Cervical Artery Stenoses in Sickle Cell Disease

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Dear Sir,

Ischemic stroke is a common complication of sickle cell disease (SCD). Approximately 1 in 10 patients with this disease has a stroke before the age of 20 years, and 20% have evidence of brain infarction on MRI [1–3]. It is the primary cause of stroke in children [2]. Ischemic stroke in these patients is usually associated with an intracranial internal carotid (IC) fork stenosis or occlusion. Here we report a patient with SCD, ischemic stroke and multiple stenoses of the extracranial carotid and vertebral arteries.

Case Report

A 19-year-old man was admitted for acute stroke. He was homozygous for the SCD trait. He had not received a regular follow-up but had never had any serious complication of the disease. He used to smoke 10 cigarettes/day. On examination he had dense right hemiplegia and anesthesia, right hemianopsia, global aphasia, somnolence, and gaze deviation to the left. The body temperature was 37°C. ECG was normal. A computed tomography scan showed early ischemic signs in the left middle cerebral artery (MCA). Carotid ultrasound demonstrated a hypoechoic occlusion of the left carotid bulb. Transcranial Doppler (TCD) showed no flow in the intracranial carotid artery and left MCA. The patient was given intravenous rt-PA (0.9 mg/kg). A post-treatment TCD showed partial recanalization of the MCA occlusion with the appearance of a blunted flow signal. CRP was decreased to 5 mg/l, cholesterol LDL was 0.8 g/l, and total hemoglobin (Hb) was 10.3 g/dl. Hb electrophoresis results were as follows: SHb

97.8%; A2Hb 2.2%, and AHb undetectable. Despite thrombolysis, blood transfusion exchanges, and anti-edematous treatment, the patient's condition deteriorated. A decompressive craniectomy was performed on the 4th day. At 6 months, the patient remained hemiparetic and was unable to walk, but his dysphasia had markedly improved. The modified Ranking score was 4. Screening for thrombophilia (protein C and S, factor VII, antithrombin III and lipoprotein (a) plasma levels, search for antiphospholipid antibodies, factor V

Leyden and prothrombin A 20210 mutations) was negative.

The first magnetic resonance angiography (MRA), performed on day 3, showed occlusion of the left IC artery at the level of the bulb. The left posterior communicating artery partially perfused the distal intracranial carotid artery and the left MCA. There was stenosis of the post-bulbar right IC, occlusion of the vertebral arteries on V3 for the left and V4 for the right, with muscular anastomoses which perfused distally (fig. 1). The posterior intracranial circula-

Fig. 1. The cervical time of flight (TOF) showed occlusion of the left IC at the level of the bulb (arrow), the post-bulbar stenosis of right IC (broken arrow) and the occlusion of the vertebral arteries (the right on V4 and the left on V3; arrowhead) with muscular anastomoses (small arrows).

tion and all right-sided intracranial vessels were angiographically normal. No intramural hematoma was seen in the extracranial arteries on the T1 sequence. A repeat MRA at 6 months showed complete recanalization of the MCA. Occlusion of the left cervical IC and vertebral arteries and stenosis of the extracranial right IC remained unchanged. We did not see any irregular caliber vessels on the circle of Willis.

Discussion

Ischemic stroke in SCD has long been associated with intracranial T-carotid artery stenosis. Studies with TCD have shown that the prevalence of such stenoses is 50% in patients with SCD and 80% in a subgroup with ischemic stroke [4]. Furthermore, the presence of intracranial T-carotid stenosis as detected by TCD in asymptomatic children is strongly predictive of future ischemic stroke [3, 5, 6]. Most intracranial carotid stenoses develop during the first decade of life [2]. Stenoses affect the supraclinoid carotid and, to a lesser degree, the first segment of MCA and anterior cerebral artery [6–12]. Moyamoya collaterals are associated in approximately 30% of patients with stroke [13, 14]. Histological examination of the carotid wall in symptomatic patients shows intimal hyperplasia and fragmentation of the internal elastic membrane with superimposed thrombus. The mechanisms underlying the development of intracranial carotid stenosis may include recurrent endothelial injury by sickled cells, with inflammatory and prothrombotic factor production, high blood flow resulting from chronic anemia, reduction in nitric oxide levels and exposure of the carotid wall to free hemoglobin in the cavernous sinus [3, 15–17].

In the present case, there was no evidence of intracranial artery stenosis. The left MCA was initially occluded, but recanalized after thrombolysis without residual stenosis on control MRA. The posterior circulation perfused the left distal intracranial IC and the MCA. Persistent stenoses and occlusions were exclusively located in the extracranial carotid and vertebral arteries. Spontaneous multiple dissections are unlikely because there was no evidence of intramural hematoma on MRI, and stenoses did not show any trend to-

ward regression on the 6-month control MRA. Other classical causes of extracranial carotid and vertebral stenosis/occlusion such as atherosclerosis, arteritis and fibromuscular dysplasia are also unlikely because of the patient's young age, the location of stenoses, and the lack of systemic inflammation or thrombophilia. Thus, the possibility remains that the cervical artery stenoses were secondary to SCD. This would be an exceptional association because we could not find any previous report of cervical artery stenosis in SCD. However, most series have included only children and our patient is a young adult. Furthermore, the present case prompted us to look for extracranial carotid or vertebral stenosis using ultrasound in patients with SCD referred to our neurosonology unit for intracranial artery stenosis screening. We found no cervical artery stenosis in a consecutive series of 15 patients: 7 girls, 8 boys (mean age 17.2, range 8–30 years; 7 older than 15 years).

In conclusion, the present report suggests that ischemic stroke in SCD may be exceptionally associated with extracranial carotid and vertebral arteriopathy.

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