Cerebral venous sinus thrombosis (CVST) is a cerebrovascular disease that is caused by a number of factors, including hypercoagulability and vessel wall damage. Sjögren’s syndrome (SS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration of the exocrine glands. CVST could be caused by autoimmune diseases. According to previous reports, the most frequently reported autoimmune diseases which could cause CVST are systemic lupus erythematosus and antiphospholipid syndrome. Reports of SS leading to CVST are scarce. Here, we present a case of a 51-year-old woman who was diagnosed with SS-induced CVST. We tease out knowledge about the pathogenesis, feature of clinic symptom, treatment, and prognosis of SS-associated CVST, and illustrates how a detailed patient history can contribute to an accurate diagnosis.

Abstract

Cerebral venous sinus thrombosis (CVST) is a cerebrovascular disease that is caused by a number of factors, including hypercoagulability and vessel wall damage. Sjögren’s syndrome (SS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration of the exocrine glands. CVST could be caused by autoimmune diseases. According to previous reports, the most frequently reported autoimmune diseases which could cause CVST are systemic lupus erythematosus and antiphospholipid syndrome. Reports of SS leading to CVST are scarce. Here, we present a case of a 51-year-old woman who was diagnosed with SS-induced CVST. We tease out knowledge about the pathogenesis, feature of clinic symptom, treatment, and prognosis of SS-associated CVST, and illustrates how a detailed patient history can contribute to an accurate diagnosis.

Keywords: Autoimmune diseases, cerebral venous sinus thrombosis, Sjögren’s syndrome

INTRODUCTION

Sjögren’s syndrome (SS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration of the exocrine glands. The frequency of nervous system involvement is not high, and reports of SS leading to cerebral venous sinus thrombosis (CVST) are rare. Here, we present a case of a 51-year-old woman who was diagnosed with CVST, although she had no history of risk factors for venous thrombosis (e.g., long-term usage of oral contraceptives, recurrent miscarriages, and diet). The patient reported a history of dry mouth for 1 month. Clinical and laboratory tests for autoimmunity, including a tear secretion test and labial salivary gland biopsy, confirmed a diagnosis of SS. This case may raise awareness that autoimmune diseases, such as SS, can lead to CVST. Screening SS biomarkers are necessary for CVST patients without common risk factors.

CASE REPORT

A 51-year-old woman presented to our hospital with vomiting, delirium for 12 h, weakness in all four limbs, abnormal behavior, and aconuresis. For approximately 1 month, she had experienced xerostomia, and she had been febrile, especially in the afternoon. The patient had no history of risk factors for venous thrombosis (e.g., long-term usage of oral contraceptives, recurrent miscarriages, and diet) and no family history of thrombotic disease. On examination, the patient was unconscious, and her blood pressure was 133/88 mmHg. Myodynamia of all four limbs was diminished, and electrospensive cone bundle pathology and neck stiffness were present. Cranial nerve examination was unremarkable, and Kernig’s sign was negative. Laboratory investigations showed anti-SS-related antigen A (anti-Ro/SSA) antibodies (+++), anti-SS antigen B (anti-SSB) antibodies (+++), beta 2 glycoprotein antibody (−), antiphospholipid antibody (−), and anti-nuclear ribonucleoprotein/Sm antibodies (+) and an increased immunoglobulin G level (23.2 g/L). The function of blood coagulation including detection of thrombin time, prothrombin time, activated partial prothrombin time, international normalized ratio, prothrombin time activity percentage, and fibrinogen is normal. The activity of Protein C, Protein S, and antithrombin is normal. The level of homocysteine is normal. Lumbar puncture revealed an elevated intracranial pressure (240 mmH2O), but cerebrospinal fluid cell count and protein levels were normal. Antinuclear antibodies, immunoglobulin G4, rheumatoid factor, and C-reactive protein levels were also normal. Neurological imaging aided diagnosis. Brain computed tomography demonstrated a bilateral low-density shadow on the thalamus [Figure 1a], and brain magnetic resonance imaging suggested deep vein thrombosis associated with brain edema [Figure 1b-f]. Magnetic resonance venography images showed that the straight sinus, vein of Galen, left middle cerebral vein, and inferior sagittal sinus were...
not visible [Figure 1g and h]. Color Doppler ultrasonography of the lymph nodes in the salivary glands and their drainage area implied that the outline of the bilateral parotid gland and submandibular gland were unclear, with a coarse heterogeneous echo pattern in the parenchyma. Blood flow parameters were increased, and the surrounding soft tissue was thickened and hyperechoic. Schirmer’s I test: 1 mm in 5 min for both eyes. Schirmer’s II test: 4 mm in 5 min for both eyes. Labial salivary gland biopsy confirmed a diagnosis of SS [Figure 2]. After diagnosis, a rheumatologist prescribed oral hydroxychloroquine sulfate and total glucosides of peony. In addition, the patient was treated with anticoagulants, diuretics, and antibiotics. Subsequently, the patient’s symptoms improved.

**Discussion**

CVST is a rare type of ischemic cerebrovascular disease, accounting for <1% of all strokes. SS is a chronic

![Figure 1](image1.png)

**Figure 1:** Computed tomography showing symmetrical bilateral low-density alterations in the thalamus with tissue swelling and mass effect (arrows, a). Magnetic resonance imaging showing bilateral abnormal signals on T2-weighted images and hyperintensities in the thalamus, suggesting hemorrhage (arrows, b and c). Fluid-attenuated inversion recovery images showing mixed signal (d and e), and alteration of signal intensity in the mesencephalon (f-h). Images of the straight sinuses and vein of Galen are difficult to detect, suggesting deep venous thrombosis

![Figure 2](image2.png)

**Figure 2:** Pathology result of the labial salivary gland biopsy, stained with H & E. (a) Lymphocyte infiltration with a focus score >1 meets the diagnostic criteria for xerostomia (×100). (b) >50 lymphocytes/4 mm² (×200)

| Table 1: The characters of Sjögren’s syndrome associated cerebral venous sinus thrombosis |
|---|---|---|---|---|---|---|
| Age | Gender | SS symptom before CVST occurs | Thrombosis site | Positive antibodies | Treatment | Prognosis |
|---|---|---|---|---|---|---|
| 44-year-old | Female | Recurrent otitis; mucosal dryness; recurrent hands’ arthralgias | Left TS | ANA (+++), pANCA, anti-Ro/SSA antibodies anti-La/SSB antibodies RA test | IV heparin followed by oral anticoagulant hydroxychloroquine | Fully recovered and no relapse in 3-year follow-up |
| 43-year-old | Female | Oral and ocular Sicca syndrome Recurrent cavities | Left TS | ANA (+++), ENA, anti-Ro/SS-A antibodies | IV heparin followed by oral anticoagulant hydroxychloroquine | Fully recovered and no relapse in 5-year follow-up |
| 50-year-old | Female | None | Left TS | Anti-Ro/SSA antibodies anti-dsDNA antibodies Lupus anticoagulant antibodies | IV heparin followed by oral anticoagulant hydroxychloroquine | Fully recovered and with no relapse at the 6-month follow-up |
| 51-year-old | Female | Xerostomia and fever for a month | The straight sinus Vein of Galen Left middle cerebral vein Inferior sagittal sinus | Anti-Ro/SSA antibodies (+++) anti-La/SSB antibodies (+++) nRNP/Sm antibodies (+) | IV heparin followed by oral anticoagulant hydroxychloroquine | Fully recovered and no relapse in 3-month follow-up Clinical and radiological release, but no follow-up record |
| 41-year-old | Female | None | TS | Anti-Ro/SSA antibodies anti-La/SSB antibodies | Steroids and warfarin | |

SS=Sjögren’s syndrome, CVST=Cerebral venous sinus thrombosis, ANA=Antinuclear Antibody, ENA=Extractable nuclear antigens, SSB=Sjögren’s syndrome antigen B, Ro/SSA=Sjögren’s-syndrome-related antigen A, TS= Transverse Sinus
inflammatory autoimmune disease, mainly involving the exocrine glands. Evidence suggests that 68% of primary SS patients experience abnormalities of the central nervous system.  However, SS cases causing CVST is an uncommon phenomenon. In the current case study, the patient had xerostomia, and serum anti-SSA and anti-SSB antibodies were detected. These findings combined with the results of her labial salivary gland biopsy led to a diagnosis of SS. Common risk factors for CVST were absent, as the patient had no history of head injury, smoking, alcohol abuse, or long-term use of oral contraceptives or other medications. No family history of thrombotic disease and negative results of genetic thrombophilia tests make the conclusion of genetic thrombophilia ruled out. Although there is no gene test for the patient, according to the latest research, the benefit of gene test is limited and do not fit for the case. Therefore, we propose a causal relationship between CVST and SS in this patient. According to the literature, the most frequently reported autoimmune diseases which could cause CVST are systemic lupus erythematosus and antiphospholipid syndrome. To the authors’ knowledge, only four other cases of CVST in SS has been reported. The characters of these cases were summarized in Table 1. It could be seen from the table that all patients are females above 40 years old. Four of them subjected to a thrombosis at transverse sinus, while the case author report had a thrombosis site at the straight sinus and vein of Galen. Unfortunately, we did not get the data about how long it takes for an SS patient to develop CVST as there is no description in the reports.

The mechanism of SS-induced neurological dysfunction remains unknown. In the central nervous system, SS-induced vasculitis of small and medium-sized veins and small arteries localized in and around the subcortical white matter may result in acute cerebral infarction or cerebral hemorrhage. In addition, CVST in SS may be caused by immune-mediated nerve injury.

What maybe worthy to mention is that there are 2%–5% SS patients do not have xerostomia and xerophthalmia symptom. It might be wise to detect autoimmunity antibodies to find a possible cause for CVST patient without common risk factors, even they do not have the typical symptom of SS.

The treatment of CVST involves anticoagulants, followed by symptomatic treatment. The management of SS-induced CVST involves immunosuppressive agents administered with anticoagulant therapy, as shown in Table 1. However, in the absence of relevant clinical trials, the utilization of these drugs is based on the empirical data. In previous reports, hydroxychloroquine is the most common drug. The prognosis of SS-associated CVST patients is favorable according to previous reports and the current case. Patients had no clinical or radiological relapse and fully recovered at as long as a 5-year follow-up.

In conclusion, we report a case of CVST as a rare central nervous system complication of SS. The risk factors for cerebrovascular disease, such as diabetes mellitus, smoking, and alcohol dependency are rarely seen in patients with SS, who usually present with symptoms such as dry eyes and mouth that can be overlooked by clinicians. In cases of CVST of unclear etiology, we recommend considering a diagnosis of SS with nervous system involvement, and including tests for autoimmunity in the clinical evaluations.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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