Sjögren’s Syndrome Presenting as Ischemic Stroke

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Background We describe a young woman who presented with minor stroke as a first clinical symptom of Sjögren’s syndrome (SS) in the absence of well-known risk factors for cerebrovascular disease.

Case Description The medical history included recurrent miscarriages and sun rashes, which directed the diagnosis toward immunologic disorders such as systemic lupus erythematosus and antiphospholipid antibody syndrome, which are often associated with stroke. Only complete laboratory testing, including SSB antibody studies, and ophthalmologic and salivary gland evaluation revealed the correct diagnosis.

Conclusions Sjögren’s syndrome should be considered among the causes of stroke, especially in a young female patient. (Stroke. 1994;25:2276-2279.)

Key Words • risk factors • Sjögren’s syndrome • young adults • cerebrovascular disorders
Magnetic resonance images show two areas of hyperintensity on T2-weighted image (right panel) and corresponding hypointensity on T1-weighted image (left panel) in the territory of the left middle cerebral artery, involving the cortex of the insula and the globus pallidum. R indicates right; L, left.

showed two areas of hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images in the territory of the left middle cerebral artery, involving the cortex of the insula and the globus pallidum (Figure). An ophthalmologic examination revealed an abnormal break time and a rose bengal score greater than 4, diagnostic of keratoconjunctivitis sicca.9 Minor salivary gland biopsy revealed more than one focus of lymphocytes in 4 mm2 of tissue, thus determining a grade IV lymphocytic adenitis according to the Chishol-Mason scale and confirming the diagnosis of SS.10

The patient was treated with steroid and immunosuppressive therapy (dexamethasone, 20 mg once a week, and methotrexate, 7.5 mg once a week). In the following months she also presented with an autoimmune thyroiditis, which improved after adequate therapy. We continued to follow up the patient for more than 2 years, and she did not present with any other cerebral ischemic symptoms.

Discussion

In this patient the onset and time course of the neurological symptoms as well as the MRI findings suggest the occurrence of a minor stroke in the vascular territory of the left middle cerebral artery.

Normal carotid duplex scan and cerebral angiography ruled out disease of the extracranial and intracranial large arteries as a possible cause of stroke. A possible cardioembolic mechanism was considered, but transthoracic and transesophageal echocardiography ruled out the presence of relevant cardiac and aortic abnormalities. The only detectable cardiac abnormality was thickening of the mitral valves, which is not in itself considered an independent risk factor for cardiac embolism to the brain.11 Additionally, Hess12 found that only the combination of antiphospholipid antibodies and mitral valve abnormalities was associated with brain embolism. In our patient antiphospholipid antibodies were negative on more than one occasion. Finally, we did not find any detectable cardiac arrhythmias.

Because of her young age and the absence of vascular and cardiac risk factors for cerebrovascular disease, hematologic and immunologic abnormalities were considered in the etiopathogenesis of the stroke. A congenital or acquired deficiency of inhibitory coagulation factor proteins such as antithrombin III, protein C, and protein S, which has been established as probable cause of ischemic stroke in both young and old patients,13,14 was ruled out. Possible immunologic abnormalities were then considered. The clinical clues that alerted us to the presence of an underlying immunologic disorder were the presence of three miscarriages and sun rashes in her medical history. The possibilities of antiphospholipid antibody syndrome and systemic lupus erythematosus, often associated with stroke,15,16 were considered. Our patient did not fulfill established criteria for systemic lupus erythematosus or for antiphospholipid antibody syndrome. On the other hand, the presence of antinuclear antibodies and anti-SSB antibodies, a quite specific marker for SS,17,18 led us to perform more thorough testing for SS. The ophthalmologic testing and the salivary gland biopsy confirmed the diagnosis of SS, according to the criteria of the most recent classification of SS.17 Moreover, the association with autoimmune thyroiditis and vitiligo frequently described in SS, a
well-known polyglandular (exocrine and endocrine) autoimmune disease, completed the clinical presentation in our patient.

Approximately 25% of SS patients present with CNS complications and approximately 10% to 20% with PNS complications. The entire nervous system, the peripheral and cranial nerves, and the ganglia may be involved during SS. A necrotizing vasculitis of the gray matter of the insula and globus pallidus was described for PNS complications during SS. On the other hand, a vasculitis with monocytic, lymphocytic, and neutrophilic infiltration is described in a brain biopsy in a case of reversible dementia associated with SS. A vasculitis of the gray and white matter is described in association with cardiomyopathy, but this was not true in our case. This is the first well-documented large-artery minor stroke occurring in a young woman in whom no cause other than uncomplicated SS has been found.

The etiopathogenesis of the neurological damage in SS seems to be immunologically mediated. The most common mechanism of PNS and CNS involvement during SS is due to vasculitis of small vessels. Necrotizing vasculitis involving the entire nervous system has been described in two autopsy cases of SS. T- and B-lymphocytic perivascular leptomeningeal and intraparenchymal chymal infiltration is described in a brain biopsy in a case of a reversible dementia associated with SS. A vasculitis of the gray and white matter is described in association with clinical symptoms of polyneuropathy in SS patients. Antinuclear autoantibodies have also been described for PNS complications during SS. On the other hand, a vasculitis is observed in a biopsy in a patient affected by sensory neuropathy, suggesting another possible cellular-mediated mechanism.

According to Alexander, brain autopsies in SS patients who died in association with severe CNS complications showed minute microhemorrhages and/or microinfarcts associated with extensive small parenchymal endothelial damage secondary to a few mononuclear perivascular infiltrations. According to the author, this type of vasculopathy would be progressive and cause clinical symptomatology only when larger lesions involve a clinically critical region of the brain.

No more than 20% of patients affected by SS have abnormal cerebral angiography suggestive of brain vasculitis. In our patient normal cerebral angiography ruled out the presence of extracranial and intracranial arterial diseases but gave us limited information about possible small-vessel disease. Brain biopsy, potentially diagnostic for inflammatory disease or small-vessel vasculitis, was refused by the patient.

CNS involvement during SS may be studied noninvasively with MRI. This seems to be the most sensitive among the noninvasive tests for SS, being able to detect lesions in more than 75% of patients, whereas computed tomographic scan of the brain is positive in only 20% of patients. MRI abnormalities may include areas of increased signal intensity on T2-weighted images and decreased signal intensity on the corresponding T1-weighted images. The lesions may be located in the periventricular deep white matter and less frequently in the gray matter. In our patient the involvement of the gray matter of the insula and globus pallidus was demonstrated by the MRI.

In our patient the stroke represented the clinical onset of SS. Only a thorough exclusion of other common causes of stroke and a complete hematologic and immunologic screening for disorders rarely associated with cerebral vascular disease revealed the diagnosis.

In conclusion, we believe that young stroke patients without well-known risk factors for stroke should also be evaluated for SS, even in the absence of other clinical symptomatology. The laboratory screening should include immunologic tests such as antinuclear antibodies and anti-SSA and/or anti-SSB antibodies; ophthalmologic and salivary gland evaluation should be performed only if the immunologic screening for SS is positive.

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