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A Case of Superficial Siderosis with Elevated Anti-Ro/SSA Antibody

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Abstract

Superficial siderosis (SS) of the central nervous system is a rare disorder that is caused by chronic or recurrent hemorrhage in the subarachnoid space via a dural defect at the spinal level. The most common clinical features of SS include slow-progressive sensorineural deafness, cerebellar symptoms, and pyramidal tract signs. Considering that SS can present with broad clinical manifestations, for precise diagnosis, this disease must be understood. Anti-Ro/SSA antibodies are commonly detected in patients with Sjögren's syndrome and are utilized as markers for autoimmune diseases. In this report, we present a unique pathological condition in which SS coincided with a positive anti-Ro/SSA antibody test result. During the diagnosis of gait disturbance, an elevation in anti-Ro/SSA antibody was detected, and steroid pulse therapy was initiated as the initial treatment for autoimmune diseases. Head magnetic resonance imaging (MRI) revealed extensive hypointensity as a dark band that surrounded the intracranial basal structures and cerebellar hemispheres. Spinal MRI indicated ventral longitudinal intraspinal fluid collection extending from C7 to T5 as well as a defect in the ventral T2-3 dura mater. Intraoperative visualization revealed that the intradural venous plexus was the source of bleeding that caused the SS. To our knowledge, this report is the first to discuss the presence of anti-Ro/SSA antibodies in patients with SS. The role of anti-Ro/SSA antibodies in the pathophysiology of SS remains unclear; therefore, to confirm a possible association, further research and accumulation of cases are required.

Keywords: superficial siderosis, dural defect, intradural venous plexus, anti-Ro/SSA antibody

Introduction

Superficial siderosis (SS) of the central nervous system is a rare disorder caused by chronic or recurrent hemorrhage in the subarachnoid space, with hemosiderin deposition in the subpial layer of the brain and spinal cord, which leads to neuronal damage.[1)] Based on its etiology, SS can be classified into two subtypes.[1)] Type 1 or classical SS, which predominantly involves the posterior fossa, including the cerebellum and vestibulocochlear nerves, is mostly caused by chronic bleeding from a dural defect at the spinal level. Type 2 or secondary SS is caused by an isolated subarachnoid hemorrhage from an aneurysm rupture, arteriovenous malformation, trauma, or a tumor. The association between spinal dural defects and the etiology of SS type 1 is a relatively recent discovery.[1)]

The most common clinical features of SS include slow, progressive sensorineural deafness, cerebellar symptoms (ataxia, kinetic tremor, nystagmus, and dysarthria), and pyramidal tract signs. Other clinical symptoms of SS include myelopathy, bladder and bowel dysfunction, somatic sensory dysfunction, dementia, anosmia, anisocoria, and headache.[2)] For precise diagnosis, SS, considering that it can present with broad clinical manifestations, must be understood.

In this report, we present a unique pathological condition in which SS type 1 coincides with anti-Ro/SSA antibody positivity. An elevation in anti-Ro/SSA antibodies, a marker of autoimmune disease, was detected while diagnosing gait disturbance, and steroid pulse therapy was car-

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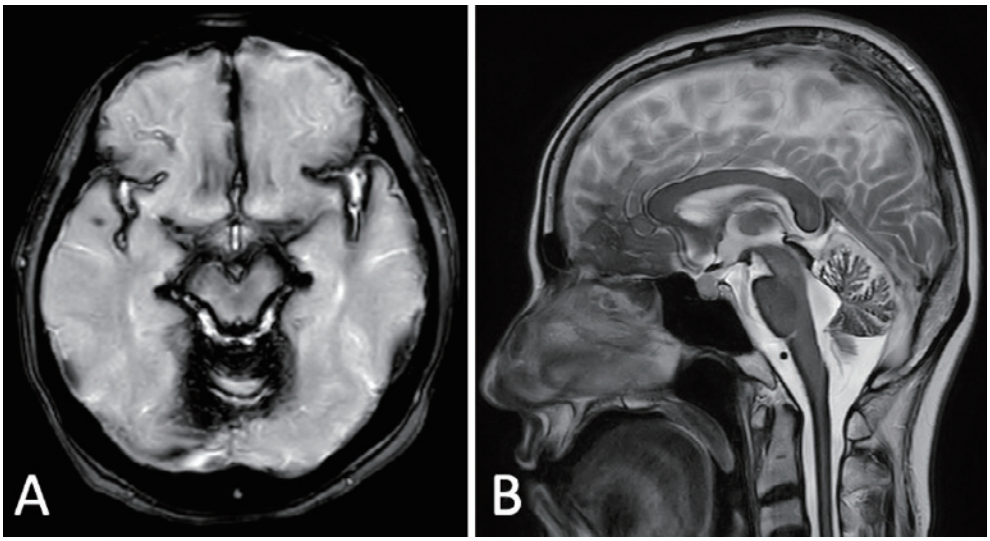

Fig. 1
A Axial T2*-weighted MR images of the brain showing extensive hypointense rims that surround the intracranial basal structures.
B Sagittal T2-weighted MR images showing cerebellar atrophy and spinocerebellar degeneration.
MR, magnetic resonance

ried out as the initial treatment for autoimmune diseases. Head magnetic resonance imaging (MRI) revealed extensive hypointensity as a dark band that surrounded the intracranial basal structures and cerebellar hemispheres. Spinal MRI indicated ventral longitudinal intraspinal fluid collection extending from C7 to T5, as well as a defect in the ventral T2-3 dura mater. Intraoperative visualization revealed that the intradural vein plexus was the source of bleeding that caused the SS. To our knowledge, this report is the first to discuss the presence of anti-Ro/SSA antibodies in an SS case, which requires further research.

Case Report

A 52-year-old woman presented to our department with a 7-year history of leg weakness and progressive gait impairment. Five years earlier, she had visited the neurology department of a nearby hospital and underwent a detailed examination for suspected neurological disease. Blood tests revealed anti-Ro/SSA antibody positivity with a level >1200 U/mL [reference interval (RI) < 10 U/mL], an immunoglobulin G level of 1973 mg/mL (RI 870-1700 mg/mL), antinuclear antibody level of ×40 (RI < ×40), anti-Sm antibody level of 1.1 U/mL (RI < 10 U/mL), anti-La/SSB antibody level of 7.1 U/mL (RI < 10 U/mL), and anti-Scl-70 antibody level of <1.0 U/mL (RI < 10 U/mL). The patient did not meet the diagnostic criteria for Sjögren's syndrome (SjS) or any other autoimmune disease based on the available data. She was diagnosed with autoimmune encephalitis and received steroid pulse therapy (methylprednisolone, 1 g/day). Subsequently, the weakness in both lower extremities and ataxia of the trunk and extremities improved, and oral steroid administration was tapered off (prednisolone, 5 mg/day) as an outpatient. One year later, the patient tested positive for anti-Ro/SSA antibodies, at a level of 1100 U/mL.

However, during the outpatient follow-up, her symptoms gradually deteriorated, and she noticed a gradual hearing loss for 3 years prior to consultation. Neurological examination revealed horizontal nystagmus in the direction of gaze, dysarthria, trunk ataxia, extremity hyperreflexia, positive pathological reflexes in the upper and lower extremities, left-dominant temperature, pain anesthesia at T6, and lower urinary and fecal incontinence.

T2*-weighted MRI showed areas of extensive hypointensity on the surfaces of the bilateral temporal lobes, base of the frontal lobes, cerebellar folia, and brainstem (Fig. 1A). Figure 1B confirms that cerebellar atrophy with spinocerebellar degeneration was observed. Brain MRI showed no vascular pathology, tumors, or hematoma. A lumbar puncture was performed; the results were as follows: xanthochromic cerebrospinal fluid (CSF), hyperproteinorachia [72.5 mg/dL (RI < 40 mg/dL)], 4 leukocytes/mm^3, red blood cell positivity [exact number not mentioned], and normal glucose levels.

Cervicothoracic T2-weighted MRI revealed an intraspinal fluid-filled cavity ventrally from C7 to T5 (Fig. 2A). The doctor in charge suspected SS due to bleeding from the dural defect, and the patient was referred to our hospital for further treatment. Constructive interference in steady-state (CISS) MRI study revealed a dural defect in the right ventral dura at the level between T2 and T3 (Fig. 2B). To repair the suspected dural defect, the patient underwent neurosurgery using the posterior midline approach and

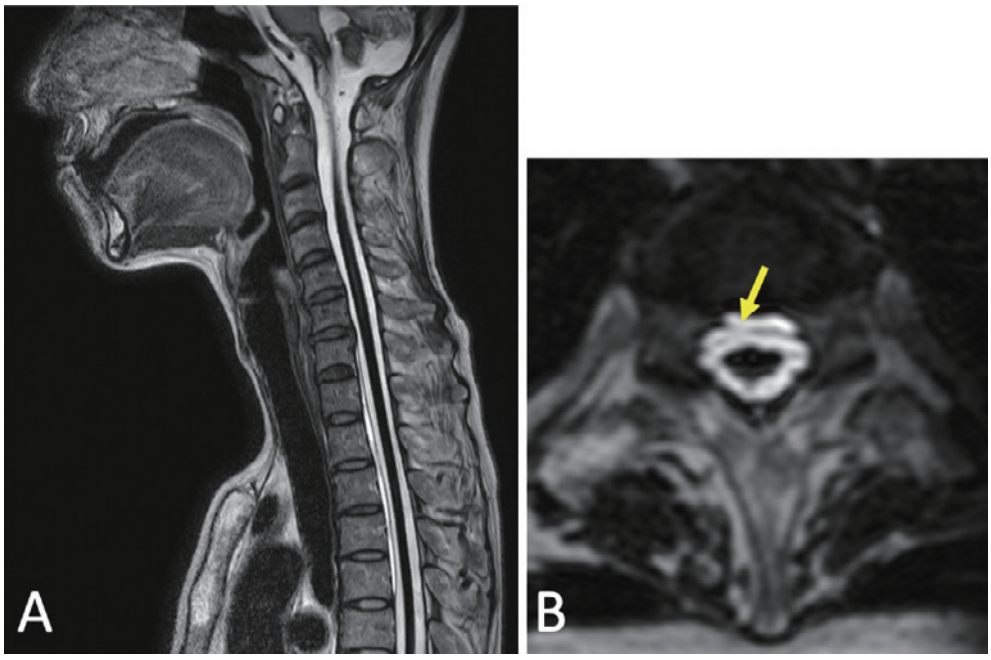

Fig. 2 Preoperative CISS MR images of the spine.
A Sagittal image showing the longitudinal intraspinal fluid-filled cavity from C7 to T5.
B Axial image. The *yellow arrow* indicates the dural defect between T2 and T3.
CISS, constructive interference in steady-state; MR, magnetic resonance

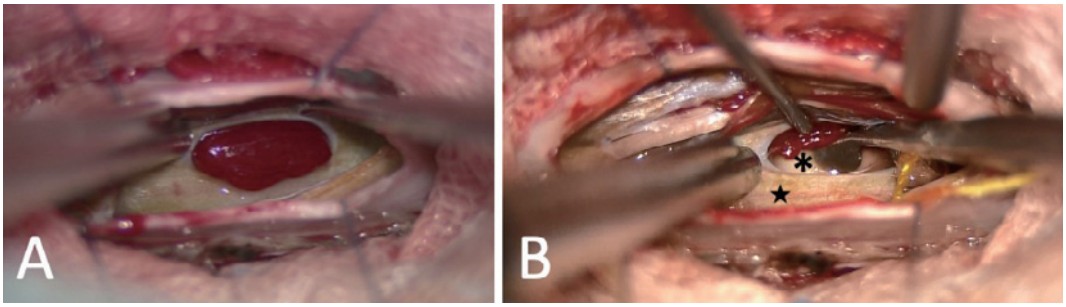

Fig. 3 Intraoperative images.
A Defects in the inner layer of the ventral dura and the protruding intradural venous plexus.
B The *asterisk* indicates the outer dural layer, and the *star* denotes the inner dural layer.

targeted laminectomy. An oral and written informed consent was given to the patient and her family prior to the treatment. The dorsal dura was cut, and a dark brown arachnoid membrane was observed immediately below. After minimally retracting the spinal cord, the dentate ligament was cut, and a defect in the inner layer of the ventral dura and protruding red tissue were confirmed (Fig. 3 A). Initially, the red tissue was assumed to be a hematoma; however, when coagulated, the venous hemorrhage gradually flowed. Coagulation was carried out as minimally as possible. The wall anterior to the coagulated vessel was another dural layer, identified as the outer dura (Fig. 3B); thus, the vessel was considered to be the intradural venous plexus. A collagen matrix was placed, and using 7-0 PDS, three stitches were carried out. A week after the operation, MRI revealed complete regression of the ventral longitudinal intraspinal fluid-filled cavity (Fig. 4A, B), suggesting that the dural defects were successfully repaired. With the aid of rehabilitation therapy, her symptoms gradually improved after surgery.

Discussion

In this report, we present a unique case of SS type 1 with a coincidental finding of anti-Ro/SSA antibody positivity. Anti-Ro/SSA antibodies as well as anti-La/SSB antibodies have been found in patients with SjS and are also associated with systemic lupus erythematosus. Nevertheless, these can also be positive in other systemic autoimmune diseases.[3] Both target three cellular proteins, namely,

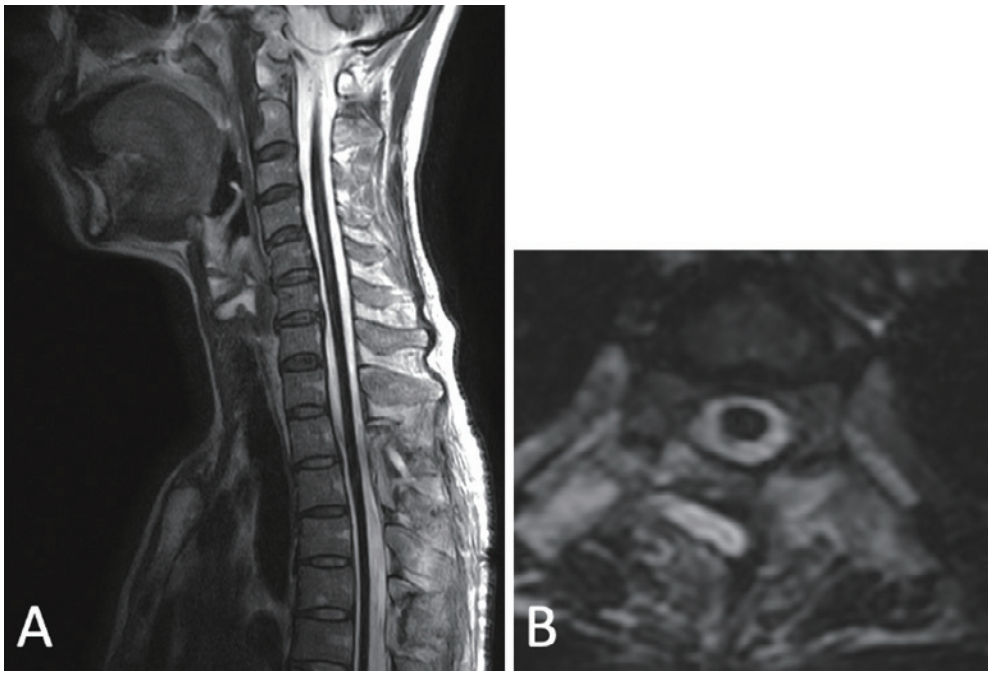

Fig. 4 Postoperative sagittal (A) and axial (B) CISS MR images of the spine.
There is no intraspinal fluid collection and no dural defect.
CISS, constructive interference in steady-state; MR, magnetic resonance

Ro52/TRIM21, Ro60, and La48, which are classified based on their molecular weight.[4] Tetsuka et al. collectively reported on 14 patients previously diagnosed with SjS who also developed cerebellar degeneration.[4] In all patients, serum anti-Ro/SSA antibodies were positive. Anti-Ro/SSA antibodies have been shown to exert differential actions on two target proteins, namely, Ro52/TRIM21 and Ro60.[5] In the Purkinje cells, high Ro52/TRIM21 expression has also been observed. These results indicate that anti-Ro/SSA antibodies are likely responsible for cerebellar degeneration in patients with SjS.[4] Atrophy of the cerebellum is a common finding;[1] hence, the pathophysiology of the elevation of anti-Ro/SSA antibodies in the present case may be related to cerebellar atrophy or degeneration. No previous studies have reported an association between SS pathology and the presence of anti-Ro/SSA antibodies. The role of anti-Ro/SSA antibodies in the pathophysiology of SS is still unclear; therefore, to confirm a possible association, further research and accumulation of cases are required. We checked reports of elevated anti-Ro/SSA antibodies in degenerative diseases, including spinocerebellar degeneration; however, we did not find clear information in this regard.

The location of the fluid cavity in patients with SS has been debated previously.[6-8] The spinal dura mater comprised an outermost loosely arranged fibroelastic layer, a middle fibrous portion, and an innermost cellular layer (dural border cell layer),[9] indicating that it can be separated into several compartments. Hosokawa et al. and Yoshii et al. showed evidence of dural dissection in which a defect was found within the dura mater and not beyond the outermost dura mater.[6,7] In contrast, Cheng et al. reported that the CSF freely communicated between the subarachnoid space and the epidural space through the pore penetrating the dural layer.[8] In the present case, the color of the deepest wall through the dural defect was the same as that of the dura mater (Fig. 3B), which indicates that the dural defect might be located within the dura mater. In the ventral side of the spinal cord, dural defects are frequently observed. The spinal cord is difficult to mobilize. These anatomical factors complicate observation inside the cavity from the dorsal side of the spinal cord.

If the entire layer of the dura mater is perforated, the CSF continues to leak, and the intracranial pressure begins to decline, which leads to spontaneous intracranial hypotension (SIH). SIH manifests primarily as an orthostatic headache, whereas SS manifests as hearing loss and gait impairment, although the clinical features of both conditions may overlap. SIH and SS are characterized by prominent vascularity on MRI, which is evident as leptomeningeal enhancement or prominent intradural or epidural veins. Owing to these similarities, it has been suggested that these two conditions may be closely related and can occur simultaneously.[2,10] Recently, Kawahara et al. found that the dural sac at the thoracic level shifted anteriorly in patients with SIH due to a CSF leak through the dural defect. They named these findings the dural sac shrinkage sign.[11] In the present case, no signs of dural sac shrinkage on the spinal MRI were observed. Clinically, the

intracranial pressure was normal, and the patient did not complain of orthostatic headache as in SIH. Therefore, we believe that the pathophysiology of this patient is similar to that described by Yoshii and Hosokawa.[6,7]

In cases of SS associated with anti-Ri antibodies, medical management in the form of corticosteroids has been reported to be successful; nevertheless, no other published studies have reported on the role of steroids in the treatment of SS.[12] Given the neuropathologic findings of SS, including microglial activation, reactive gliosis, and arachnoiditis, the broad anti-inflammatory effects of steroids could indeed be beneficial in SS.[13] However, the cause of hemosiderin deposition cannot be prevented via steroid therapy, and efforts must be made to determine the cause of SS and repair it surgically, as continued exposure of neural tissues to neurotoxic hemosiderin deposits can result in progressive neurological disturbances.

In conclusion, we report a rare case of coincidental SS and anti-Ro/SSA antibody positivity. We posit that the elevation of anti-Ro/SSA antibody levels was due to degradation of the cerebellum. Cranial MRI, as well as spinal MRI, will provide useful information in cases with anti-Ro/SSA antibody positivity and suspected autoimmune disease.

Conflicts of Interest Disclosure

All authors have no conflicts of interest to declare.

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