CLINICAL VIGNETTE

A Patient with Q Fever Endocarditis Versus Libman Sacks Endocarditis

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Case Report

A 51-year-old female presented to the emergency room with 2 weeks of worsening shortness of breath, like she was "suffocating". She reported exertional dyspnea, paroxysmal nocturnal dyspnea, and orthopnea. She denied fevers, chills, night sweats, chest pain, lower extremity edema, palpitations, presyncope, or syncope.

Her past medical history was significant for diabetes, lupus and chronic obstructive pulmonary disease. She reported pericarditis with mild to moderate pericardial effusion two years prior. The patient's outpatient medications included insulin, metformin/sitagliptin, aspirin, atorvastatin, and ranitidine. She used tobacco and smoked crack cocaine but denied intravenous drug use. She denied recent travel outside of Los Angeles but did report extensive contact with homeless people. Family history was negative for premature coronary disease or sudden cardiac death.

On presentation the blood pressure was 121/50, heart rate of 113, respiratory rate of 24, with oxygen saturation of 98% on room air. Her physical exam was significant for poor dentition with several missing teeth, patchy alopecia, mildly elevated jugular venous pressure and multiple murmurs. She had a 2-4/6 diastolic murmur at the left upper sternal border, ⅛ systolic murmur at the left upper sternal border and a 2/6 holosystolic murmur at the apex with radiation to the axilla. She had hepatomegaly, but no lower extremity edema. Splinter hemorrhages were noted scattered throughout her digits, primarily on the left hand.

Labs included negative troponins, a white blood cell count of 8.4, hemoglobin 9.2, hematocrit 29.6, platelet count 523, ESR of 68, CRP 2.5, an unremarkable chemistry panel, and an elevated BNP of 670. She had a normal c3and c4, ANA >1:1280, anti ds DNA EIA 335, negative B2 Glycoprotein ab, low titer cardiolipin IgM antibodies and borderline DRVVT.

EKG showed sinus tachycardia at a rate of 109.

Echocardiogram demonstrated normal left ventricular size, borderline septal-left ventricular hypertrophy, normal LV ejection fraction of 60% to 65%, moderate thickening and calcification of the mitral anterior and posterior leaflets, and a mobile mass on the anterior mitral valve leaflet. There was severe mitral regurgitation, severe aortic regurgitation, mild aortic stenosis, mild to moderate tricuspid regurgitation, moderate pulmonary hypertension with PA pressure of 55 to 60 mmHg, and a moderately dilated left atrium. There was no evidence of pericardial effusion on this study.

Transesophageal echocardiogram showed valvular vegetation involving both mitral leaflets with severe mitral regurgitation, and moderate-to-severe aortic regurgitation.

She underwent right and left heart cardiac catheterization which showed no significant coronary artery disease, 4+ aortic insufficiency, pulmonary hypertension (PA pressure 67/27), and elevated wedge pressure of 25 mmHg.

Abdominal CT showed moderate to severe hepatomegaly.

Blood cultures were negative. Bartonella serologies were negative. The patient had markedly positive IgG antibodies (Phase I IgG 1:4096, Phase II IgG 1:2048) for Coxiella burnetii, the causative agent of Q fever. Infectious Diseases felt this could also be due to cross-reactivity to SLE associated antibodies, however, recommended treatment with doxycycline and hydroxychloroquine.

The final diagnosis was to be made at the time of valve replacement with pathological assessment of valves with differential being Q-fever endocarditis versus Libman-Sacks endocarditis.

However, our patient refused surgery and therefore definitive diagnosis at this time in unknown.

Diagnostic criteria for infective endocarditis

The most commonly accepted criteria are the Duke criteria. Diagnosis requires 2 major criteria OR 1 major and 3 minor criteria OR 5 minor criteria [1].

Major criteria include:

- Positive blood cultures for IE
    - Typical microorganism for infective endocarditis from two separate blood cultures
    - Persistently positive blood culture
    - Single positive blood culture for Coxiella burnetii or antiphase I IgG antibody titer >1:800
- Evidence of endocardial involvement
    - Positive echocardiogram for IE
    - New valvular regurgitation

Minor criteria include:

- Predisposition with predisposing heart condition or intravenous drug use
- Fever - 38.0°C (100.4°F)
- "Vascular phenomenon" such as emboli to organs or the brain, hemorrhages in the mucous membranes around the eyes
- Immunologic phenomena - glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
- Positive blood cultures that do not meet the strict definitions of a major criterion.

Q Fever Endocarditis

Q fever is a ricketsial disease caused by Coxiella burnetii and is a zoonosis that can present as an acute or chronic illness. Endocarditis is the most serious form of chronic Q fever, with a mortality rate of up to 24% in one study[2]. Risk factors include previous valvular disease or immunocompromise[3,4]. It is more common in men over the age of 40 and exposure to cattle is frequently found[5].

Presenting symptoms of Q fever endocarditis include heart failure, valve dysfunction, or constitutional symptoms such as fever, chills, fatigue, weight loss, anorexia, and night sweats. Fever is usually low-grade and is only present in two-thirds of cases at the beginning of the disease. Peripheral manifestations include splenomegaly, hepatomegaly, digital

clubbing, purpuric rash, microscopic hematuria, and embolic manifestations, including embolic stroke [5,6].

Laboratory findings include non-specific results such as elevated erythrocyte sedimentation rate in almost all patients, and anemia, thrombocytopenia, and hematuria in about 50 percent of patients with Q fever endocarditis[5] Rheumatoid factor can also be present, but it was not elevated in our patient.

Q fever is diagnosed definitively with antibody testing to phase-I and phase-II antigens. Titers of >200 for IgG and >50 for IgM against phase II suggests a recent Q-fever infection. An IgG titer > 800 against phase 1 suggests chronic infection[7].

Libman-Sacks Endocarditis

Libman-Sacks Endocarditis refers to sterile large verrucous valvular lesions composed of immune complexes, mononuclear cells, fibrin-platelet thrombi[8,9]. These valvular lesions can be seen in patients with systemic lupus erythematosus (SLE) and patients with high titer antiphospholipid antibodies (aPL). There is a stronger association between verrucous endocarditis in SLE patients who have aPL compared with those who do not have aPL[8,10,11]. The manifestation of verrucous endocarditis in SLE is not associated with disease activity as compared with other SLE systemic manifestations[8,10].

The diagnosis of Libman-Sacks endocarditis can be particularly challenging. In the majority of cases Libman-Sacks endocarditis is asymptomatic, however, complications such as valvular insufficiency, systemic emboli and secondary infective endocarditis can occur leading to significant morbidity. Serial negative cultures, low to normal white blood cell count and high aPL titers have been found to be helpful in distinguishing Libman-Sacks from infective endocarditis[8].

Echocardiography and especially TEE is the most widely used imaging modality for evaluation of vegetative endocarditis[8,11,12]. Unfortunately, it is difficult to distinguish infective endocarditis from sterile verrucous endocarditis and their possible coexistence further complicates this. Libman-Sacks lesions appear more smooth and gelatinous and usually involve left sided valves and most commonly are found on the posterior leaflet of the mitral valve[11].

However, they can potentially involve any of the four valves in addition to the chordae tendinae and papillary muscles[8].

The most definitive diagnosis is made via histopathological evaluation of the lesions confirming the presence of fibrin-platelet thrombi, hematoxylin bodies, mononuclear cell infiltrate and the lack of polymorphonuclear leukocyte cell infiltrate[8]. Immunoglobulins and complement can be seen by immunofluorescence. This unfortunately could not be done in our patient as she refused surgery for valvular repair or replacement.

Definitive treatment of Libman-Sacks endocarditis usually requires valve replacement and or repair. Immunosuppressive therapy including gluco-corticoids has not shown benefit in the treatment of Libman-Sacks valvular endocarditis. Anticoagulation may be indicated in patients with thromboembolic disease and in patients with aPL associated disease (which was not the case with our patient). No significant evidence supports anticoagulation in patients without systemic thromboembolic disease. Prophylactic antibiotics can be considered in patients with valvular damage especially in setting of immune suppression in SLE patients though no studies have supported this and AHA guidelines for antimicrobial prophylaxis do not include native valvular damage as part of the high-risk population requiring propohylaxis antibiotics prior to procedures.

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