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CLINICAL VIGNETTE

A Young Woman with a Hypercoagulable Stroke and PFO

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A 30-year-old woman with history of polycystic ovarian syndrome (PCOS), obesity, and peptic ulcer disease presented to primary care with headache, nausea, and visual disturbance. Six days prior to presentation she awoke with a bi-temporal headache. The pain was similar to her typical tension headaches but unusual in that it was persistent and associated with visual disturbance and nausea. She continued going to work without medical evaluation until two days later, when she was involved in a motor vehicle accident where she sideswiped another car while changing lanes. She was evaluated at an outside emergency department where she additionally reported difficulty in focusing on objects in both eyes. Her physical and neurologic exams were non-focal and she was discharged home with a diagnosis of migraine without brain imaging. Her symptoms persisted and she presented to primary care clinic as a new patient. On examination she had a visual field deficit in the left lower quadrant in both eyes. MRI brain identified a subacute infarct in the area of the right middle cerebral artery (MCA) and the patient was admitted to the hospital for further evaluation.

An MR angiogram of the brain and neck during hospitalization confirmed occlusion of the right MCA but showed no other vascular abnormalities. As she was beyond the window for thrombolysis and/or thrombectomy, anticoagulation with heparin was initiated. Laboratory testing was notable for a hemoglobin A1c =5.5%, LDL =114 mg/dL, HDL =36 mg/dL and negative antinuclear antibody (ANA), double-stranded DNA (dsDNA), and antineutrophil cytoplasmic antibodies (ANCA) results. A hypercoagulation workup was negative for anticardiolipin and beta-2-glycoprotein antibodies, but dilute Russell's viper venom time was elevated, consistent with a positive lupus anticoagulant. This lab was drawn prior to receiving any heparin products. There was no evidence of deep venous thrombosis (DVT) of the left leg on Doppler ultrasound. Transthoracic echocardiogram showed normal left ventricular ejection fraction, and agitated saline bubble study showed mild right to left interatrial shunting consistent with small patent foramen ovale (PFO) without atrial septal defect. Transesophageal echocardiogram confirmed the presence of a PFO. No arrhythmia was present on ECG.

The patient was subsequently bridged to Warfarin to a goal INR of 2.5-3.5, and her oral contraceptive (OCP) was discontinued. She was discharged to physical therapy without further complications. Cardiology recommended PFO closure, which she received 3 months after her stroke.

Discussion

This young patient presented with intractable headache and left lower quadrantanopia and was diagnosed with a subacute ischemic right MCA stroke. Given her young age, new laboratory evidence of antiphospholipid syndrome, and chronic usage of an estrogen-containing OCP for PCOS, the most likely cause of her stroke was an in situ arterial thrombus secondary to a hypercoagulable state. Though her presentation was severe, strokes and transient ischemic attacks are the most common arterial events in patients with the antiphospholipid syndrome. Fortunately, her deficits were mild, though her quadrantanopia still persists. Her clinical case was further complicated by the presence of a PFO.

Secondary prevention of thrombosis in antiphospholipid syndrome is challenging and depends on the location of the clot. Venous thrombosis can be treated with warfarin with targeted INR of 2-3.^{1,2} Arterial thrombosis management is less clear with options including INR ranges of 2-3 with the addition of low dose aspirin or higher targeted INR > 3 as there appears to be a dose related affect with higher INR goals having less propensity towards clotting.³ Higher INR goals have to be balanced with bleeding risks. There is insufficient evidence on the utility of direct oral anticoagulants in secondary prevention in this patient population, but available evidence suggests they may be less effective. Secondary prevention of thrombosis has been studied with Warfarin vs. Rivaroxaban and higher recurrent embolic events were seen.⁴

Despite treatment, the rate of thrombotic recurrence has been shown to be quite high, up to 9.1 cases per 100 patient-years.³ What is the role for further secondary prevention with PFO closure? The GORE, REDUCE, and CLOSE trials have added to the mounting evidence that PFO closure reduces the risk of recurrent strokes, but the patients studied generally had cryptogenic strokes with moderate to large PFO shunting or ASD.⁵ Patients with hypercoagulable states are often excluded from these trials, due to the concern of thrombus formation on intracardiac devices. Although there is limited data on outcomes in this population it has been shown PFO closure can be done without a significant risk of thrombus formation.⁵

The decision to perform PFO closure was therefore based on a consideration of this patient's specific factors, including her young age, desire for future pregnancy which might contraindicate Warfarin use, potential for thrombotic recurrence despite

anticoagulation, and potential for a catastrophic event given the severity of her initial presentation.

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