Letter to the Editor

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Brain-to-Brain Paradoxical Embolism through Patent Foramen Ovale after Cerebral Vein Thrombosis

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Dear Sir,

Patients with right-to-left shunt due to patent foramen ovale (PFO), especially if associated to atrial septal aneurysm, are at increased risk of stroke [1–5]. Although there are many possible mechanisms of stroke in these subjects (in situ formation of thrombus, atrial vulnerability, other comorbidities), paradoxical embolism is thought to be one of the most important causes of stroke, yet difficult to be proven [6–8]. Ultrasonographic examination of the venous system as well as CT or MRA studies can identify a venous source in no more than 20% of subjects with cryptogenic stroke [7–10].

We report a case of stroke in a young man with a large PFO, in which the only source of paradoxical embolism was the presence of a recent cerebral venous thrombosis.

Case Report

We investigated a right-handed 50-year-old man, admitted to our Stroke Unit in June 2004, for headache, dizziness and delirium, followed by mild left hemiparesis. MRI and MRA showed the presence of venous thrombosis of sagittal sinus and right transverse and sigmoid sinuses, without parenchymal brain lesions. Screening for thrombophilia did not show any abnormality. The patient had been diagnosed 4 years before as having a non-Hodgkin lymphoma and had undergone bone marrow transplantation 3 years before. He was at that time in therapy with cyclosporine. No hematologic abnormalities, nor hyperhomocysteine, nor genetic mutations of coagulation factors were found; in particular, we searched for MTHFR mutation, prothrombin G20210A mutation and factor V Leyden mutation, and none was found. He was treated with intravenous heparin (5,000 IU bolus, followed by continuous infusion of 1,000 IU/h), with complete resolution of symptoms. Color-coded duplex sonography of the cervical arteries showed no carotid or vertebral disease, and arterial transcranial Doppler ultrasound was unremarkable. A venous color-Doppler of the legs did not show the presence of venous thrombosis, yet it cannot completely exclude this condition. A second cerebral MRI and MRA examination showed partial recanalization of transverse and sigmoid sinuses, and the persistence of thrombosis of sagittal sinus. Then the patient was discharged with oral anticoagulants (warfarin) with a suggested International Normalized Ratio interval of 2–3.

After 10 months, warfarin was stopped and replaced with aspirin, 100 mg, because of the occurrence of bilateral spontaneous subdural hematoma.

Two months later he was admitted again to our Stroke Unit for sudden onset of vertigo, nausea, vomiting and cerebellar ataxia. Neurological examination showed horizontal nystagmus and dysmetria of the right limbs. The acute cerebral CT scan was normal, while a CT scan, performed after 48 h, showed a right cerebellar infarction with mass effect. MRI confirmed the presence of the recent right cerebellar ischemic infarction, associated with other recent bilateral temporal and occipital small areas of arterial ischemia, with neuroradiological characteristics of possible small embolic lesions. Moreover, MRA showed slow flow in the left tranverse sinus, suggesting a recent episode of cerebral venous thrombosis. A traditional digital subtraction angiography showed no arterial lesions, but confirmed slow flow, expression of recent venous thrombosis, in the left transverse sinus, previously patent. Thrombolytic therapy was not performed because of the clinical history and because of the long time interval from onset (>5 h). To identify the cause of the ischemic stroke in the still young patient, a transcranial Doppler with gaseous contrast was done, and a large right-to-left shunt was demonstrated, with 9 microbubbles at rest and curtain effect during Valsalva maneuver [11, 12]. Then a transesophageal echocardiography confirmed the presence of a large PFO without atrial septal aneurysm. The clinical workup (venous Duplex of legs, abdominal echography, total body CT scan with contrast medium, MRA of pelvic veins) failed to show venous sources of paradoxical embolism other than the thrombus in the left transverse sinus. During his stay in our Stroke Unit, the patient was monitored as usual, and continuous ECG did not show atrial fibrillation or other potentially emboligenic dysrhythmia. The patient got better, and he was discharged with a mild right ataxic syndrome, with oral anticoagulant therapy. Then the opportunity to undergo transcatheter closure of the PFO was discussed with the patient.

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Discussion

PFO can be the cause of stroke when it occurs in young subjects without other clear cause of stroke [1–5]. Nevertheless, a venous source of emboli is not often found [6–8]. A recent MRI study reported the presence of thrombosis of pelvic veins in 20% of subjects with cryptogenic stroke and PFO [9].

Cerebral venous thrombosis can be due to local flogistic factors as well as to thrombophilic conditions. In our case the original cerebral vein thrombosis was thought to be caused by thrombophylic state due to non-Hodgkin lymphoma or to cyclosporine therapy [13–18]. The possibility of an intravascular lymphomatosis was excluded by the value of circulating white blood cells, which was normal, and by the clinical course [19].

As the patient had subdural hematomas, warfarin was stopped after the first episode of cerebral vein thrombosis, and probably the thrombotic process in the cerebral vein restarted, facilitated by the venous stasis due to the incomplete recanalization of the first episode. This was probably the mechanism of the last paradoxical embolic event.

Patients with cryptogenic stroke and PFO have high probability to be affected by coagulopathies and venous thrombosis [20–25]. Moreover, the presence of coagulopathies does not obviate the search for venous thrombosis [8]. Lethen et al. [7], studying with phlebography 53 patients with stroke or transient ischemic attack due to PFO, found the presence of deep vein thrombosis in 9.5%. Cramer et al. [9] reported pelvic vein thrombosis in 20% of patients with cryptogenic stroke. In our case, the patient had neither coagulopaties nor mutation of coagulation factors, and the intravascular pathology was the cause of cerebral venous thrombosis. Valdueza et al. [26] reported presence of microemboli in the jugular vein in 3 out of 6 subjects with sagittal sinus thrombosis. We did not search for microemboli in the jugular veins, but Duplex showed bilateral patency of the veins. In our case, the presence of PFO was the cause of paradoxical embolization from the cerebral veins to the brain.

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