Antiphospholipid antibody syndrome causing acute myocardial infarction in a young adult

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KEYWORDS:
Myocardial infarction; Antiphospholipid antibody syndrome; Factor V Leiden; Hypercoagulable state; Anticoagulation; Young adult

Myocardial infarction (MI) is more frequent in patients older than 45 years of age; however, it can occur in young patients and it is important to include in the differential diagnosis of chest pain. In this case, a 29-year-old male presented to the emergency department with chest pressure. Electrocardiography revealed an acute ST elevation MI. The patient was found to have a mixed hypercoagulability disorder, including antiphospholipid (aPL) antibody syndrome, which led to the infarction. aPL antibody syndrome is a common cause of acquired hypercoagulability in the general population. It is a clinical syndrome characterized by repeated arterial and venous thrombosis, recurrent fetal loss, and positive antibody tests. Asymptomatic patients with low titer aPL antibodies require no treatment. Asymptomatic patients with moderate to high titer aPL antibodies are managed with low-dose aspirin, as are patients with a history of pregnancy-related complications. Patients with more severe manifestations, such as venous or arterial thrombosis, are managed with lifelong administration of warfarin.

Case report

A 29-year-old male presented to the emergency department with a two-day history of progressively increasing chest pain. He stated the pain was left-sided, substernal, and began while he was sitting. The pain at presentation was a 10 out of 10 on a pain scale and associated with nausea, sweating, shortness of breath, and radiation to his left arm and jaw. He denied fever, chills, abdominal pain, dizziness, blurry vision, or headaches. It was described as dull in nature and felt like “a piano was sitting on my chest.” All other review of systems was negative. He denied any trauma to his chest. He had never experienced chest pain like this. He had a past medical history of ulcerative colitis, which was in remission, and he was supposed to be taking sulfasalazine, but admitted he rarely used it because his “stom-ach” felt fine. He denied any allergies. He was a nonsmoker, denied any illicit drug use, and was a social drinker. His father developed hypertension in his 60s, and his maternal grandfather had coronary disease diagnosed in his 70s. He denied any family history of premature or sudden death of anyone younger than age 55.

At arrival to the emergency department, he was pale, diaphoretic, and tachycardic at 110 bpm, which then slowed to 83 bpm after a few minutes. His blood pressure was 110/70, respiratory rate was 22 breaths/min, temperature was 98.5°F, and his oxygen saturation was 100% on room air. There was no peripheral edema and all his pulses were normal. Heart auscultation was regular without any murmurs, rubs, or gallops. His lungs were clear without any rhonchi or rales. His abdominal, neurological, and rectal examinations were all normal. A portable chest x-ray was clear. A 12-lead electrocardiogram was performed and showed sinus rhythm with ST-segment elevation in the anterior precordial leads (Fig. 1). He was given aspirin, nitroglycerin sublingual tablets followed by intravenous...
nitroglycerin, IV heparin, and eptifibatide. While this was being done, the physician covering the acute myocardial infarction (MI) service was alerted.

The patient’s initial troponin I level was 10.27. His initial basic metabolic panel was unremarkable, as was his urine analysis, prothrombin time, partial thromboplastin time, and international normalized ratio (INR). He had a leukocyte count of 16.3 and a hemoglobin and hematocrit of 12.1 and 35.9, respectively. His urine drug screen was negative for phencyclidine, benzodiazepines, cocaine, amphetamines, tetrahydrocannabinol, opiates, and barbiturates.

The patient was taken to the catheterization lab, where he was found to have a near 100% occluded left anterior descending artery and a 90% occlusion of his right coronary arteries. Cardiac stenting was attempted but was unsuccessful because of the density of the clot. The cardiologist successfully performed a thrombectomy of his left anterior descending artery clot. His IV heparin was continued throughout the hospitalization. An echocardiogram performed later that morning showed a 40% ejection fraction and slight septal wall motion abnormalities. Because of his young age, more laboratory tests were ordered for analysis, which were run from his initial “preheparin” treatment, including lupus anticoagulant, factor V Leiden, prothrombin gene mutation, proteins C and S levels, homocysteine level, and factor VIII levels.

While he was recovering in the intensive care unit (ICU), his hypercoagulable laboratory results returned. His factor V Leiden was heterozygous and he was positive for the lupus anticoagulant. Antithrombin III, proteins C and S, homocysteine level, factor VIII level, and anti-nuclear antibody were normal. His chest pain had been resolved and two days later he was resting comfortably when he complained again of chest pain. He then suffered a ventricular fibrillation cardiac arrest while in the ICU and was successfully resuscitated. He was intubated during the cardiac arrest and, after recovering, was not able to be extubated. Fourteen weeks after his initial labs, lupus anticoagulant was still positive as was a high titer B2-glycoprotein-I antibody (an antiphospholipid [aPL] antibody). Unfortunately, he continued to have recurrent deep vein thrombosis while in the ICU and he eventually died from a pulmonary embolism. The family declined an autopsy.

Discussion

When approaching a patient such as this, it is vital to understand the differential diagnosis of MI in young adults. The causes of MI in adults younger than 45 years can be divided into four groups: (1) atheromatous coronary artery disease, (2) non atheromatous coronary artery disease, (3) MI related to substance abuse, and (4) hypercoagulable states.1

Atheromatous coronary disease begins in childhood. In a study of 760 young adults who died of various causes, advanced coronary disease was found in 20% of men and 8% of women between the ages of 30 and 34 years.2 The etiology of atheromatous coronary artery disease in young persons is similar to older individuals, with high lipids, diabetes, and smoking being major risk factors.1 Nonatheromatous coronary artery disease can be caused by congenital abnormalities, such as myocardial bridging (a tunneling
phenomenon that can result in arterial constriction) and coronary artery aneurysm. The third major cause—recreational drug use—is common among young patients. Cocaine use was found to be associated in 48% of young adults who presented to the emergency department with nontraumatic chest pain. Patients with cocaine-related MI cannot be distinguished clinically from other causes. Therefore, patients who lack cardiac risk factors, especially young patients, should have urine cocaine screening routinely performed.

The fourth cause—hypercoagulability—is a rare but important cause of MI in young people, as illustrated in this case. The differential diagnosis of the hypercoagulable state can be divided into congenital and acquired. Congenital causes include antithrombin III deficiency, protein C deficiency, protein S deficiency, homocystinuria, dysfibrinogenemias, hyperlipidemia, and factor V Leiden mutation. Acquired causes include oral contraceptive use, lupus anticoagulant, myeloproliferative disorders, essential thrombocythemia, polycythemia vera, paroxysmal nocturnal hemoglobinuria, heparin-associated thrombocytopenia, prothrombin complex concentrate infusion, nephrotic syndrome, pregnancy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, malignancy, sickle cell anemia, hyperviscosity syndromes, previous venous thrombosis, and venous trauma (Table 1).

Although it rarely causes MI, aPL antibody syndrome is a common cause of acquired hypercoagulability in the general population. It is a clinical syndrome characterized by repeated arterial and venous thrombosis, recurrent fetal loss, and positive antibody tests. aPL antibodies are autoantibodies directed against proteins that bind to phospholipids, including cardiolipin and B2-glycoprotein-I. Patients with aPL antibody syndrome are at increased risk of recurrent arterial or venous thrombosis or pregnancy loss. aPL antibodies are found among young, otherwise healthy people at a prevalence of 1% to 5% for both cardiolipin antibodies and lupus anticoagulant antibodies. Among patients presenting with thrombosis, the prevalence of aPL antibodies is much higher, in the range of 4% to 21%. Among patients with aPL antibodies, the absolute risk of developing new thrombosis is low (1% per year) in otherwise healthy patients without prior thrombotic events; may be moderately increased (up to 10% per year) in women with recurrent fetal loss without prior thrombosis; and is highest (10% in the first year) in patients with a history of venous thrombosis who have discontinued anticoagulant drugs within 6 months. Finally, among patients with systemic lupus erythematosus, the prevalence of aPL antibodies can be as much as 30% for anticardiolipin antibodies and as much as 34% for the lupus anticoagulant.

The clinical spectrum of disease for aPL antibody syndrome varies. It can present as vascular events, systemic manifestations (eg, livedo reticularis, thrombocytopenia, hemolytic anemia, nephropathy, cardiac valve disease), catastrophic antiphospholipid syndrome, or asymptomatic aPL positivity. As far as vascular events, this syndrome can present with arterial or venous thrombosis. Stroke and transient ischemic attack are the most common presentations of arterial thrombosis, whereas deep vein thrombosis is the most common presentation of venous thrombosis. Catastrophic aPL syndrome is a rare and severe form of aPL syndrome that commonly occurs with thrombotic microangiopathy, thrombocytopenia, widespread thromboses, and microangiopathic hemolytic anemia.

A diagnosis of definite aPL syndrome requires the presence of at least one of the clinical criteria (vascular thrombosis or complications of pregnancy) and at least one of the laboratory criteria. The laboratory criteria required to make the diagnosis are lupus anticoagulant on two or more occasions at least 12 weeks apart, anticardiolipin antibody on two or more occasions at least 12 weeks apart, or anti-β2 glycoprotein-I antibody on two or more occasions at least 12 weeks apart.

Therapy for antiphospholipid syndrome involves anticoagulation for thrombosis or pregnancy prophylaxis. Treatment is less well-defined for the associated nonthrombotic complications and atypical complications, and for asymptomatic patients. Limited data support anticoagulant therapy in asymptomatic aPL-positive patients. Current recommendations from a recent consensus statement favor low-dose aspirin in asymptomatic patients. Asymptomatic patients with low titer aPL antibodies require no treatment. Asymptomatic patients with moderate to high titer aPL antibodies are managed with low-dose aspirin, as are patients with a history of pregnancy-related complications. Patients with more severe manifestations, such as venous or arterial thrombosis, are managed with life-long warfarin. Just as important in these patients is the avoidance of reversible thrombotic risk factors such as smoking or oral contraceptive use. Patients with arterial or venous thrombosis require long-term anticoagulation therapy. Previous

### Table 1 Differential diagnosis of hypercoagulable state

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<th>Congenital</th>
<th>Acquired</th>
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<td>Antithrombin III deficiency</td>
<td>Oral contraceptive use</td>
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<td>Protein C deficiency</td>
<td>Venous trauma</td>
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<td>Protein S deficiency</td>
<td>Lupus anticoagulant</td>
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<td>Homocystinuria</td>
<td>Myeloproliferative disorders</td>
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<td>Dysfibrinogenemias</td>
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<td>Hyperlipidemia</td>
<td>Polycythemia vera</td>
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<td>Factor V Leiden</td>
<td>Paroxysmal nocturnal Hemoglobinuria</td>
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<td>Heparin-associated thrombocytopenia</td>
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<td>Prothrombin complex concentrate infusion</td>
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<td>Disseminated intravascular coagulation</td>
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retrospective studies suggest that long-term, high-intensity (INR 3-4) warfarin was most effective in preventing recurrent thromboembolic events, but the necessity of high-intensity anticoagulation has become controversial. A more recent prospective randomized controlled trial of two intensities of warfarin therapy in 114 aPL antibody–positive patients with previous thrombosis followed for a mean of 2.7 years concluded that moderate (INR 2-3) and high (INR 3-4) intensity anticoagulation were similarly effective. Current American College of Chest Physicians (ACCP) guidelines recommend initial INR range of 2 to 3, but INR range 2.5 to 3.5 for recurrent thrombotic events, or if the patient has any additional thromboembolic risk factors.

The patient in this case had a history of ulcerative colitis, which, according to the patient, was in remission. Patients with inflammatory bowel disease (IBD) frequently suffer from macrovascular thrombosis. The incidence of arterial and venous thromboembolism in patients with ulcerative colitis and Crohn’s disease is between 1% and 8%, rising to an incidence of 39% in some postmortem studies. The risks for thrombosis in IBD has been attributed to a state of hypercoagulation caused by elevated levels of plasma fibrinogen and factors V, VII, and VIII; as well as thrombocytosis and abnormal platelet aggregation. Interestingly, positive aPL antibodies, in addition to antibodies against β2-glycoprotein-I, have been found in patients with IBD. According to some studies, a trend toward an association between anticardiolipin antibodies and worsening thrombotic disease was identified; however, the associations were not strong enough to be statistically significant. In addition, the presence of β2-glycoprotein-I antibodies does not seem to be related to thrombotic risk in IBD. Although levels of anticardiolipin antibodies appear to be elevated in patients with IBD, elevated anticardiolipin antibody levels appear to play no role in the pathogenesis of thromboembolic events in patients with IBD.

The patient in this case also happened to be heterozygous for the factor V gene mutation. Studies on whether factor V Leiden mutation itself increased the risk of acute MI are ambiguous. A small prospective controlled trial concluded that frequency of factor V Leiden mutation was higher among patients with MI. However, another small study addressed patients presenting with acute MI to assess whether factor V Leiden increases the risk of arterial thrombosis. This particular study showed no evidence of an association between factors V Leiden and acute MI. A 1999 study specifically looked at the potential synergy between factor V Leiden and aPL syndrome. This study showed an increased risk of thrombosis in patients with a factor V Leiden mutation and the aPL antibody syndrome.

Conclusions

Hypercoagulability is a rare cause of MI, but should be included in the differential for young patients, along with coronary disease, anatomical abnormalities, and substance abuse. aPL antibody syndrome is associated with various conditions, including arterial and venous thrombosis and pregnancy-related complications. Diagnosis of aPL syndrome is based on a combination of clinical history and laboratory testing. If a clinical scenario is present, initial testing should include lupus anticoagulant, anticardiolipin antibodies, and β2-glycoprotein-I, if available. Laboratory testing should be repeated in 12 weeks. Therapy for aPL syndrome involves anticoagulation for thrombosis or pregnancy prophylaxis. Current recommendations from a recent consensus statement favor low-dose aspirin in asymptomatic patients. Asymptomatic patients with moderate to high titer aPL antibodies are managed with low-dose aspirin, as are patients with a history of pregnancy-related complications. Patients with more severe manifestations, such as venous or arterial thrombosis, are managed with lifelong warfarin. Current ACCP guidelines recommend an initial INR range of 2 to 3, but an INR range 2.5 to 3.5 is suggested for recurrent thrombotic events or if the patient has any additional thromboembolic risk factors. Early recognition and treatment in these patients can be lifesaving.

References


