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Disappearance of Microembolic Signals after Heparin in Acute Cerebral Ischemia due to Cyanotic Heart Disease with Polyglobulia

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Introduction

Patients with congenital cyanotic heart disease have many hematologic and hemostatic abnormalities [1–5] and are probably at increased risk of cerebral infarction [6, 7]. Although there are many studies on the efficacy of long-term anticoagulation in cardioembolic stroke prevention, there are few data on stroke prevention in subjects with congenital cyanotic heart disease; moreover, there is no evidence on the efficacy of intravenously administered heparin in modifying the rate of embolic events in these particular cases. We report a case of congenital cyanotic heart disease, with accompanying hematological abnormalities, who developed episodes of transient ischemic attacks and numerous microembolic signals (MES) on transcranial Doppler (TCD) recordings, modified by heparin infusion.

Case Report

We investigated a right-handed 29-year-old woman, known to suffer from a complex congenital cyanotic heart disease. She had pulmonary atresia, ventricular septal defect, right aortic arch, and systemic origin of pulmonary circulation and was operated on at the age of 10 years with a procedure in the left chest, uniting two collaterals to the left lung and connecting them to the left subclavian artery. She then suffered from the effects of advancing pulmonary hypertension and obstructive disease, with secondary polyglobulia. On February 3, 2004, during a therapeutic phlebotomy for polyglobulia (hematocrit 63%), she showed a sudden onset of moderate motor aphasia, with reduced verbal fluency, and a mild hemiparesis with hemiparesthesias on the right side. These symptoms disappeared spontaneously within 1 h, but an identical episode occurred a few hours later, with complete clinical resolution.

The day after, she was admitted to our stroke unit. Neurological examination as well as cerebral CT scan and carotid duplex were normal. We could not perform MRI because of claustrophobia. She was already treated with an antiplatelet agent (aspirin 325 mg).

The clinical evaluation showed moderate cyanosis with digital clubbing. The hematocrit value on admission was 57.5%, hemoglo-

bin was 17.3 mg/dl, and the red blood cell count was 7.5 million cells/ml.

On February 5, 2004, during a second therapeutic phlebotomy, she developed a further episode of right hemiparesis and hemihypesthesia, with motor aphasia. Acute EEG monitoring contributed to exclude the diagnosis of seizures. Color-coded duplex sonography of the cervical arteries showed no carotid or vertebral disease, and TCD was unremarkable. Then bilateral TCD monitoring was performed during the attack (Multidop DWL-X4; DWL Elektronische Systeme, Sipplingen, Germany) which showed several MES on both middle cerebral arteries (35 MES on the right and 64 MES on the left within 25 min of recording) [8, 9]. Considering the occurrence of the ischemic event during antiplatelet therapy, and the very high rate of bilateral MES, heparin infusion was started, with an intravenous bolus of 5,000 U and continuous infusion of 1,000 U/h. The MES completely disappeared immediately after the intravenous bolus. The symptoms resolved within 1 h, and no further MES were recorded during the following 30 min. Long-term oral anticoagulation with warfarin was started, and a daily TDC monitoring did not show any MES during the following 7 days. The patient was treated with phlebotomies (accompanied then by isovolemic fluid replacement) two times a week, coupled with anticoagulant therapy. No further neurological symptoms appeared, and the patient was discharged from the stroke unit after 1 week, free from any neurological symptoms or signs, under oral anticoagulant medication. The hematocrit on discharge was 48%, and the international normalized ratio (for clotting time) was 2.7.

Discussion

We reported the case of a 29-year-old woman, affected by congenital cyanotic heart disease, who developed transient ischemic attacks during periodical therapeutic phlebotomies. We detected transient MES on both middle cerebral arteries during one of these episodes. As the patient was taking an antiplatelet agent, and since the hematocrit value was high, the clinical events were thought to be due to hyperviscosity and microembolization of red cell aggregates. The MES recorded disappeared completely after heparin infusion, and the episode completely resolved soon after.

The presence of MES during acute cerebrovascular ischemic events is well known [10–15]. In particular, it has been suggested that bilateral MES can be the expression of a cardioembolic source, as opposed to unilateral MES which are more frequent in the presence of a carotid source [10, 12, 13]. MES recording can give information on stroke pathogenesis in individual cases, classifying stroke as cardioembolic, lacunar, or atherosclerotic [10–17], and may identify patients with continuing embolization. Finally, MES have an independent predictive value of a poor clinical outcome [13, 18, 19]. The localization of an active embolic source can help in identifying patients at risk of recurrent stroke as candidates for more aggressive antiplatelet therapy and for monitoring drugs for early recurrence prevention [20, 21].

While antiplatelet therapy has been shown to reduce MES occurrence in the acute phase of stroke [22], and in symptomatic arterial stenoses [23], it has been reported that heparin has no effect on presence and frequency of MES [24]. Nevertheless, other authors [25] have reported a correlation between coincidence of reduction in the rate of embolization in patients with acute stroke and therapy with warfarin plus antiplatelet agents.

Hyperviscosity is considered to be of crucial importance in the pathogenesis of ischemic events in patients with polyglobulia [26–29]; hyperviscosity and hypoperfusion enhance thrombus formation, promoting embolization of fresh thrombi [30]. Moreover, administration of heparin is known to cause a reduction of viscosity and also of markers of thrombus formation [31]. In our patient, who was already treated with aspirin, immediately after the infusion of heparin, there was a progressive reduction in the rate of embolization, ending with no recordable MES. The reduction of MES immediately after heparin infusion may be interpreted as expression of a reduction of red cell aggregates and increased washout of emboli [26, 32–34]. In fact, after long-term anticoagulation coupled with regular isovolemic phlebotomies, no further MES and no symptoms developed.

To our knowledge, this is the first case of reduction of MES after heparin infusion in a subject with cardioembolic stroke due to cyanotic heart disease and polycythemia. This case report stresses the importance of TCD monitoring in acute stroke and suggests that heparin can influence positively the cerebral blood flow in case of secondary polyglobulia due to cyanotic heart disease.

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