Acute Myocardial Infarction in a Patient With Systemic Lupus Erythematosus and Normal Coronary Arteries

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Although cardiac manifestations such as pericardial, myocardial, and valvular involvement are common in patients with systemic lupus erythematosus (SLE), coronary artery involvement is less frequent. Clinical manifestations of coronary artery disease in SLE can result from accelerated atherosclerosis, arteritis, abnormal coronary flow reserve, spasm, and thrombosis. In SLE, the classic valvular abnormality consists of noninfective, verrucous vegetation. Thickening of the leaflets due to inflammation followed by fibrosis is common, occurring in about 50% of patients, whereas vegetations are present in about 40%. Mitral valve involvement is most common, with valvular regurgitation more frequent than valvular stenosis. The tricuspid valve and the aortic valve may also be affected. Its frequency varies widely: 13% to 74% in the general population. We report a case of a woman with acute myocardial infarction and normal coronary arteries, who was subsequently diagnosed with Libman-Sacks endocarditis and SLE.

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Key words: Systemic lupus erythematosus • Libman-Sacks endocarditis • Acute myocardial infarction • Verrucous vegetation

A 40-year-old woman with no significant past medical history presented to the emergency room with a 30-minute history of chest pain, nausea, and diaphoresis. An electrocardiogram (ECG) showed evolving ST-segment elevation in the inferior leads, with a rise in cardiac enzymes consistent with acute inferior wall myocardial infarction. An emergent coronary angiography showed no significant obstructive lesions in any of the major coronary vessels. The patient was treated with a calcium channel blocker and nitrates and given a presumptive diagnosis of vasospastic angina.

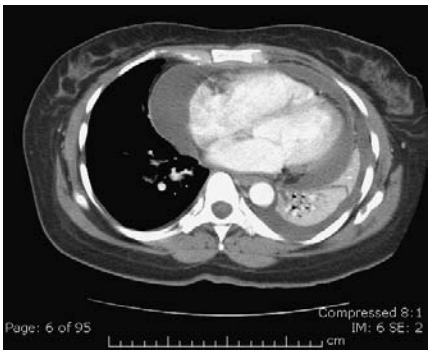

Figure 1. *Computed tomography scan showing a moderate-to-large pericardial effusion.*
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border. Abdominal examination revealed minimal abdominal tenderness with mild distension. A 2-D echocardiogram and computed tomography (CT) scan (Figure 1) showed a moderate-to-large pericardial effusion with early tamponade physiology. She was admitted to the cardiac intensive care unit for close monitoring of her effusion and underwent serial echocardiograms. Serum amylase and lipase were normal, and the obstruction series did not show any evidence of intestinal obstruction. CT scan of the abdomen revealed moderate ascites with no signs of perforation, inflammation, or obstruction, and upper gastrointestinal endoscopy showed an erosive gastritis. Chest x-ray showed an increased cardiac silhouette and bilateral pleural effusions. A repeat echocardiogram performed 3 days later showed no change in the size of the effusion, but did show new visible masses on the ventricular surface of the mitral valve. Her laboratory examination was significant for a normocytic normochromic anemia and hyponatremia, with normal renal function. A serum antinuclear antibody test was positive and the erythrocyte sedimentation rate was high (Table 1). Hepatitis B surface

After the angiography, the patient again developed chest pain, with elevated rising cardiac enzymes. Reevaluation of the angiogram showed a thromboembolic occlusion distally in one of the diagonal branches. A 2-dimensional (2-D) echocardiogram showed normal left ventricular function with no valvular disease. The patient was found to be hypothyroid and depressed, for which she was started on levothyroxine sodium and sertraline, respectively. She was subsequently discharged home on aspirin, metoprolol, and atorvastatin.

The patient returned 2 weeks later with chest pain. A repeat echocardiogram showed a small pericardial effusion. She was treated with high-dose ibuprofen for pericarditis and subsequently discharged home. The patient again returned a week later with shortness of breath, severe abdominal pain, and vomiting. She also complained of mild chest pain when lying flat. She was hemodynamically stable and had no pulsus paradoxus. On examination, she was in moderate respiratory distress, breathing at a rate of 40 and saturating 100% on room air. Her cardiac examination was remarkable for a friction rub at the lower left sternal

Table 1
Laboratory Values

	Values	Reference Values
Serum ANA	1:640 Speckled pattern	< 1:80
Pericardial fluid ANA	1:640 Cytoplasmic rim pattern	< 1:80
Pleural fluid ANA	1:640 Cytoplasmic rim pattern	< 1:80
Factor V mutation	Negative	Negative
Anti-ds-DNA Ab	680 U/mL	< 100
Anti-ribonucleoprotein Ab	1555 H U/mL	< 100
Anti-smith Ab	1597 U/mL	< 100
Cardiolipin IgG	13 H GPL U/mL	0-10
Cardiolipin IgM	7 MPL U/mL	0-9
ESR	119	0-20 mm/1st h
Protein C	78%	74%-151%
AT III	95%	75%-135%
Factor V	149	70%-120%
Rheumatoid factor	< 1:1	< 1:1
C3 complement	62	88-201 mg/dL
C4 complement	19	16-47 mg/dL
Albumin	2.6	3.5-5.2 g/dL
LDH	263	100-200 IU/L
BNP	130	0-100 pg/mL
PT	14.3	12.1-16.6
PTT	22.6	22.7-33.9
Homocysteine	13.6	5-15 Umol/L

ANA, antinuclear antibody; ds, double-stranded; Ab, antibody; Ig, immunoglobulin; ESR, erythrocyte sedimentation rate; AT, antithrombin; LDH, lactate dehydrogenase; BNP, B-type natriuretic peptide; PT, prothrombin time; PTT, partial thromboplastin time.

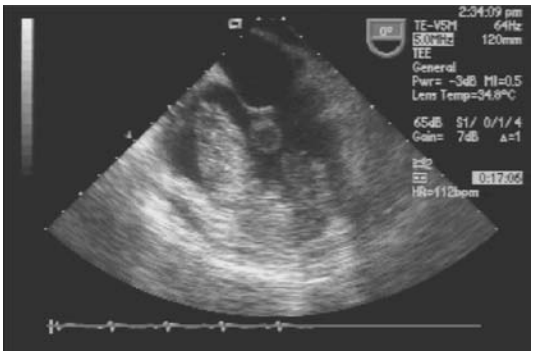

Figure 2. *Transesophageal echocardiography showing a large, smooth-edged mass (Libman-Sacks endocarditis) attached to the anterior mitral leaflet.*
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antigen was positive, and liver function tests were within normal ranges, except for a low serum albumin (Table 1). Urinalysis showed nephrotic range proteinuria (> 3 g/24 h). Transesophageal echocardiography (TEE) showed 2 smooth-edged masses measuring about 1 cm × 1 cm, each attached to the anterior and posterior mitral leaflets, respectively (Figure 2).

The patient was started on antibiotics after blood cultures were obtained, and she was given a presumptive diagnosis of infective endocarditis. She continued to remain afebrile. It was decided not to start her on steroids until an infectious etiology was ruled out. She was not anticoagulated for the valvular vegetations, out of concern that hemorrhage could develop within the pericardium. Pleurocentesis revealed an exudative fluid with negative Gram stain and cultures, and cytology showed reactive mesothelial and inflammatory cells with no malignant cells. An ECG showed low voltage with electrical alternans (Figure 3). Her antibiotics were stopped after blood cultures did not reveal any growth and evidence suggested a non-bacterial endocarditis.

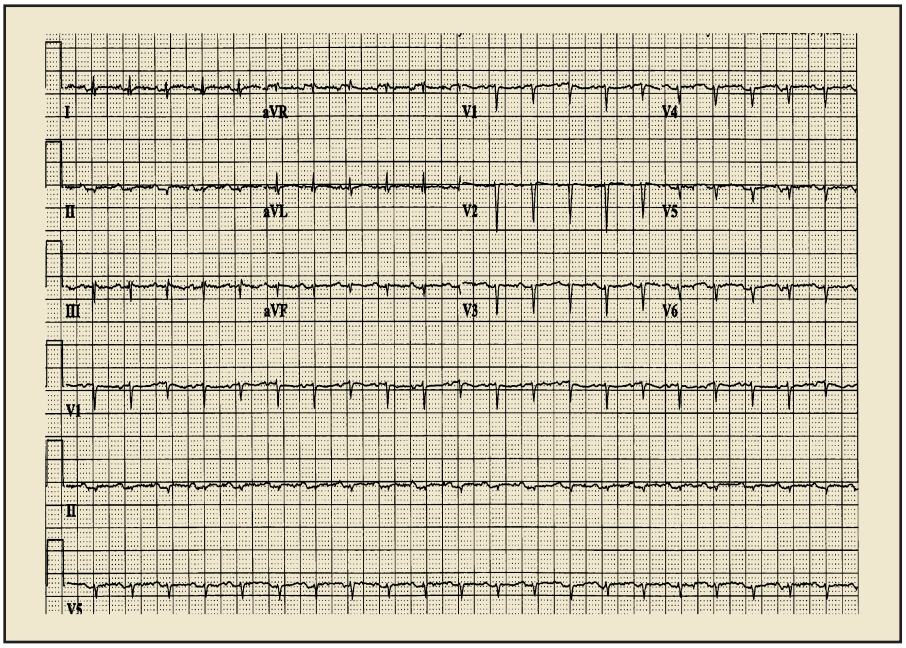
On day 5, the patient became hypotensive and tachycardic, with echocardiographic evidence of tamponade, and she underwent pericardiocentesis with removal of 900 mL of bloody, non-clotting pericardial fluid. Considering the high likelihood of a connective tissue disease, she was started on steroids on day 6. She continued to remain hypotensive and tachycardic, and a repeat TEE showed a moderate-sized pericardial effusion, mainly localized around the right atrium without signs of compression of the cardiac chambers or right ventricular diastolic collapse.

Because of her symptoms, she underwent a left anterior thoracotomy, which revealed a small pericardial fluid accumulation with adhesive pericarditis. A pericardial biopsy was performed, and 500 mL of pleural fluid was removed. Her hypercoagulability workup (protein C, antithrombin III, homocysteine, factor V mutation) was negative. The tests for serum anti-smith, anti–double-stranded DNA, and anti-ribonucleoprotein antibodies were positive (Table 1). Pleural and pericardial fluid antinuclear antibody tests were positive, with a cytoplasmic rim pattern. Pericardial biopsy showed inflammatory changes consistent with lupus pericarditis. The patient was discharged home in stable condition on steroids (prednisone 60 mg once daily). For follow-up, she was instructed to obtain a rheumatology consultation for management of her systemic lupus erythematosus (SLE) and to visit a renal clinic for an outpatient renal biopsy.

Discussion

Although cardiac manifestations such as pericardial, myocardial, and

Figure 3. *Low-voltage electrocardiogram with electrical alternans.* www.medreviews.com



valvular involvement are common in patients with SLE, acute myocardial infarction (AMI) as a consequence of embolization to the coronary arteries from verrucous endocarditis is rare. In SLE, the classic valvular abnormality consists of noninfective, verrucous vegetation that was first described by Libman and Sacks in 1924.[1] Thickening of the leaflets due to inflammation followed by fibrosis is common, occurring in about 50% of patients, whereas vegetations are present in about 40%. Mitral valve involvement is most common, with valvular regurgitation more frequent than valvular stenosis. Neither the presence of nor changes in valvular disease are temporally related to disease activity, therapy, or the duration of SLE. Although verrucous endocarditis most frequently involves the mitral valve, the tricuspid valve and the aortic valve may also be affected. Its frequency varies widely: 13% to 74% in the general population.[2-11] Verrucae are small in size (1 mm to 4 mm in diameter), and consist of accumulations of immune complexes, mononuclear cells, hematoxylin bodies, fibrin, and platelet thrombi that accumulate near the edge of the valve. Verrucous endocarditis is typically asymptomatic. However, verrucae can fragment and produce peripheral embolization, and, on rare occasions (as described in this case report), coronary embolization and AMI.

Although blood cultures are negative in verrucous endocarditis, infective endocarditis can develop on already damaged valves.[12] Therefore, blood cultures and echocardiography should be performed in a patient with SLE who develops fever and a new murmur. Infective endocarditis cannot be reliably distinguished from verrucous endocarditis on echocardiogram, so any new valvular vegetations should be treated as infective until proven otherwise. Antibiotic prophylaxis can be considered for patients undergoing procedures associated with a high risk of developing bacteremia, such as dental care. Clinical examination is minimally helpful in identifying valvular involvement in these patients. Still, cardiac auscultation should be performed at most visits, followed by echocardiography for the evaluation of significant or changing murmurs or changing cardiac function. The prevalence of significant valvular dysfunction in Libman-Sacks endocarditis is 3% to 4%, with 1% to 2% of patients requiring valve surgery. Corticosteroids and cytotoxic therapy have no effect upon the progression of valvular dysfunction. There are no published prospective, randomized, controlled treatment trials in patients with valvular disease or other thrombotic complications attributed to SLE.[13] On the basis of a large, retrospective, nonrandomized study, anticoagulation therapy with high-intensity warfarin (resulting in an international normalized ratio ≥ 3) is now recommended in patients with SLE with antiphospholipid antibodies who have a confirmed major thrombosis.[13,14] This therapeutic regimen will substantially reduce the high incidence of recurrent thrombotic events, estimated to be 69% without anticoagulant therapy. Low-dose aspirin (75 mg/d) alone resulted in a marginal benefit.

Blood cultures and echocardiography should be performed in a patient with systemic lupus erythematosus who develops fever and a new murmur.

An even more problematic area is the treatment of patients with isolated valvular masses but no evidence of systemic embolization. Should these patients be offered anticoagulant therapy? The benefit of anticoagulant therapy must be weighed against the associated bleeding complications. The embolic event rate in patients with SLE and valvular vegetations has not been clearly defined. In contrast, warfarin therapy resulting in an international normalized ratio of greater than or equal to 3 will cause hemorrhage in 1 of 14 patients per year, and serious hemorrhage in 1 of 50 patients per year.[13] Since the embolic event rate is unknown, the decision to use warfarin therapy in patients with valvular vegetations but with no evidence of systemic embolization needs to be individualized, with careful attention to the risk-benefit ratio.

The relationship between antiphospholipid antibodies and coronary artery disease is controversial. Suggestive evidence implies that patients without clinical documentation of SLE but with antiphospholipid antibodies are at increased risk of cardiovascular disease. Even if an association does exist between antiphospholipid antibodies and coronary artery disease, whether the antiphospholipid antibodies are causative or form as an immune response to myocardial ischemia or necrosis is unclear.[15] To address this issue, Vaarala and colleagues[16] used a nested case-control design in the Helsinki Heart Study and found that anticardiolipin antibody levels were an independent predictor of coronary artery disease.

AMI in patients with SLE should, in general, be evaluated and treated as it is in patients without lupus. The role of primary percutaneous coronary intervention or fibrinolytic therapy in patients with AMI and

Libman-Sacks endocarditis is not well established. Because thrombotic occlusions due to peripheral embolization from Libman-Sacks endocarditis generally involve small distal coronary vessels, these patients may often not be suitable for primary percutaneous coronary intervention. Antiplatelet therapy with aspirin should be prescribed and the steroid dose should be reduced. Aggressive management of risk factors, including diabetes mellitus, hypertension, hyperlipidemia, smoking, and obesity, should be undertaken. ■

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Main Points

- Infective endocarditis cannot be reliably distinguished from verrucous endocarditis on echocardiogram, so any new valvular vegetations should be treated as infective until proven otherwise.
- Neither the presence of nor changes in valvular disease are temporally related to disease activity, therapy, or the duration of systemic lupus erythematosus (SLE).
- Antibiotic prophylaxis can be considered for patients undergoing procedures associated with a high risk of developing bacteremia, such as dental care.
- Cardiac auscultation should be performed at most visits, followed by echocardiography for the evaluation of significant or changing murmurs or changing cardiac function.
- Corticosteroids and cytotoxic therapy have no effect upon the progression of valvular dysfunction.
- Acute myocardial infarction in patients with SLE should, in general, be evaluated and treated as it is in patients without lupus.