive of transverse myelitis (Figures 1a, 1b).

A diagnosis of TM was made and the patient was treated initially with intravenous methylprednisolone (1 gm/day for 5 days), followed by gradually tapered oral prednisolone over the subsequent 8 weeks. During the outpatient follow-up period, a total recovery was achieved. However, 5 weeks after prednisolone withdrawal, the patient started to complain again about a gradually aggravated weakness and numbness in both the upper and lower extremities. Oral prednisolone was reintroduced (40 mg/d) and tapered over a period of 8 weeks, followed by prompt clinical response. Since then the patient remains free of symptoms for 9 months.

**Discussion**

The term transverse myelitis (TM), a rare disorder of the spinal cord, implies an inflammatory process that interrupts most of the large tracts across the greater part of the horizontal extent of the cord at the level of the lesion. The disease may result from several viral or bacterial infections,[6,7] insufficient blood flow,[7] or autoimmune diseases, including systemic lupus erythematosus (SLE), SS and PBC.[1,3] The association of TM with PBC has been very rarely reported and only in association with SS.[3,4]

The clinical picture of TM includes partial or complete paraplegia or quadriplegia, decrease or loss of deep reflexes, sensory impairment and varying degrees of bladder and bowel disturbance. In most cases the peak occurs in the first week with the level of involvement set at the onset and the nadir is reached within 3 weeks.[2,6]

In our case, the diagnosis of TM fulfilled all the settled inclusion and exclusion criteria.[2] The onset was sudden and the cervical spinal cord was immediately involved. Our patient did not develop primary respiratory insufficiency and she has had a complete neurological recovery.

The precise pathogenesis of TM in patients with PBC is unknown. Additionally, there appears to be no relation between the severity of the liver disease and the presence of TM in patients with PBC and concomitant TM.[3] In the subgroup of patients where PBC is accompanied by SS, the potential mechanisms include immunological injury of spinal vessels and/or the spinal cord driven by reactive T-cells and/or the presence of anti-neuronal antibodies.[8] Moreover, in a recent study, the presence of Ro (SS-A) without clinically evident SS has been proposed to associate with recurrent TM, indicating their potent direct pathogenetic role.[9]

The sudden onset of symptoms, the absence of MS and tuberculosis, and the response to steroids suggest that the subsequent pathology in our case involved an autoimmune process and practically ruled out an infectious aetiology. Nevertheless, the absence of pathology in Schirmer’s test, slit lamp examination, unstimulated salivary flow measurement, and lip biopsy in combination with the absence of ocular or oral symptoms excluded sicca syndrome or true SS despite the presence of ANA and Ro (SS-A), scoring 1 out of 6 criteria according to Vitali et al.[4] The autoimmune nature of the TM process combined with the absence of a well-defined autoimmune process other than the underlying PBC, allows us to hypothesize that TM was really PBC-related in this patient.

The prognosis of TM is variable, with about one-third of the patients progressing to a syndrome indistinguishable from spinal muscular atrophy. Our patient’s rapid primary response, in spite of the very acute course of the disease, may be well ascribed to the early use of methylprednisolone.[10]

**References**