

Recurrent strokes under anticoagulation therapy: Sticky platelet syndrome combined with a patent foramen ovale

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ABSTRACT

The sticky platelet syndrome (SPS) is a congenital disorder characterized by platelet hyperaggregability to epinephrine and/or adenosine diphosphate; this predisposes affected individuals to acute myocardial infarction, ischemic optic neuropathy, recurrent venous thromboembolism, and transient ischemic cerebral attacks and strokes. Here, we describe an unusual case with recurrent cerebrovascular accidents due to SPS, in the presence of a patent foramen ovale (PFO). We report an unusual case of a 56-year-old female patient with a PFO, who suffered from recurrent strokes despite long-term medication with clopidogrel for SPS. The patient underwent successful transcatheter closure of the PFO, and, in addition, she has been placed on low-dose acetylsalicylic acid. After 18-month follow-up, she demonstrated an intact atrial septum without any vegetations on the percutaneous device until today. She has had no further thromboembolic events.

Key words: Cryptogenic stroke, patent foramen ovale, sticky platelet syndrome

INTRODUCTION

Ischemic stroke is associated with multiple etiologies and diverse pathogenic mechanisms. Despite numerous studies suggesting a relationship between paradoxical embolism from a patent foramen ovale (PFO) and cerebrovascular accidents, the role of a PFO as a risk factor for cerebral ischemia remains controversial.^[1] Otherwise it is well known that coagulation disorders like sticky platelet syndrome (SPS) are also common in young patients with ischemic stroke.

SPS is a congenital disorder characterized by platelet hyperaggregability to epinephrine and/or adenosine diphosphate (ADP), thus increasing the risk of acute myocardial infarction, ischemic optic neuropathy, recurrent venous thromboembolism, and transient ischemic cerebral attacks and strokes.^[2] In this paper, we report a case of successful treatment of recurrent strokes due to SPS in a patient with a PFO that was managed by transcatheter closure and anticoagulation with low-dose acetylsalicylic acid.

CASE REPORT

This report describes a 56-year-old female patient with a PFO who suffered from recurrent strokes despite long-term medication with clopidogrel for SPS. In 1997, the patient was diagnosed with a transient ischemic attack (TIA) with initial right-sided hemihypesthesia followed by

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discrete, accented brachiofacial hemiparesis. After 20 h, all symptoms resolved. Cardiovascular and neurological examinations were unremarkable. The patient was discharged without any residual defects.

In December 2007, the patient was admitted because of acute sensomotoric aphasia as well as a right-sided discrete, distinctive, accented brachiofacial hemiparesis. Magnetic resonance imaging (MRI) of the brain was performed and she was diagnosed with an ischemic stroke. The cardiovascular examination was unremarkable. After thrombolytic, occupational, and speech therapy, the patient was discharged without complaints.

In view of the suspected allergy to acetylsalicylic acid, a permanent anticoagulant with clopidogrel was prescribed (75 mg daily).

Despite the long-term anticoagulant treatment with clopidogrel, the patient was admitted again in December 2008 with global aphasia. While exercising, she suddenly felt nauseated and dizzy, and had speech difficulty. During admittance, the patient was well oriented and cardiopulmonary stable, however, not able to communicate verbally or in writing. Motoricity, sensibility, and word understanding seemed to be well conserved. Demand or requests were followed up promptly. Immediate investigations revealed an ischemic cerebrovascular accident in the area of the media cerebral arterial distribution. A systemic thrombolytic therapy was prescribed which resulted in regression of symptoms. However, during this admission, transthoracic and transesophageal echocardiogram revealed a PFO. She was treated with intravenous heparin and later prescribed warfarin. The patient recovered without any residual defects and was discharged in a fortnight with continued rehabilitative therapy. Three months later, the anticoagulation regime was changed from clopidogrel to subcutaneous heparin and a series of hypercoagulability studies was performed. The results were positive for SPS type II. As a result, the anticoagulant treatment was adjusted to include low-dose acetylsalicylic acid (100 mg/day). The analysis at 1 month demonstrated a therapeutic effect of the low-dose acetylsalicylic acid medication. In addition, the closure of the PFO was performed under transesophageal echocardiography control at a specialised center in April 2009. After percutaneous closure, the patient received clopidogrel (75 mg/day for 6 months) additionally. The postoperative course was unremarkable and the patient was discharged after 5 days. An intact atrial septum with a correct positioning of the implanted device was seen in the 18-month follow up. She has since had thrombotic events,

is free of pain, and able to do well in activities of daily living. Patient's children were also evaluated for hypercoagulable states, although neither reported a previous thrombotic event. The daughter showed heterozygosity for SPS and both sons had no coagulation disorders.

DISCUSSION

The cause of stroke remains unknown in roughly one-third of patients, despite extensive investigation. The presence of a PFO, a remnant of the fetal circulation that is present in approximately 25% of the general population, has been linked to an increased risk of ischemic stroke, especially in cases without an alternative explanation (cryptogenic strokes).^[3-5] And it is well known that recurrent thromboembolic events are more frequent in patients who have had a PFO associated with paradoxical embolism.^[6,7] Otherwise, inherited hypercoagulable states like deficiencies of specific coagulation inhibitors or platelet hyperactivity can also result in thromboembolic events.

Hyperactivity of platelets was found in SPS and was first described in 1983.^[8] SPS appears to be transmitted with an autosomal pattern and about two-thirds of the affected patients have a positive family history of thromboembolic disease.

It has been noted in previous studies that an increased sympathetic activity associated with emotional stress results in a higher level of epinephrine, which is accompanied by an increased platelet reactivity with unexplained arterial and/or venous thrombotic events.^[9]

SPS was identified as a cause of thromboembolic kidney graft infarction,^[10] arterial microemboli in the fingers,^[11] peripheral arterial occlusion,^[12] and stroke.^[13] Treatment of SPS is acetylsalicylic acid medication, as it inhibits platelet aggregation and prevents recurrent thromboses^[14].

In our case, the etiology of patient's neurological events is more than difficult to explain. The PFO or SPS might have caused the recurrent strokes. A second possibility, which might be especially important in our case, is the combination of SPS and PFO which further increases the recurrent strokes than either etiology alone.

Due to this, the decision to treat PFO was made. However, to date, there is a considerable uncertainty about the optimal management of patients with PFO and stroke, with treatment strategies including systemic anticoagulation,^[15] open-heart surgery,^[16-18] and transcatheter PFO closure^[19,20] having been proposed to reduce the risk of recurrent events.

The patient was informed of the options of treatment, and she decided to undergo percutaneous closure. We are convinced that the decision in this case was correct and safe, because the percutaneous closure of PFO is a safe procedure associated with a high success rate and a low incidence of periprocedural complications and recurrences of thromboembolic events.^[20]

We believe that SPS is a frequent disease predisposing to vascular events but often remains undiagnosed as long as no second insult to the coagulation system or vasculature occurs. In this case report, the third cerebrovascular accident in combination with the diagnosis of a PFO led to extended investigations of the hemostatic system. One should keep in mind that the therapy with warfarin, if the SPS were responsible for the recurrent strokes, was not adequate to prevent further vascular complications.

CONCLUSIONS

This case report highlights the importance of thorough investigations of the hemostatics system of patients who experience thrombotic events, especially under anticoagulation therapy. As demonstrated in this report, the combination of hemostatitic abnormality and a PFO is unique in the current stroke literature.

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