Image Diagnosis: Splenic Infarction Associated with Oral Contraceptive Pills in a Healthy Young Woman

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CASE PRESENTATION

A 23-year-old white woman with no significant medical history presented to the Emergency Department with 3 days of progressively worsening left upper quadrant abdominal pain. She described the pain as a constant, "pressure-like" pain, radiating to her back and associated with nausea. She denied any vomiting, constipation, diarrhea, fever, chills, rigors, night sweats, weight loss, loss of appetite, dysuria, hematuria, urinary frequency, history of trauma, or personal history or family history of thromboembolism. She had never smoked and denied any alcohol or illicit drug use. She had been taking oral contraceptive pills (OCP)—norgestimate and ethinyl estradiol—for several years.

Physical examination revealed a normal body mass index and tenderness in the left upper quadrant of the abdomen. Laboratory work-up showed a white blood cell count of 13.5 K/µL, with an absolute neutrophils count of 10.8 K/µL, hemoglobin of 14.2 g/dL, platelet count of 249 K/µL, serum sodium of 136 mmol/L, serum potassium of 3.1 mmol/L, creatinine of 0.8 mg/dL, lipase of 15 U/L, and LDH of 175 IU/L. Urine analysis was unremarkable, and blood cultures were negative. Further laboratory work-up revealed a partial thromboplastin time of 21.2 seconds (23.0-36.9 s) and a prothrombin time of 13.5 seconds (12.0-14.7 s). Hypercoagulability work-up was negative for factor V Leiden or prothrombin gene mutations. Her antithrombin III activity was 106% (80%-120%), protein C activity was 175% (70%-160%), protein S activity was 91% (65%-140%), activated protein C resistance ratio was 2.53 (2.00-4.00 ratio),

Figure 1. An axial-view contrast-enhanced computed tomography scan of the abdomen, taken at presentation to the Emergency Department. The arrows show a diffusely hypodense spleen, indicating massive splenic infarction.

and fibrinogen was normal. Anticardiolipin IgG, anticardiolipin IgM, antibeta-2 glycoprotein IgM, anti-eta-2 glycoprotein IgG, and lupus anticoagulant were all negative. Paroxysmal nocturnal hemoglobinuria panel, hepatitis B and C panel, antinuclear antibody panel, and HIV-1 and HIV-2 Ab screens were also negative. High-performance liquid chromatography results were negative for sickle cell trait. Peripheral blood smear showed leukocytosis with neutrophilia, with no evidence of dysplastic changes or immature myeloid or lymphoid cells, including blasts. The red blood cells were normal in morphology without schistocytes or spherocytes.

A computed tomography (CT) scan of the abdomen revealed a 5.7 cm x 3.0 cm x 3.3 cm wedge-shaped area of nonenhancement in the superior and medial aspect of the spleen, most consistent with an infarction (Figures 1 and 2). A CT scan of the chest was negative for pulmonary arteriovenous malformation, and venous
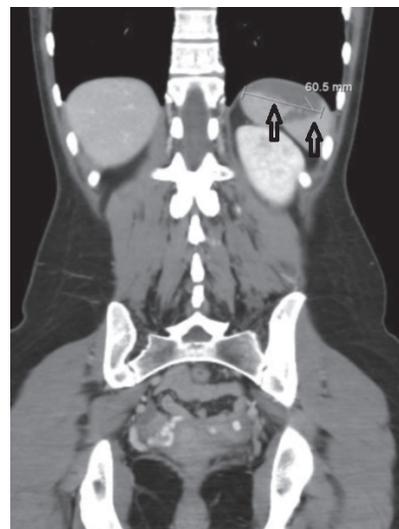

Figure 2. A coronal-view contrast-enhanced computed tomography scan of the abdomen. The arrows indicate a wedge-shaped area of decreased density of the spleen.

Doppler ultrasound of the lower extremities was negative. The splenic artery and vein appeared normal with no evidence of arterial occlusion or venous thrombosis. An echocardiogram showed a normal ejection fraction, with no regional motion abnormalities and no vegetation, though there was a small physiologic right-to-left shunt.

The patient was advised to discontinue the OCP. Because OCP use has been associated with increased risk of thromboembolic events,[1-3] and because our patient was symptomatic because of her splenic infarct, she was started on anticoagulation therapy with a full dose of enoxaparin 1 mg/kg twice a day and warfarin 5 mg oral daily. Once her international normalized ratio

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reached the goal of 2-3, we discontinued the enoxaparin with a plan to continue warfarin for 3 months, because OCP use was considered a reversible risk factor.[3] During the next month, our patient's abdominal pain resolved. She continued her anticoagulation regime for a total of 3 months, and had not experienced any recurrence on last follow-up 12 months later.

DISCUSSION

Splenic infarction is caused by arterial or venous occlusion. The infarction may involve part of the spleen (segmental) or the entire spleen. Most patients present with sudden onset of left upper quadrant abdominal pain; however, some patients may be asymptomatic, with so-called "silent splenic infarction."[4] Splenic infarction is associated with a heterogeneous group of diseases such as bacterial endocarditis, splenic embolism, sickle cell disease, and hematologic malignancies.[5-8]

Splenic infarction can be asymptomatic, though the most common initial presentation symptoms are left upper quadrant pain (33%) and fever and chills (27%).[8] The most common sign for splenic infarction is left upper quadrant tenderness, seen in 35% of patients.[8] Splenomegaly may be present in up to 10% of patients. Leukocytosis ($\geq 10,000/\mu L$) is present in 58% of cases,[8] with elevated lactate dehydrogenase levels in 71% of cases.[9] Causes of splenic infarction include cardioembolism (22%), hypercoagulable states (22%), septic emboli (10%), and hematologic disease (10%).[8] In a review by Antopolsky et al,[8] approximately 17% of patients with splenic infarction were otherwise healthy, and 2% were taking OCP.

The mechanism of splenic infarction depends on the underlying etiology; for example, in sickle cell disease vascular occlusion is attributed to crystallization of the abnormal hemoglobin during periods of hypoxia or acidosis.[10] Splenic embolization may be caused by various cardiovascular conditions, including a left atrial or ventricular mural thrombus in the setting of an acute myocardial infarction or atrial fibrillation, as a complication of cardiac catheterization, or a nonthrombotic emboli as seen in bacterial endocarditis.[11] In cancer patients, the predominant etiology

is thought to be the underlying malignancy-associated hypercoagulable state, and is associated with a shorter survival.[12] Diagnosis of splenic infarction is made by CT scan, which characteristically shows wedge-shaped, linear, or peripheral round hypodense areas in the spleen.[8]

OCPs increase the natural incidence of venous thrombosis of 1-2/10,000 women per year by 3 to 4 fold.[13] OCP use has also been associated with thrombosis in unusual sites. Arul et al[14] reported a case of splenic infarction secondary to celiac thrombosis in a young female on OCP. Khomand et al[15] described a case series of 9 female patients who presented with cerebral vein thrombosis and used a short course of OCP. Estrogen influences hemostasis by increasing the levels of clotting factors (VII, VIII, X, fibrinogen) and plasminogen, by lowering antithrombin III and protein S levels, and by altering activated protein C resistance. Activated protein C is a zymogen that inactivates factor Va. With increased activated protein C resistance, such inhibition is not in effect and the coagulation cascade proceeds. The net effect of combination pills is a procoagulant effect. The overall hemostatic effect is partly caused by estrogen (found in all pills but at different doses) and partly caused by the type of progestogen. Third-generation pills that contain desogestrel were found to cause a greater increase in factor II and factor VII levels.[1-3]

An extensive work-up, as was performed in our case, is recommended to explore the etiology of splenic infarction. In our case, a CT scan with contrast did not show any splenic venous or arterial occlusion, and OCP use was thought to be the major predisposing factor. OCP may contribute to a hypercoagulable state with microangiopathy ultimately causing splenic infarction. Treatment of splenic infarction depends upon the underlying cause. In our patient, an OCP-associated prothrombotic state was the probable etiology, and thus short-course anticoagulation therapy was recommended. American College of Chest Physicians guidelines on antithrombotic therapy and prevention of thrombosis recommend anticoagulation over no anticoagulation in symptomatic patients with splenic vein

thrombosis. Duration of anticoagulation therapy is similar to that recommended in deep-vein thrombosis guidelines, with three months for provoked and more than three months for unprovoked thromboemboli.[16] The role of splenectomy in the setting of massive spleen infarction remains unclear.[17]

CONCLUSION

A sudden onset of left upper quadrant abdominal pain is the most common symptom of splenic infarction. A detailed history and physical examination and an extensive work-up, with particular attention to medication list, is important in detecting the underlying etiology of splenic infarction. In our patient, we recommended discontinuation of OCP use and short-term anticoagulation therapy for treatment of symptomatic OCP-associated splenic infarction. ❖

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