Title

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CLINICAL VIGNETTE

Libman-Sacks Endocarditis in a Young Woman

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Case Presentation

A 21-year-old-woman with history of systemic lupus erythematosus, class III lupus nephritis, and chronic normocytic anemia presented to the emergency department for 5 days of lower extremity edema , dyspnea and pleuritic chest pain. The patient's home medications included hydroxychloroquine, mycophenolate, ferrous sulfate, prednisone, pantroprazole, ondansetron, calcium carbonate, and cholecalciferol. Initial physical exam was notable for 2+ bilateral lower extremity edema and a fine blanching rash on her bilateral forearms. No murmur or crackles were appreciated. Initial laboratory studies were remarkable for hemoglobin 6.8 g/dL, hematocrit 22.1%, B-type natriuretic peptide 171 pg/dL, 2+ protein and 2+ blood on urinalysis. Creatinine was normal at 0.46 mg/dL. Chest x-ray demonstrated a trace right pleural effusion and right atelectasis. Ultrasound of bilateral lower extremities was negative for thrombosis. Of note, patient had a prior borderline positive diluted Russell viper venom time (DRVVT) in 2015, which had not been repeated to date.

Transthoracic echo was performed to evaluate etiology of lower extremity edema, which demonstrated mitral valve thickening and moderate mitral valve regurgitation. Transesophageal echo demonstrated a 0.6 x 0.6cm vegetation on the posterior leaflet of the mitral valve, thickening of the posterior leaflet, and moderate to severe mitral regurgitation. These findings were highly suspicious for Libman-Sacks endocarditis. Blood cultures were negative, ruling out infective endocarditis. DRVVT, cardiolipin antibody, and beta-2-glycoprotein labs were sent to evaluate for antiphospholipid syndrome and returned negative. Patient was started on heparin gtt following a negative CT head and transitioned to enoxaparin upon discharge.

Discussion

Libman-Sacks endocarditis is a rare and interesting diagnosis. It is a form of nonbacterial thrombotic endocarditis (NBTE) that occurs specifically in individuals with underlying autoimmune diseases, connective tissue diseases, or hypercoagulable states. Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APLS) are the most common of these underlying conditions. The clinical presentation and diagnosis of NBTE are the same regardless of the underlying disease, so this discussion will focus on NBTE in general.

NBTE occurs as a result of endothelial damage followed by deposition of fibrin and platelets that form a vegetation.[1,2] Vegetations can form on any endocardial surface, but the most common sites are on the surfaces of undamaged valves. The left-sided valves (aortic and mitral) are affected more frequently than the right-sided valves.[3]

Before modern echocardiography, the disease was rarely diagnosed before death. Thus, the true prevalence of NBTE is difficult to ascertain because most data are based upon post-mortem examinations. More recent studies based on echocardiography findings may be more accurate. In a series of studies by Reisner et al, 32% of patients with primary antiphospholipid syndrome, 63% of those with myeloproliferative disorders, and 19% of those with solid malignant tumors were found to have NBTE.[4]

Typically, patients with NBTE are asymptomatic, and thus the disease goes undetected until a complication occurs. Complications of NBTE include valvular dysfunction (most commonly regurgitation) and systemic embolization.[4] Initial presentation as a result of valvular dysfunction, however, is uncommon.

Interestingly, the vegetations in NBTE are more vulnerable to embolization than those in infective endocarditis, perhaps because of the lack of an inflammatory reaction at the vegetation site.[3] In fact, systemic embolization occurs in almost 50 percent of cases of NBTE and can have devastating consequences.[5] Frequent sites of embolization include the brain, spleen, kidney, mesenteric vasculature, and the lower extremities.[1] Patients most commonly present with a new neurological deficit as a result of a cardioembolic stroke. In one study, 87% of SLE patients with cerebrovascular disease were found to have NBTE.[6] Thus, NBTE should be strongly considered in a patient with SLE presenting with neurological deficits.

If NBTE is suspected, diagnostic evaluation should include blood cultures to distinguish NBTE from infectious endocarditis. Disseminated intravascular coagulation (DIC) should also be ruled out as a potentially life-threatening etiology. Unfortunately, there is no laboratory testing specific to NBTE. Instead, laboratory evaluation is aimed at searching for an underlying condition, such as an autoimmune disease or hypercoagulable state, that may increase the patient's risk for NBTE. Since cancer is the most common cause of NBTE, age-appropriate cancer screening should be pursued. Further testing should include anti-nuclear antibody, lupus anticoagulant, and antiphospho-

lipid antibodies (anti-cardiolipin and beta2-glycoprotein I antibodies). Diagnostic imaging should begin with a transthoracic echocardiogram (TTE). If negative, but suspicion remains high, a transesophageal echocardiogram (TEE) should be obtained for further evaluation. TEE has been shown to be a more sensitive test for detecting valvular vegetations, particularly those < 5 mm in diameter.[7,8]

Lifelong anticoagulation and treatment of the underlying disease are the mainstays of therapy. Therapeutic dose low-molecular-weight heparin (LMWH) should be prescribed over warfarin or a direct oral anticoagulant, as previous studies have suggested that warfarin is less effective in preventing recurrent thromboembolism.[3,5] Surgical intervention is rarely pursued but is sometimes considered in patients with recurrent embolic strokes.

In this case, a young female patient with SLE presented with shortness of breath and lower extremity edema as a result of moderate mitral regurgitation, an uncommon initial presentation of NBTE. Our patient was retested for antiphospholipid syndrome, as she had had a borderline DRVVT in the past, which was negative. This case therefore highlights the importance of considering NBTE particularly in patients with SLE or APLS who present with symptoms suggestive of heart failure.

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