

Multiple Cerebral Arterial Occlusions in a Young Patient with Sjögren's Syndrome: Case Report

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WE DESCRIBE A case of a young patient with multiple occlusions of major cerebral arteries and Sjögren's syndrome. This 17-year-old female patient experienced repeated transient ischemic attacks of right hemiparesis, speech disturbance, and unconsciousness. Angiography revealed progressive occlusion of the bilateral carotid and vertebral arteries. Examinations, including a serological test, a rose bengal test, Ga scintigraphy, and a biopsy of the parotid gland, indicated Sjögren's syndrome. The patient was successfully managed with bypass surgery. Patients with Sjögren's syndrome may experience progressive occlusion of the major cerebral arteries resembling that of moyamoya disease. (Neurosurgery 38:592-595, 1996)

Key words: Cerebral arterial occlusion, Moyamoya disease, Multiple infarction, Sjögren's syndrome, Vasculitis

Recurrent ischemic attacks caused by progressive multiple occlusion of the main intracranial arteries in children or young patients may occur in moyamoya disease or in association with diseases such as neurofibromatosis (7), sickle cell anemia (11), Down's syndrome (10), inflammation, and collagen disease (13). Moyamoya disease produces spontaneous occlusion of the intracranial terminal portions of the bilateral internal carotid arteries associated with the collateral vascular network in the base of the brain or the transdural collateral supplies (12, 13). The pathogenesis of moyamoya disease is unknown. Suzuki and Takaku (12) suspect an autoimmune mechanism. However, there have been few case reports in which moyamoya disease was associated with autoimmune disease (6). We describe a patient with subclinical Sjögren's syndrome who experienced cerebral ischemic attacks and a brain stem stroke caused by progressive occlusion of the bilateral internal carotid

and vertebral arteries. We also discuss the cerebral arterial occlusions seen in this patient in relation to moyamoya disease and Sjögren's syndrome.

CASE REPORT

This 17-year-old female patient had an 8-year history of occasional transient attacks of unconsciousness that especially occurred when she hyperventilated while playing a melodica or exercising. Recently, she developed several transient ischemic attacks with speech disturbance and right hemiparesis and fell into a depressive state 3 months before admission.

At admission, she had a low-grade fever and was depressed; she rarely laughed or spoke. Neurological examination revealed slurred speech and mild weakness of the right hand.

Serological examinations were positive for rheumatoid factor (RF), antinuclear antibody, and anti-Ro/SS-A antibody. The RF titer, assayed by the latex

fixation method, was 1:45 (normal RF titer, <25). Antinuclear antibody, detected by the immunofluorescent technique was 1:160 (normal antinuclear antibody, <20). Anti-Ro/SS-A antibody, determined by the Ouchterlony double diffusion technique, was 1:4 (normal anti-Ro/SS-A antibody, undetectable). Decreased lacrimation was suspected, because the results of the rose bengal and fluorescent tests were positive; the results of the Schirmer test were negative. Decreased salivary secretion was detected by a gum test; only 3.6 ml of saliva was obtained (normal salivary secretion, >10 ml). Whole-body Ga scintigraphy showed high uptake in both the parotid and submandibular glands. A biopsy of the parotid gland demonstrated almost complete loss of the gland structure with fatty degeneration and mild infiltration of inflammatory cells. These data indicated a diagnosis of Sjögren's syndrome, although the patient had exhibited no clinical manifestation of the syndrome, such as dry eye, dry mouth, or connective tissue disease.

Magnetic resonance imaging revealed multiple lacunal infarctions in both the basal ganglia and the paraventricular regions (Fig. 1). Carotid angiograms demonstrated occlusion of the bilateral internal carotid arteries at the C3 level just distal to the ophthalmic artery, providing collaterals to form a fine vascular network in the base of the brain (Fig. 2). Meningeal arteries arising from the ophthalmic arteries or external carotid arteries also contributed to the transdural anastomosis over the convexity. Cerebral blood flow images, studied by single photon emission computed tomography (SPECT) using ^{99m}Tc-hexamethylpropyleneamine oxime, revealed a low perfusion area in the left frontoparietal region.

Because the patient twice developed transient ischemic attacks with right hemiparesis after admission and a SPECT study revealed hypoperfusion of the left hemisphere, a parietal branch of the superficial temporal artery (STA) was anastomosed to a cortical branch of the middle cerebral artery (MCA) and a

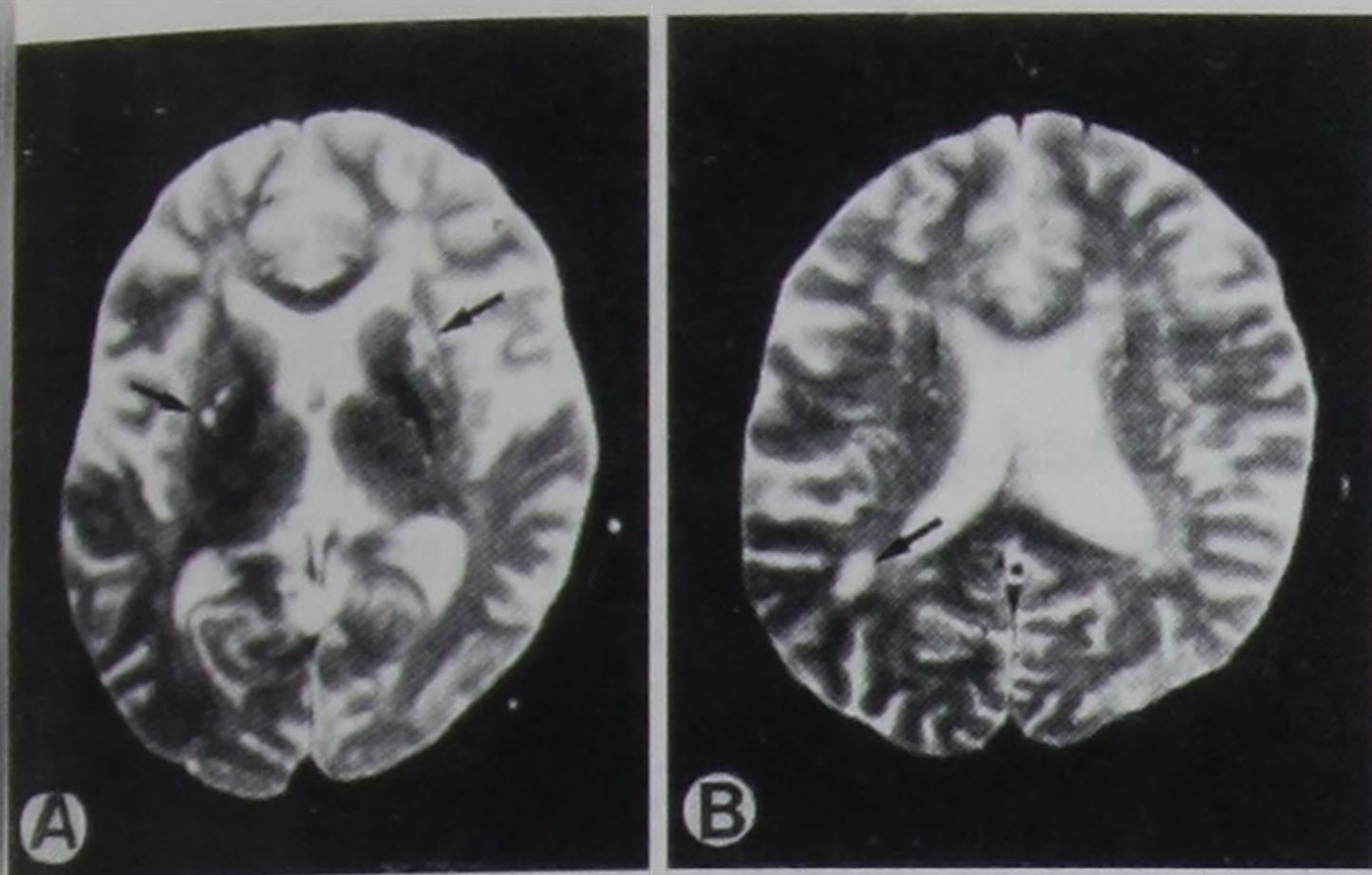


FIGURE 1. The T2-weighted magnetic resonance images (repetition time, 2300 ms; echo time, 90 ms) reveal multiple areas of increased signal intensity in both basal ganglia (*A*, arrows) and the paraventricular white matter (*B*, arrow).

frontal branch of the STA was placed on the frontal cortical surface (encephaloarteriosynangiosis) on the left side. Angiography performed 3 months after surgery demonstrated patent bypass grafts that provided blood flow to the MCA branches in the frontal and parietal cortices (*Fig. 3*). The left vertebral artery was occluded at the foramen magnum, and its meningeal branches formed collaterals to the basilar and posterior inferior cerebellar arteries (*Fig. 4A*). The right vertebral artery was patent. Leptomeningeal anastomosis

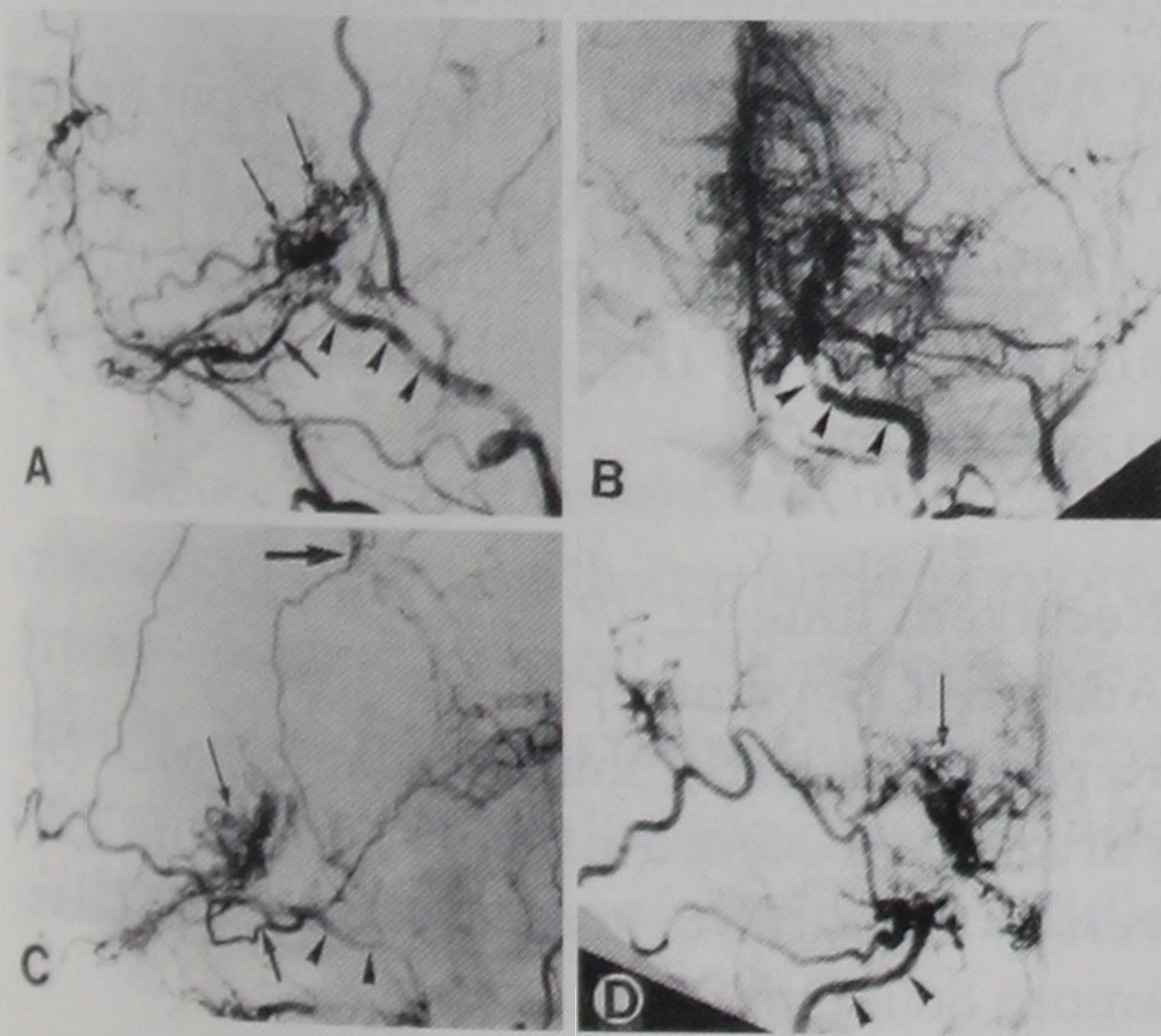


FIGURE 2. Left (*A*, *B*) and right (*C*, *D*) common carotid angiography. Lateral (*A*, *C*) and frontal (*B*, *D*) views demonstrate occlusion of the internal carotid artery (arrowheads) at the C3 portion just distal to the origin of the ophthalmic artery (short arrows), providing a transdural anastomotic network (long arrows) by way of its meningeal branches. A transdural anastomosis from the distal portion of the right STA (*C*, thick arrow) is faintly seen over the right hemisphere.

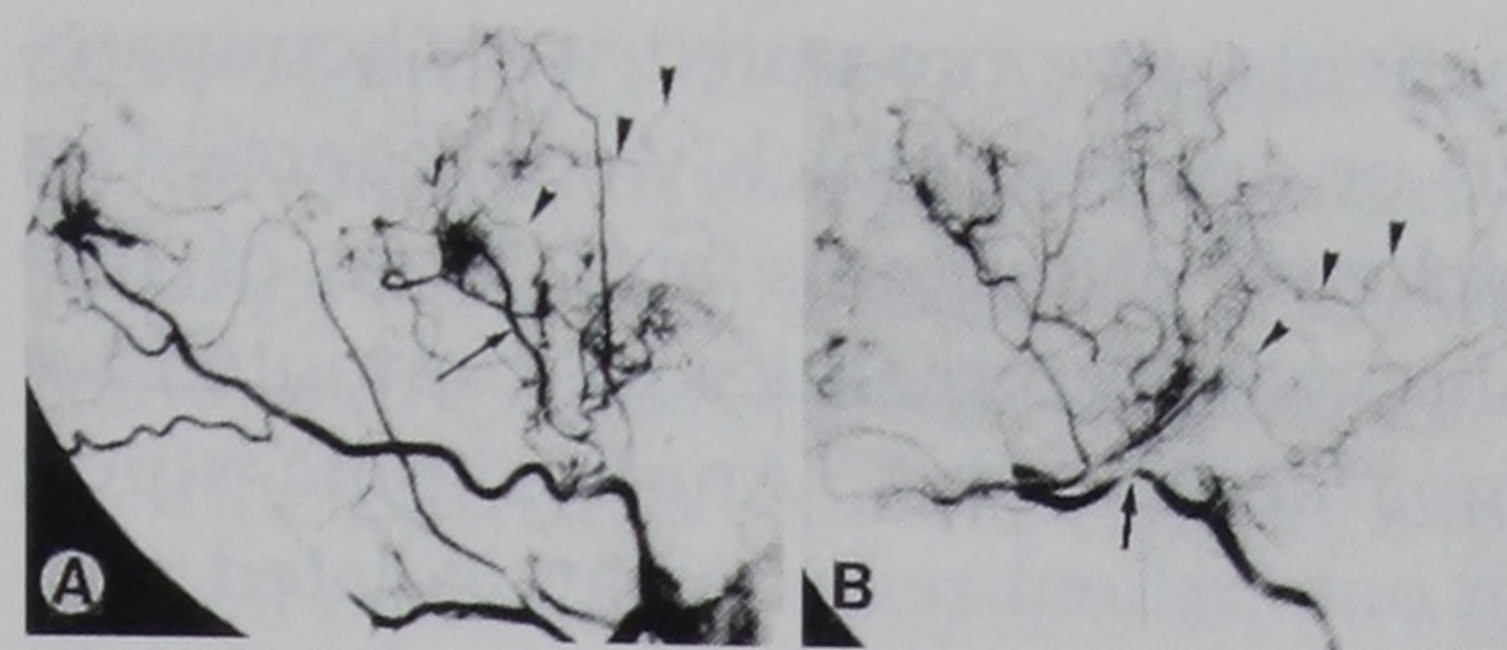


FIGURE 3. Left external (*A*) and internal (*B*) carotid angiography in the lateral projection 3 months after surgery demonstrates the patency of the STA (*A*, arrow) to MCA anastomosis with filling of the temporal and parietal branches (arrowheads). The internal carotid artery was occluded at the C3 portion (*B*, arrow).

was observed at the base of the brain; it originated from the bilateral posterior cerebral arteries (*Fig. 4B*). There were no postoperative ischemic attacks involving the left hemisphere.

One year after surgery, ischemic attacks recurred with left arm weakness. The patient exhibited typical psychiatric symptoms of manic-depressive disorder. A SPECT study revealed a decrease in the cerebral blood flow to the right hemisphere, and a second bypass operation was performed. This time, encephaloduroarteriosynangiosis (8) was performed using the frontal and parietal branches of the right STA because a transdural anastomosis from the distal portion of the STA branches was faintly observed over the right hemisphere. The postoperative course of the patient was uneventful, and she was discharged 2 weeks after surgery. However, 1 month later, she suddenly developed dysarthria and weakness of the left hand and was readmitted. T2-weighted magnetic resonance imaging performed 2 weeks after this event revealed a high-intensity area in the right pons (*Fig. 4C*). Vertebral angiograms demonstrated abrupt occlusion of the right vertebral artery (*Fig. 4D*), which had been patent on the angiogram obtained 1 year earlier (*Fig. 4B*). The intracranial blood flow was maintained with a transdural anastomosis via both internal and external carotid arteries, including the STA bypass grafts, and via meningeal arteries originating from both extracranial vertebral arteries. The collaterals from the right STA used for encephaloduroarteriosynangiosis were seen over the right

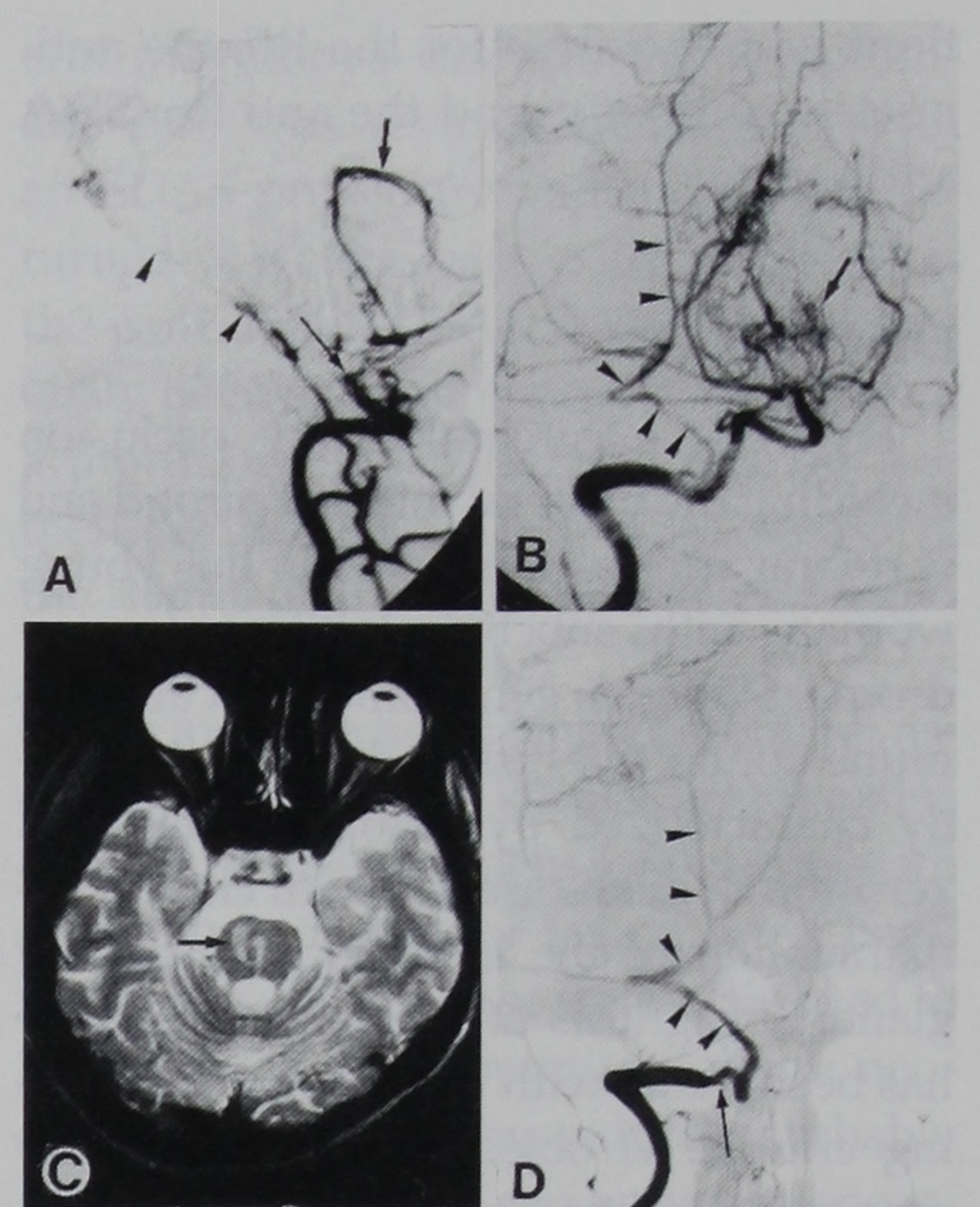


FIGURE 4. *A*, lateral view of a left vertebral angiogram showing the abrupt termination of flow (long, thin arrow) in the left vertebral artery at the foramen magnum. The basilar artery (arrowheads) and the posterior inferior cerebellar artery (thick arrow) are seen by way of the meningeal branches. *B*, right vertebral angiogram reveals patent right vertebral artery, basilar artery, and posterior cerebral arteries providing a fine vascular network in the base of the brain (arrow). A meningeal branch (arrowheads) originating from the vertebral artery makes a transdural anastomosis. *C*, T2-weighted magnetic resonance image obtained 2 weeks after the second operation demonstrates pontine infarction on the right side (arrow). *D*, right vertebral angiogram obtained 3 months after the second operation reveals abrupt termination of flow in the right vertebral artery at the foramen magnum (arrow) just distal to the meningeal branch (arrowheads) providing collaterals to the cerebellum.

hemisphere, although these were less developed than the collaterals from the left STA-MCA bypass graft. The dysarthria and the clumsy hand syndrome gradually improved, and the patient was discharged in good condition except for mild dysarthria. In the past 4 years, the patient has had no more ischemic attacks and her manic-depressive disorder is well controlled by medication. Follow-up serological examina-

tions were positive for the RF, the anti-nuclear antibody, and the anti Ro/SS-A antibody.

DISCUSSION

Progressive cerebral artery occlusion including the bilateral internal carotid and vertebral arteries was noted in this young woman with subclinical Sjögren's syndrome. Sjögren's syndrome is an autoimmune connective tissue disorder primarily characterized by xerophthalmia and xerostomia in association with chronic inflammation of the lacrimal and salivary glands. Diagnosis of Sjögren's syndrome has been made with the use of the following criteria: 1) objective evidence of diminished lacrimation (rose bengal or fluorescent test); 2) objective evidence of diminished salivation (gum test); 3) positive minor salivary gland biopsy; and 4) evidence of a systemic autoimmune process, as manifested by the presence of autoantibodies, such as RF or antinuclear antibody (3). The patient described was regarded to have subclinical Sjögren's syndrome, because she met all four criteria and she exhibited no clinical manifestation of Sjögren's syndrome.

Angiographic findings resembled those seen in moyamoya disease; however, they were different from those of typical moyamoya disease in which occlusion is usually seen at the terminal internal carotid arteries (at the C1 level). The moyamoya vessels originating from the internal carotid arteries form fine vascular networks in the basal ganglia (basal moyamoya), and involvement of the vertebral arteries is rare (5, 12, 13). However, occlusion of the internal carotid artery can progress to a more proximal portion in the late stage of moyamoya disease, and the moyamoya vessels in the basal ganglia may disappear (12). Therefore, we cannot exclude the possibility that our patient was in the late stage of moyamoya disease coincidentally accompanied by subclinical Sjögren's syndrome.

The occurrence of central nervous system disorders in association with Sjögren's syndrome is considered to be rare (2). Alexander et al. (2) reported the association of major central nervous system disorders in eight patients with primary Sjögren's syndrome. Of the eight

patients, five presented with hemiparesis or aphasia, which were regarded as ischemic symptoms and three of five showed abnormalities on computed tomographic scans. Angiographic study in one patient revealed an isolated progressive stenotic lesion at the distal right internal carotid artery. Giordano et al. (4) reported a patient with Sjögren's cerebritis complicated by subarachnoid hemorrhage and bilateral superior cerebellar artery occlusion. These reports suggest that cerebral vasculitis resembling moyamoya disease can occur in patients with Sjögren's syndrome. Alexander et al. (1, 2) suggested a possible relationship between positive anti-Ro/SS-A antibody and vasculitis. Provost et al. (9) also reported a patient with positive anti-Ro/SS-A and anti-La/SS-B antibodies and cerebral vasculopathy associated with collateralization resembling the moyamoya phenomenon, although there was no other laboratory and clinical evidence of Sjögren's syndrome or systemic lupus erythematosus. This is interesting, inasmuch as Suzuki and Takaku (12) have suggested that the cause of moyamoya disease is related to an autoimmune mechanism because tonsillitis and infections around the neck were frequently present in the history of patients with moyamoya disease and because the disease resembled Takayasu's arteritis or Kawasaki disease. In our patient, the progressive multiple occlusions of the major intracranial arteries may have resulted from vasculitis caused by the autoimmune mechanism involved in Sjögren's syndrome.

The effective treatment of occlusive cerebrovascular disorders associated with Sjögren's syndrome is not established, because the association of both disorders is considered to be rare and the details of treatment results were lacking in most of these reports (1, 2, 4, 9). Corticosteroids might be effective (2), although no corticosteroids were used in our patient because she exhibited no clinical manifestation of Sjögren's syndrome. We regarded central nervous system involvement in our patient as a moyamoya-like disorder, because angiographic findings in our patient resembled those seen in patients with moyamoya disease. Because surgical

therapy to augment the collateral circulation is considered to be promising as a treatment to prevent the recurrence of ischemia in moyamoya disease (13), we performed direct and indirect bypass operations using superficial temporal arteries on both sides in our patient. The second operation, an encephaloduroarteriosynangiosis procedure on the right hemisphere, was delayed until the patient became symptomatic and SPECT demonstrated a decrease in the cerebral blood flow to the right hemisphere, because the clinical course of such a patient with a rare association of multiple cerebral arterial occlusions and Sjögren's syndrome was unknown. Except for a brain stem stroke that occurred shortly after the second operation, our patient has had no further ischemic attacks in the 3 years since her bilateral bypass operation. Her manic-depressive disorder is effectively controlled by medication. Bypass surgery might be an effective treatment to prevent the recurrence of ischemia in patients with multiple occlusion of major cerebral arteries and Sjögren's syndrome.

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REFERENCES

1. Alexander EL, Craft C, Dorsch C, Moster R, Provost TT, Alexander GE: Necrotizing arteritis and spinal subarachnoid hemorrhage in Sjögren syndrome. *Ann Neurol* 11:632-635, 1982.
2. Alexander GE, Provost TT, Stevens MB, Alexander EL: Sjögren syndrome: Central nervous system manifestations. *Neurology* 31:1391-1396, 1981.
3. Fox RI, Robinson CA, Curd JG, Kozin F, Howell FV: Sjögren's syndrome proposed criteria for classification. *Arthritis Rheum* 29:577-585, 1986.

4. Giordano MJ, Commins D, Silbergeld DL: Sjögren's cerebritis complicated by subarachnoid hemorrhage and bilateral superior cerebellar artery occlusion: Case report. *Surg Neurol* 43:48-51, 1995.
5. Handa J, Handa H: Progressive cerebral arterial occlusive disease: Analysis of 27 cases. *Neuroradiology* 3:119-133, 1972.
6. Hattori T, Niikawa S, Ohkuma A, Takenaka K, Deguchi K: Moyamoya disease associated with progressive systemic sclerosis: A case report. *Jpn J Stroke* 12:436-442, 1990.
7. Lamas E, Lobato RD, Cabello A, Abad JM: Multiple intracranial arterial occlusions (moyamoya disease) in patients with neurofibromatosis. *Acta Neurochir (Wien)* 45:133-145, 1978.
8. Matsushima Y, Fukai N, Tanaka K, Tsuruoka S, Inaba Y, Aoyagi M, Ohno K: A new surgical treatment of moyamoya disease in children: A preliminary report. *Surg Neurol* 15:313-320, 1980.
9. Provost TT, Moses H, Morris EL, Altman J, Harley JB, Alexander E, Reichlin M: Cerebral vasculopathy associated with collateralization resembling moyamoya phenomenon and with anti-Ro/SS-A and anti-La/SS-B antibodies. *Arthritis Rheum* 34:1052-1055, 1991.
10. Schrage GO, Cohen SJ, Vigman MP: Acute hemiplegia and cortical blindness due to moyamoya disease: Report of a case in a child with Down's syndrome. *Pediatrics* 60:33-37, 1977.
11. Seeler RA, Royal JE, Powe L, Goldbarg HR: Moyamoya in children with sickle cell anemia and cerebrovascular occlusion. *J Pediatr* 93:808-810, 1978.
12. Suzuki J, Takaku A: Cerebrovascular 'moyamoya' disease. *Arch Neurol* 20:288-299, 1969.
13. Yonekawa Y, Goto Y, Ogata N: Moyamoya disease: Diagnosis, treatment, and recent achievement, in Barnett HJM, Mohr JP, Stein BM, Yatsu FM (eds): *Stroke: Pathophysiology, Diagnosis, and Management*. New York, Churchill Livingstone, 1992, ed 2, pp 721-747.

COMMENTS

These authors present an interesting case of a patient with multiple cerebral artery occlusion and Sjögren's syndrome. This patient ultimately required bilateral revascularization, one side with superficial temporal artery-middle

cerebral artery (STA-MCA) bypass and the other with an encephaloduroarterio-synangiosis (EDAS) procedure. The outcome seems to have been satisfactory.

Although I have no experience with arterial occlusion in Sjögren's syndrome patients, my group has been called upon to treat a fair number of patients with moyamoya disease because the number of neurosurgeons in our area who are comfortable with revascularization procedures has decreased. I have some misgivings about the future of revascularization, because our residents do not have nearly the amount of experience with and the exposure to these procedures that previous residents had. I do not doubt that revascularization by either STA-MCA or EDAS procedures is appropriate for patients with moyamoya disease and abnormalities such as that reported here, and I worry that a useful skill is being lost to the general neurosurgical community.

Regarding this case, if faced with a patient with moyamoya disease and a unilateral symptomatic lesion but bilateral angiographic findings, I most likely would have proposed revascularization of the contralateral asymptomatic side on a prophylactic basis some 2 to 3 months after treatment of the symptomatic side. These authors elected to wait because of the unusual nature of the case and, as has ultimately been demonstrated, revascularization of the contralateral side was required. It is unclear to me which is the procedure of choice in adult patients. Certainly, the EDAS is a simpler and quicker operation, but the morbidity of a STA-MCA bypass should also be quite low. In our most recent case of a Vietnamese national with bilat-

eral moyamoya disease, the symptomatic side was revascularized first with an EDAS procedure and the patient returned 3 weeks later with a stroke on the contralateral side, which had previously been asymptomatic. After waiting a month for the patient to recover, we then performed a STA-MCA bypass in the hemisphere that had experienced the most recent stroke.

The message here is that cerebral revascularization of some kind clearly remains an appropriate treatment for patients with moyamoya disease or (as reported here) moyamoya-like disease states. We need to make an effort to continue training neurosurgeons in these procedures, probably in certain specialized cerebrovascular centers where sufficient clinical material will still be available. For neurosurgeons uncomfortable with STA-MCA bypass now, substitution of an EDAS procedure may allow them an acceptable alternative in the treatment of these patients.

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Nagahiro et al. report the association of bilateral internal carotid arteries with Sjögren's syndrome in a 17-year-old female patient. Although the single association of these rare diseases may not indicate a pattern, the discussion by the authors regarding the autoimmune hypothesis for multiple cerebral artery occlusions is of some interest. The role of revascularization procedures in patients with progressive arterial occlusions of this sort is unproven.

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