Antiphospholipid Syndrome with Renal Artery Embolism: Case Report

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Antiphospholipid syndrome is characterized by venous and arterial thrombosis. Antiphospholipid antibodies are essential to making the diagnosis. It may be a primary disorder or it may be secondary to a connective tissue disorder. Cardiac manifestations of this syndrome include both thrombotic and degenerative valvular disease. Systemic or pulmonary embolism, as well as intravascular thrombosis, is a significant cause of morbidity and mortality. We present a case of renal infarction in a woman with polymyalgia rheumatica and a positive test for antiphospholipid antibody. [Rev Cardiovasc Med. *2002;3(4);196–201*]

Key words: Antiphospholipid syndrome • Renal infarction • Valvular disease • Abnormal thrombosis

A 68-year-old female presented to the emergency department of an urban teaching hospital complaining of right-sided abdominal pain.

History

She had been generally well until 12 hours prior to presentation. At that time a dull pain developed in the right lower quadrant of her abdomen. She denied nausea, vomiting, diarrhea, or constipation. Her past medical history was remarkable for polymyalgia rheumatica (PMR), for which she was taking prednisone daily, and a heart murmur diagnosed when she was a child. She denied alcohol, tobacco, or illicit drug use. There was no family history of connective tissue disease, premature atherosclerosis, or abnormal clotting.

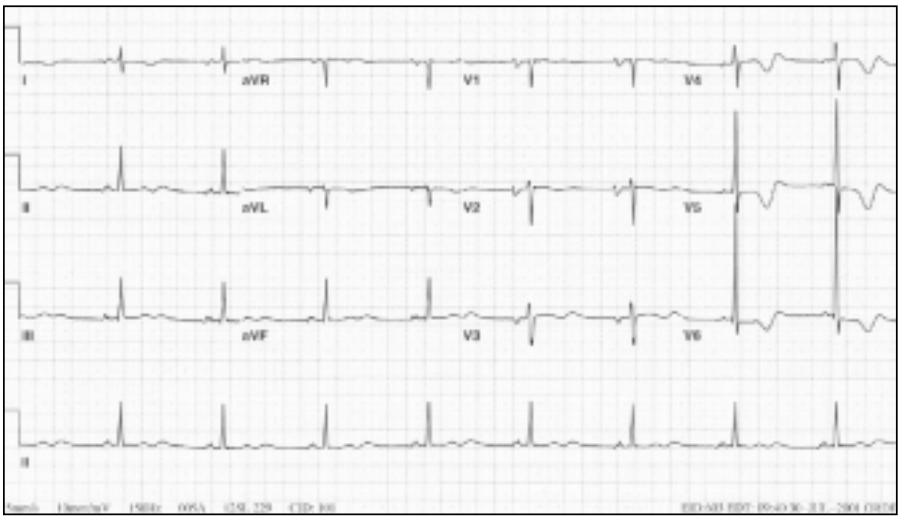

Figure 1. *Electrocardiogram at admission shows sinus bradycardia with a ventricular response rate of 51, left atrial enlargement, left ventricular hypertrophy, and T-wave inversion in leads V4–V6.*

Physical Examination

Upon admission, physical examination revealed severe hypertension of 193/99 mm Hg. There was moderate right lower-quadrant abdominal tenderness without rebound tenderness. Cardiac examination revealed a normal rate and rhythm with a physiologically split S2 and a III/VI systolic murmur loudest at the left second intercostal space near the sternal border. The lungs were clear to auscultation, and extremity examination, including peripheral pulses, was normal.

Electrocardiogram revealed sinus bradycardia at a rate of 51 (Figure 1). There was left atrial enlargement and left ventricular hypertrophy with associated T-wave inversion in the precordial leads. Mild hematuria was present on urinalysis.

Treatment

She was admitted with a diagnosis of biliary tract obstruction versus appendicitis and underwent abdominal computed tomography with contrast, which revealed infarction of the superior pole of the right kidney (Figure 2) and a suprarenal thoracoabdominal aortic aneurysm (4.5 cm at greatest diameter). There was no evidence of aortic dissection.

The cardiology service was consulted to assist in evaluation for the source of renal artery occlusion. The history of connective tissue disease provided an interesting differential diagnosis in this case of renal artery obstruction. Three major possibilities included embolic occlusion, vasculitis/inflammatory occlusion, and in situ thrombosis of the renal artery. Taking into consideration the history of PMR and its association with giant-cell arteritis (GCA), high-dose steroids were started immediately. Laboratory studies to evaluate for hypercoagulable states revealed the presence of the lupus anticoagulant and antiphospholipid immunoglobulin G (aPL IgG). Transesophageal echocardiography was obtained to assess for intracardiac thrombi.

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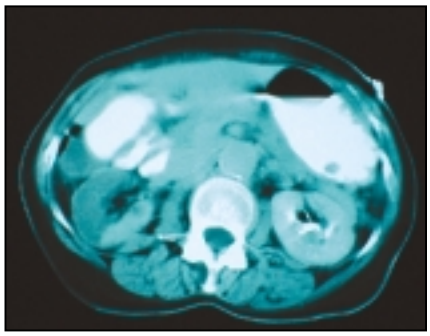


Figure 2. *Computed tomography showing infarction of the superior pole of the right kidney.*

Upon arrival to the echocardiography suite, the patient was noted to be in atrial fibrillation with a ventricular response rate of 123 (Figure 3). The examination was performed without difficulty after appropriate medications were given for rate control. The left ventricular ejection fraction was 30% with global hypokinesis. Spontaneous echo contrast was present in both atria as well as in the left ventricle and the visualized portions of the aorta (Figure 4). Thrombus was noted in the right atrium, but there was no definite left atrial or ventricular thrombus or septal defect.

The patient's history and diagnostic tests performed while in the hospital suggest three possible etiologies of renal infarction: in situ thrombosis related to secondary antiphospholipid syndrome, renal arteritis as a manifestation of GCA (given the history of PMR), and thromboembolism related to atrial fibrillation.

The patient's history of PMR led to the question of the possibility of arteritis affecting the renal artery as the cause of the infarct. Polymyalgia rheumatica is well known to be associated with GCA; 40% of patients with GCA have PMR.[1] This typically involves the aorta and its proximal branches, but not the renal arteries. It has been associated

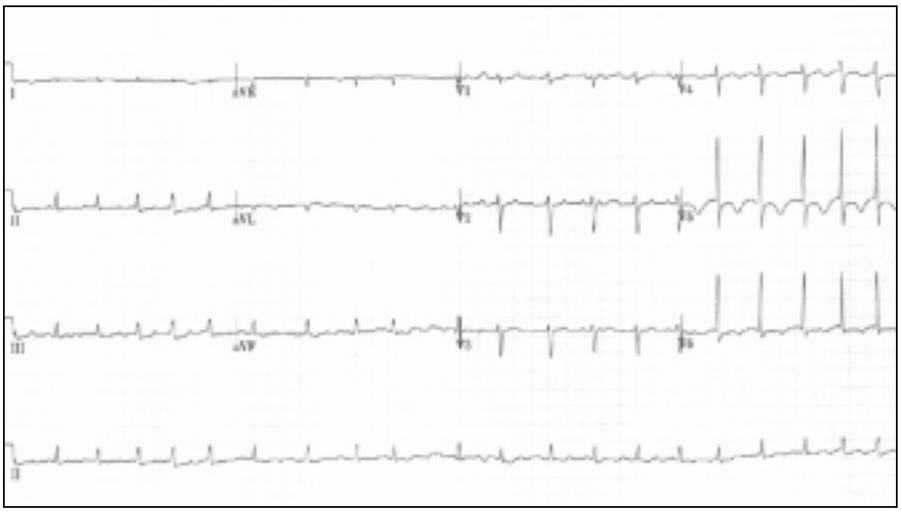
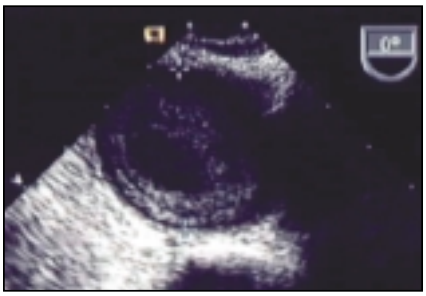


Figure 3. *Electrocardiogram upon arrival to the echocardiography suite with atrial fibrillation and a rapid ventricular response. (Note scale changed to 5 mm/mV.)*

with iliac artery obstruction from aortic dissection, however.[2] Erythrocyte sedimentation rate (ESR) is typically elevated with GCA to at least 40 mm/hr and not unusually to 80–100 mm/hr.[2] This patient's ESR was 50 mm/hr. Acute renal infarction was considered to be an unlikely first presentation of GCA, and therefore we felt there was another more likely diagnosis.

In this case, paroxysmal atrial fibrillation was discovered with telemetry monitoring in the echocardiography suite, and a presumptive diagnosis of cardioembolic renal infarction due to a dislodged left atrial thrombus was made. Anticoagulation was initiated with intravenous heparin, and steroids were tapered to preadmission doses. The patient was discharged home on warfarin sodium (Coumadin) to be continued indefinitely.

Figure 4. *Transesophageal echocardiogram view of spontaneous echo contrast or "smoke" in the descending aorta.*



With a positive antiphospholipid antibody serology, secondary APS related to polymyalgia rheumatica is very likely to have played a role in this case of renal infarction, although thromboembolism due to untreated asymptomatic paroxysmal atrial fibrillation cannot be excluded. In either case, long-term anticoagulation is indicated.

Although the true diagnosis will never be known in this case of renal infarction, it should serve as a reminder that diagnosing the etiology of abnormal thrombosis requires a broad approach. The differential diagnosis may be narrowed as indicated by the patient's history, physical exam, and the results of laboratory testing.

Discussion

Antiphospholipid syndrome (APS) is a disease characterized by venous and arterial thrombosis as well as recurrent fetal losses and thrombocytopenia. Demonstrating the presence of antiphospholipid (aPL) antibodies (anticardiolipin antibodies or the lupus anticoagulant) is essential to making the diagnosis (Table 1). It may be a primary disorder or it may be a secondary phenomenon related to an underlying connective tissue disorder.[3]

Table 1
Antiphospholipid Syndrome Diagnostic Criteria

Antiphospholipid antibodies present on multiple testing
Anticardiolipin antibodies
Lupus anticoagulant
Repeated arterial or venous thrombosis
Recurrent fetal loss in the 1st or 2nd trimester
Thrombocytopenia

Cardiac manifestations of this syndrome include both thrombotic and degenerative valvular disease (Table 2).[4] Systemic or pulmonary embolism from sterile vegetations or from intravascular thrombus is a significant cause of morbidity and mortality in APS. This disorder is easily diagnosed with laboratory tests that are widely available, and it should not be overlooked.

Rheumatic diseases such as PMR and systemic lupus erythematosus (SLE) are associated with hypercoagulability and APS. Antiphospholipid syndrome may occur as a primary disorder or as an associated syndrome with a connective tissue disease. It is diagnosed by a history of vascular thrombosis, pregnancy morbidities such as consecutive miscarriages or unexplained fetal death, and by labo-

Table 2
Antiphospholipid Syndrome Cardiac Manifestations

Valve disease
Vegetations
Leaflet thickening
Regurgitation
Stenosis (rare)
Mitral > aortic > pulmonic or tricuspid valve involved
Coronary artery disease
Native coronary artery disease
Late occlusion of bypass grafts
Restenosis of lesions after angioplasty
Intracardiac thrombus
Myocardial dysfunction

ratory studies that reveal the presence of antiphospholipid antibodies. Antiphospholipid syndrome also commonly presents with low platelets and a prolonged activated partial thromboplastin time (aPTT).[5] This patient did have a positive blood test for aPL IgG but had a normal platelet count and aPTT. There was no history of recurrent fetal loss or prior intravascular thrombosis.

Renal infarction, renal artery stenosis, and hypertension in association with APS have been described by several authors.[6–8] In a recent study, 215 patients with APS were evaluated. Forty-two had evidence of abdominal involvement, and computed tomography (CT) revealed visceral ischemia or infarction in 36 (85.7%). Twenty-two (52%) had renal involvement.[9] The prevalence of renal infarctions in this study of APS patients was 10.2%, considerably higher than the prevalence in the general population of 1.4%. A study of 14,441 consecutive autopsies identified 205 renal infarctions, but only 2 of the 205 (1%) were diagnosed antemortem.[10] Table 3 lists causes of renal infarction.

In young patients with renal infarction, primary APS should be considered, as it may be the initial manifestation of the disease.[11] Renal angiogram and CT are established methods to diagnose renal infarction. Other laboratory evidence includes leukocytosis, hematuria, elevated lactate dehydrogenase, aspartame transaminase, alanine transaminase, and alkaline phosphatase.[12] Our patient was a little unusual in that her right kidney was affected. Renal infarction occurs almost twice as often in the left as in the right kidney, likely owing to the fact that the left renal artery forms an acute angle with the aorta.[13–15]

This patient also demonstrated signs of cardiac pathology attributable to APS. Intracardiac thrombus and myocardial dysfunction are two possible cardiac findings in APS. Cardiac manifestations of this syndrome include valvular abnormalities, coronary artery occlusion and related myocardial dysfunction, diffuse cardiomyopathy, and intracardiac thrombosis (in any chamber).[9]

In patients with lupus and secondary APS, there is an increased risk of cardiac abnormalities, particularly valvular lesions. Lesions may be regurgitant or stenotic, and most commonly involve the mitral or aortic valves. In a recent study, over 75% of patients with primary APS had valvular involvement; 59% had at least one regurgitant lesion. In this small series, 13 patients had follow-up transesophageal echocardiography (TEE) after 1 year of anticoagulation or antiplatelet therapy and none showed improvement; in fact, 7 (54%) had developed new lesions.[16] This appears to be the normal course of the disease, but an isolated case of disappearance of valve lesions with anticoagulation has been reported.[17] Ten-year follow-up of another small series of APS patients revealed that 41% had a valve lesion; 13% required valve replacement.[18]

Table 3
Causes of Renal Infarction

Cardioembolic
Atherosclerosis
Valvular heart disease
Myocardial infarction
Atrial septal or ventricular aneurysm
Dilated cardiomyopathy
Atrial fibrillation
Trauma
Polycythemia vera
Fibromuscular dysplasia
Extra-adrenal pheochromocytoma
Arterial dissection or aneurysm
Connective tissue diseases
Systemic lupus erythematosus
Primary antiphospholipid syndrome
Polyarteritis nodosa
Systemic vasculitis
Mixed connective tissue disease
Bechet's disease
Idiopathic
Drugs
Marijuana, cocaine

Antiphospholipid syndrome is much more common in patients requiring heart valve replacement surgery than in the general population. A recent study of patients referred for valve replacement due to nonspecific valve disease found significantly more aPL antibodies in subjects than in age- and sex-matched

controls (21% vs 9%; $P < .03$). A significantly higher number of the patients with aPL antibodies had a history of arterial thrombosis than did controls (42% vs 11%; $P < .01$). Mitral regurgitation was the most common valve lesion in those with aPL antibodies (37%), followed by aortic stenosis (26%).[19]

The valvular pathology associated with APS has been well described. A study of 16 heart valves from 10 patients with APS revealed 6 with verrucous lesions and 4 with fibrocalcific changes.[20] Five valves from APS patients and three from controls were evaluated for IgM, IgG, or complement deposition. Four of the valves from APS patients demonstrated subendothelial antibody deposition, whereas none of the controls did. It was suggested that these antibodies lead to endothelial activation and to the valvular disease in APS.[20]

A significant correlation between mitral valve thickening and anticardiolipin (aCL) antibody titer has also been demonstrated. Patients with an aCL antibody titer above 40 GPL-U had a 94% chance of mitral valve thickening versus 42% in those with an aCL antibodies titer under 40 GPL-U. The investigators therefore recommend TEE evaluation of any primary APS patient with clinical findings or high aCL antibodies titer.[21] The morphology of the valve lesions in APS is nonspecific, however, and may be clinically, echocardiographically, and pathologically indistinguishable from those seen in chronic rheumatic heart disease.[22]

There may exist an association or a common pathogenesis for rheumatic heart disease and APS-induced valve pathology. Of patients with acute rheumatic fever, 80% may be positive for aCL antibodies versus 40% with inactive disease.[23] If there is a relationship, it is incompletely understood at this time.

Ischemic heart disease is another important cardiac manifestation of APS. Approximately 5% of APS patients will have myocardial infarction. There is an association with pulmonary hypertension and cardiomyopathy due to microvascular thrombosis without vasculitis.[5,24] Acute thrombosis after angioplasty and bypass graft occlusion have been reported in patients with aCL antibodies.[25] These vascular occlusions may lead to significant cardiomyopathy. Cardiac failure led to death in 17% of patients who died in an 8-year study of 354 patients with APS.[26]

These vascular occlusions may lead to significant cardiomyopathy.

There is a condition known as catastrophic APS in which there are multiple simultaneous vascular occlusions. It warrants mention due to its high mortality rate of 50%. Differential diagnosis includes SLE vasculitis, thrombotic thrombocytopenic purpura (TTP), and disseminated intravascular coagulation (DIC). In a literature review, 78% of patients with catastrophic APS had renal involvement, 66% had pulmonary involvement, 56% had central nervous system involvement, and 50% had cardiac involvement. Cardiac findings were mostly valvular (32%) or myocardial (16%). Myocardial involvement was usually due to multiple myocardial microthrombi. Treatment consists of daily plasmapheresis and systemic anticoagulation.[27]

Treatment of APS

Long-term anticoagulation is indicated for seropositive APS patients with evidence of thrombosis. Warfarin is the usual treatment in the absence of contraindications such as pregnancy. Target international normalized ratio (INR) is 3.[3] Patients who are resistant to warfarin therapy may require a higher target INR of 4.5, addition of daily aspirin, or treatment with heparin. Low-molecular-weight heparin has been used in an attempt to reduce complications such as bleeding, osteoporosis, and thrombocytopenia. Some authors recommend twice-daily dosing in an attempt to achieve a more stable level of anticoagulation.[28] ■

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