Antiphospholipid Syndrome and Homozygous Factor V Leiden Mutation in a Young Patient with Libman-Sacks Endocarditis and Stroke

To the Editor:

CASE REPORT

A 16-year-old female student presented to the hospital with sub-acute abdominal pain. She had no pertinent past medical or family history. An oral contraceptive was her only medication, and she did not smoke.

Vital signs were normal. The abdomen was sensitive but without peritoneal signs. The white cell count was $23 \times 10^9/L$. A pregnancy test was negative. While being evaluated, the patient developed a dense left hemiplegia. A cerebral computed tomography scan demonstrated a right sylvian ischemic stroke. An abdominal computed tomography scan revealed multiple infarctions in the spleen, liver, and kidneys (Figure). Transesophageal echocardiography revealed a $2 \times 3$-mm vegetation on the mitral valve. Blood cultures were taken, and antibiotics were begun for presumed bacterial endocarditis.

Cultures remained negative after many days. Thrombophilia screening revealed a lupus anticoagulant and a homozygous factor V Leiden mutation. Antibiotics were discontinued and the patient was anticoagulated. The lupus anticoagulant remained detectable 3 months later, and a diagnosis of antiphospholipid syndrome was made. The patient’s left hemiplegia recovered favorably. Indefinite anticoagulation with a target international normalized ratio of 3.0 and discontinuation of oral contraceptives were advised. Testing of her family members was not performed.

DISCUSSION

Antiphospholipid antibodies (APAs) are the most frequent cause of acquired thrombophilia. They appear in 3% to 5% of the white population, the prevalence increasing with age. Patients with antiphospholipid syndrome might present with venous or arterial thrombi or pregnancy loss in the presence of APAs. APAs exert many thrombogenic mechanisms, including: perturbation of the coagulation cascade (by decreased activation of protein C and inhibition of $\beta_2$-glycoprotein, antithrombin, and fibrinolysis); endothelial cell activation (via increased tissue factor expression and proinflammatory cytokine secretion); platelet activation (via increased thromboxane A2 synthesis); immune complex formation between APAs and $\beta_2$-glycoprotein I in membrane phospholipids of endothelial cells and platelets.

Libman-Sacks endocarditis also is known as “non-infectious” or “thrombotic” endocarditis. First described in 1924, the characteristic sterile valvular lesions were originally considered specific to lupus. It was not until 1987 that the association of these lesions with APAs was reported in the absence of lupus. Nearly a third of patients with APAs have valvular thickening from subendocardial deposition of immunoglobulin and complement, but only 4% develop true vegetations from the associated hypercoagulable state. These vegetations are small and primarily located on the mitral valve. The most frequent and morbid thromboembolic complication is cerebral infarction. Other systemic emboli are generally without consequence. Middle-aged adults are the most frequently affected.

Our patient had a positive lupus anticoagulant and a homozygous factor V Leiden mutation. The coexistence of these 2 thrombophilias is extremely rare, as the homozygous factor V Leiden mutation occurs in only 0.02% of the white population. The mutation of factor V Leiden causes a resistance in factor V to the effect of protein C. This generally manifests by venous thrombosis, although it has been associated with increased risk of stroke in children and young adults. The combination of a factor V Leiden mutation with APAs has been suggested to synergistically increase hypercoagulability, potentially leading to a more severe thromboembolic presentation in our patient. Her oral contraceptive also might have contributed.

We identified 1 case report similar to ours, describing the antiphospholipid syndrome with Factor V Leiden mutation in a young patient with Libman-Sacks endocarditis and stroke, but the Factor V Leiden mutation was heterozygous and the patient had only a transient ischemic attack. We found only 2 other cases of antiphospholipid syndrome and homozygous factor V Leiden mutation in the same patient, both presenting with Budd-Chiari syndrome.

Our case reminds us that unusual or catastrophic thromboemboli should lead to comprehensive thrombophilia screening to rule out multiple disorders. If multiple...
thrombophilic entities are identified, indefinite anticoagulation should be favored, with consideration of familial testing.

Nadesh Morissette, MD
Department of Internal Medicine
Laval University
Québec City, Québec, Canada

Todd Gorman, MD

References