Cerebral Perfusion Imaging Evaluates Pharmacologic Treatment of Unilateral Moyamoya Disease

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Unilateral Moyamoya disease presents as unilateral stenosis or obstruction of the supraclinoid internal carotid artery, which causes cerebral hypoperfusion resulting in seizures or TIA-like attacks. In severe cases, surgical treatment is performed with superficial temporal artery-middle cerebral artery anastomosis. In mild cases, conservative management is the treatment of choice. Flunarizine is a calcium ion anti-blocking agent, whose primary effect is that the cerebral vessels have been used for the treatment of postcerebrovascular disorders. Recently, it has been suggested that flunarizine could be used to treat Moyamoya disease. This report documents the efficacy of flunarizine to improve regional cerebral perfusion in Moyamoya disease.

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CASE REPORT

A 10-yr-old boy suddenly developed cataplectic attack and gait disturbance while taking a bath 1 mo prior to admission.

On evaluation, the patient complained of weakness in both lower extremities and a gait disturbance. On physical examination, motor nerve paralysis and sensory disturbance up to the L4 level were observed. The remainder of the examination was unremarkable. Routine laboratory data showed no abnormality. There was sudden remission of symptoms. A diagnosis of a psychosomatic disorder was considered. To exclude other organic diseases, MRI and magnetic resonance angiography (MRA) were performed (Fig. 1). These studies revealed obstruction of the right middle cerebral artery and Moyamoya disease was suspected. There was no lesion with high signal intensity in the brain parenchyma on MRI (proton disease-weighted images).

Two months later, the patient developed the same symptoms after severe tantrums. Speech disturbance was also observed. Although the symptoms were temporary, the patient was admitted to the hospital for further evaluation and treatment. After admission, cerebral angiography (Fig. 2) showed severe stenosis of the right internal carotid artery with a defect of the middle and anterior cerebral arteries. So-called Moyamoya vessels were identified in the area of the right basal ganglia. The left internal carotid artery was normal. The patient was diagnosed as having unilateral Moyamoya disease. Technetium-99m-HMPAO SPECT (740 MBq) was performed (Fig. 3) to evaluate blood perfusion of the brain. There were multiple hypoperfused areas: bilateral cingulate gyri, high frontal lobes, thalamus and posterior lobes. No response to acetazolamide was observed.

Since the patient's symptoms were relatively mild, conservative management with flunarizine (5 mg/day the first week, then 10 mg/day in the succeeding week) and ticlopidine hydrochloride (100 mg/day) was initiated. Four weeks later, a repeat SPECT study was performed (Fig. 3). Remarkable improvement of perfusion in the cingulate gyri and high frontal lobes was observed, and some areas in the thalamus, posterior lobes and cerebellum remained unchanged. There was no recurrence of symptoms during the next 4 wk, even during crying periods.

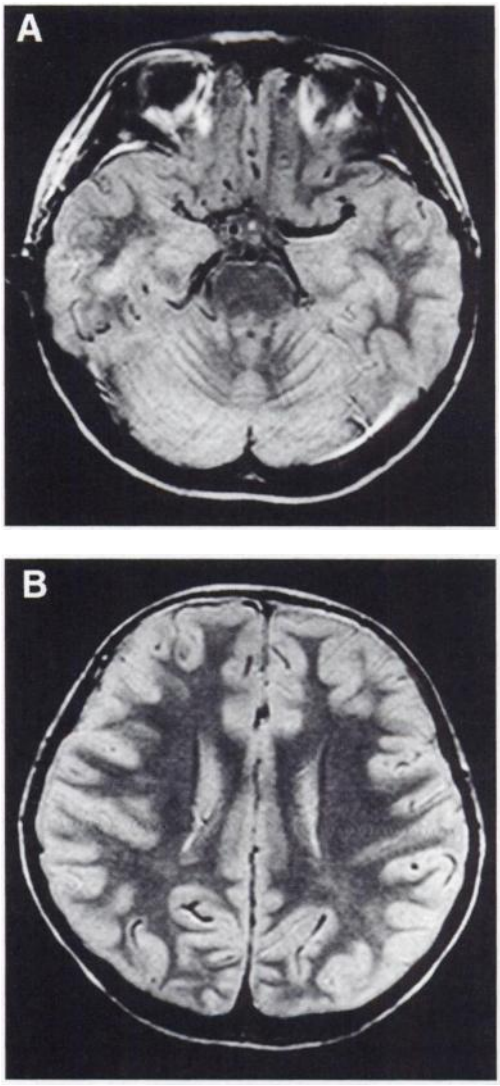

FIGURE 1. MRI shows probable right middle cerebral artery obstruction (A), but no ischemic lesions could be observed (proton density-weighted images) (B).

DISCUSSION

Moyamoya disease is caused by an obstruction or severe stenosis of the internal supraclinoid carotid arteries. Many

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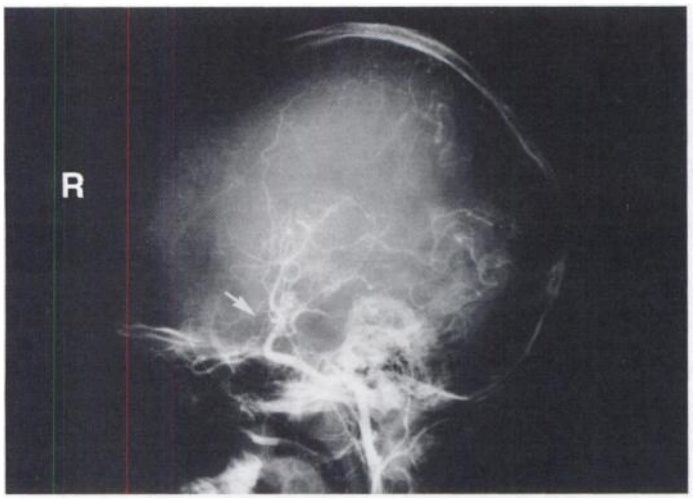

FIGURE 2. Right internal carotid angiography showed severe stenosis as visualized at the supraclinoid level in the basal ganglia area.

collateral vessels compensate for the parenchymal hypoperfusion, mainly in the middle and anterior cerebral artery areas (*1*). The response of cerebral vessels to CO_2 is usually greater than normal, whereas hypocapnia induces marked cerebral hypoperfusion. Furthermore, cerebral oxygen saturation is lower than in normal children (*2*).

Flunarizine is a strong and long acting anti-vasoconstrictor, secondary to calcium ion channel blockage in the blood vessel smooth muscle. During brain hypoxia-ischemia, it protects against endothelial cell damage (*3*). The maintenance dose is 10 mg daily and peak plasma levels are reached within 2–4 hr after oral administration (*4*).

Flunarizine has been used in therapy-resistant epilepsy, migraine and postcerebrovascular diseases, cerebral infarction and cerebral hemorrhage. Nakano et al. reported the therapeutic efficacy of flunarizine in two patients with Moyamoya disease (*5*). In those patients, the symptom was repeated and TIA-like hemiparalysis during hyperventilation was relieved after treatment. Hiyama et al. reported a case of Moyamoya disease treated successfully with Chinese medicine (*6*). They reported

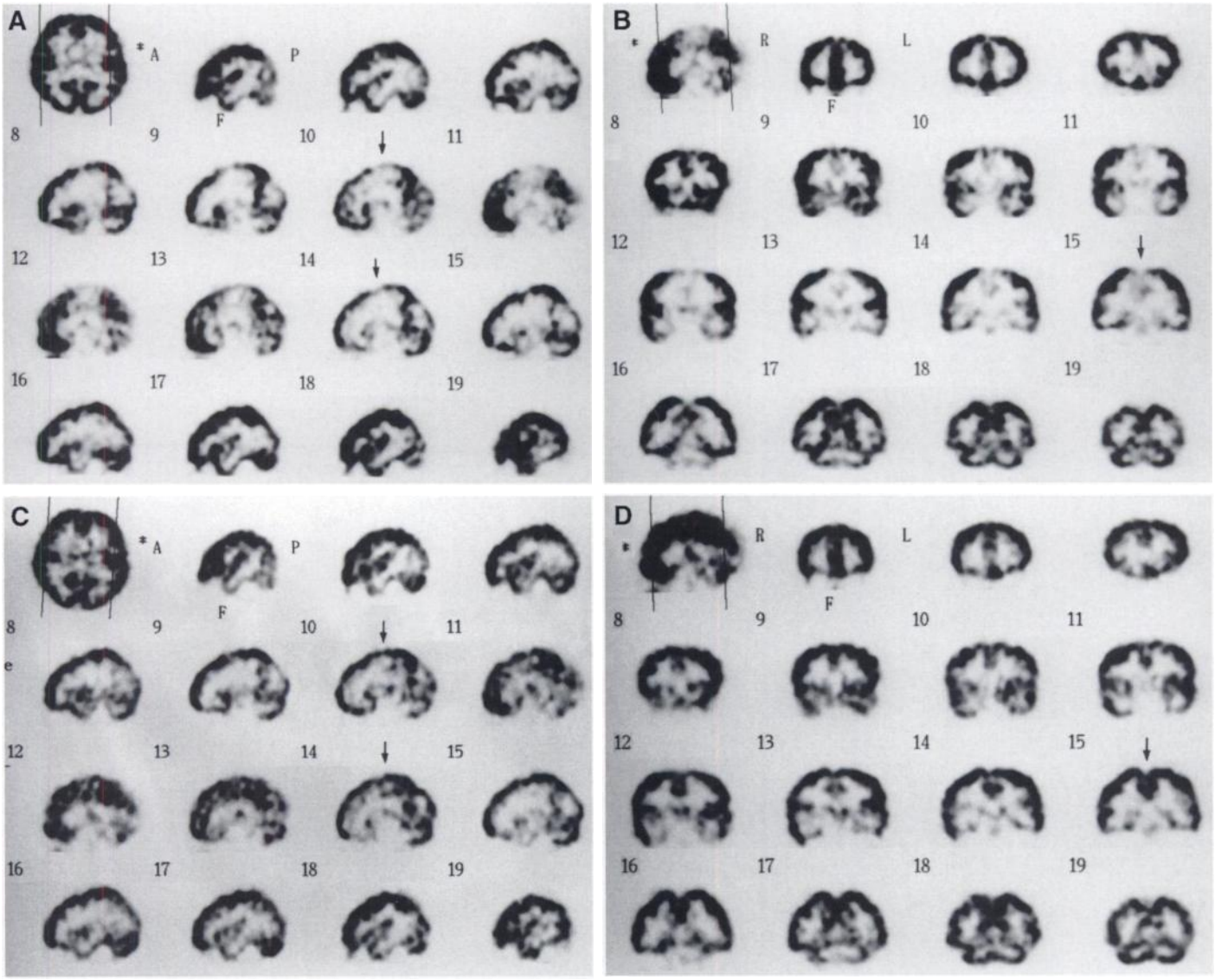

FIGURE 3. Technetium-99m-HMPAO SPECT sagittal (A) and coronal (B) images show multiple hypoperfusion areas in the brain, especially in both the high frontal lobes and cingulate gyri (arrows), before flunarizine treatment. Reperfusions in the high frontal areas and cingulate gyri (arrows) were detected after flunarizine treatment (C,D).

decreased whole blood viscosity and blood flow rate in the bulbar conjunctiva.

It is desirable to document the changes in local cerebral perfusion following therapy. Technetium-99m-HMPAO provides direct information of regional perfusion and vascular reserve of the vessels. In our patient, the collateral vessels were seen, but areas of hypoperfusion were visualized on ^{99m}Tc-HMPAO images. De Lay demonstrated that vasoconstriction at the level of the small vessels is resistant to flunarizine experimentally (*7*). Red blood cell deformability has an important role in the microcirculation of capillary vessels which lack smooth muscles (*8*). Improvement in the deformability of red blood cell and a decrease in blood viscosity with flunarizine have been reported (*9,10*). In our patient, the left anterior cerebral artery (on the side opposite of the affected right ICA) is visualized normally by angiography, but the dominant area (cingulate gyrus, high frontal lobe) showed hypoperfusion. Technetium-99m-HMPAO SPECT imaging revealed the hypoperfused area not only on the affected side, but also on the opposite side and could explain the abnormal symptoms.

CONCLUSION

We have shown improved cerebral perfusion following so-called unilateral Moyamoya disease corresponding to the pharmacologic control of symptoms. Technetium-99m-HMPAO and SPECT regional cerebral perfusion imaging are tools that can assess the effectiveness of flunarizine in patients with Moyamoya disease.

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