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Case Report

Aortic valve surgery for aortic regurgitation caused by Libman-Sacks endocarditis in a patient with primary antiphospholipid syndrome: a case report

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ABSTRACT

Antiphospholipid syndrome is an antibody mediated pro-thrombotic state leading to various arterial and venous thromboses. The syndrome can be either primary or secondary to other autoimmune diseases. Cardiac involvement, in particular valvular disease is common in patients with antiphospholipid syndrome (APS) but it is frequently underestimated as most clinicians do not routinely screen for valvular lesion in patients with APS unless they are symptomatic. Valvular disease associated with antiphospholipid syndrome often occurs as valve thickening and non-bacterial vegetation or Libman-Sacks endocarditis, with a higher propensity towards mitral valve although haemodynamically significant valvular dysfunction is rare. Valve surgery in patients with APS carries considerable early and late morbidity and mortality, usually caused by thromboembolic and bleeding events. The perioperative anticoagulation management and haemostatic aspect of APS present exceptional challenges to clinicians, surgeons, anaesthetists and laboratory personnel. Thus, the indication of valve surgery and the choice of valve remains a critical consideration in these patients. We present a successful isolated aortic valve replacement with cardiopulmonary bypass in a 48 year old lady with newly diagnosed antiphospholipid syndrome, who has severe aortic regurgitation as a result of Libman-Sacks endocarditis. Antiphospholipid antibodies were positive and the clinical data showed both negative cultures and infective parameters. Surgically resected vegetations revealed sterile fibrin fibrinous and verrucous vegetations on aortic valve. Valve replacement and the course of cardiopulmonary bypass were uneventful, and patient was discharged well.

Keywords: Antiphospholipid syndrome, Libman-Sacks endocarditis, Cardiac manifestations, Aortic regurgitation, Valve replacement surgery

INTRODUCTION

Antiphospholipid syndrome (APS) is a rare coagulative disorder with antiphospholipid antibody mediated pro-thrombotic state mainly characterised by hypercoagulable complications. Cardiac manifestations of APS include arterial or venous thromboses, valve disease, coronary artery disease, intracardiac thrombus, pulmonary hypertension and dilated cardiomyopathy. Valvular manifestation in APS is commonly associated with Libman-Sacks endocarditis.[1] Libman-Sacks endocarditis, also known as non-bacterial thrombotic, originally described in patients with systemic lupus erythematosus, is a well-known complication of antiphospholipid syndrome.[1,2] We present a successful aortic valve replacement for severe aortic regurgitation due to Libman-Sacks endocarditis in a 48 year old lady with newly diagnosed APS.

CASE REPORT

A 42 year old lady was admitted to cardiology ward complaining of worsening breathlessness, orthopnea and chest discomfort for one month. Coexisting medical conditions include chronic hypertension on treatment with 2 previous episodes of spontaneous miscarriages and 1 episode of transient ischemic attack few years ago.

Clinically, she was hemodynamically stable with a wide pulse pressure. Finger clubbing was noted with livedo reticularis rashes over bilateral upper and lower limbs without ulcers or thrombophlebitis. Her peripheral pulses were bounding with water-hammered pulse, with a grade-III diastolic murmur heard during cardiac auscultation. In addition, she has elevated jugular venous pressure, crepitation over both lung bases and bilateral pedal oedema.

Echocardiography showed a dilated left atrium and left ventricles. Severe aortic regurgitation (AR) was found with PHT of 156 ms, mean pressure gradient of 32 mmHg, and end diastolic velocity of 29 cm/s. In addition, a vegetation sized 1.2 cm^2 was seen on aortic valve. Mild mitral regurgitation (MR) was also noted with thickened anterior leaflet with mitral regurgitant ERO of 0.12 cm^2 and mitral regurgitant volume of 20 ml. There was minimal pericardial effusion seen but no intracardiac thrombus. Coronary angiography was subsequently done which showed minor disease.

Blood investigation revealed bicytopenic picture of anaemia and thrombocytopenia with elevated activated partial thromboplastin time (aPTT) of 54 s and erythrocyte sedimentation rate (ESR). Otherwise, the reports were not suggestive of infection with normal white cell count and C-reactive protein (CRP), and negative blood cultures. Further hematological investigations revealed positive antinuclear antibody (1:640), Lupus anti-coagulant (LA), anti-smith antibodies and Coombs' test. Subsequent bone marrow aspiration test and cytogenetic studies showed a grossly normal specimen. Anti-phospholipid syndrome was thus diagnosed, and therapeutic enoxaparin therapy was initiated perioperatively.

She underwent aortic valve replacement, and intraoperative exposure of aortic valve revealed verrucous thickening of aortic leafelts with vegetations involving all three cusps, with rolled edge on left coronary cusp. No perforation or destruction of cusp tissue was identified. Following excision of leaflets, a mechanical valve was implanted. The course of cardiopulmonary bypass was uneventful.

Postoperatively, oral anticoagulation therapy was started with international normalized ratio (INR) target of 2.5 to 3.5 and subcutaneous enoxaparin as bridging therapy. There was no excessive bleeding or major thromboembolic complications occurred during in-patient stay. She was well and free of complications at 6 months and one year follow-up. Clinical examinations and echocardiography demonstrated satisfactory aortic valve function. The microbiological culture of the excised vegetations revealed sterile specimens.

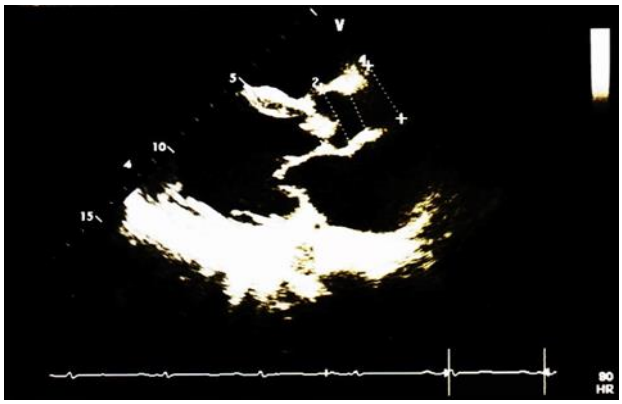

Figure 1: Transthoracic echocardiography shows thickened aortic valve with vegetations attached to aortic cusps.

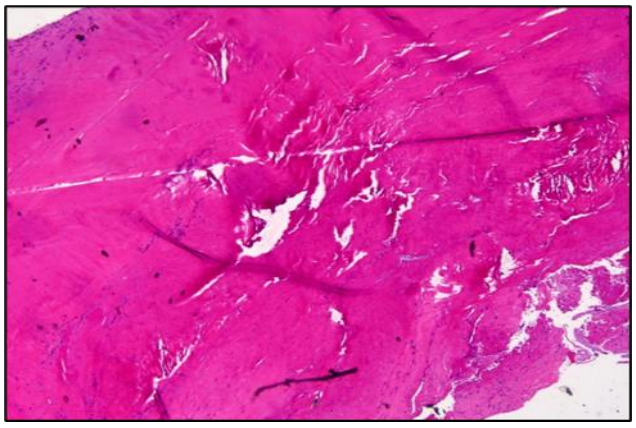

Figure 2: Eosinophilic amorphous material composed of fibrin and platelet thrombi attached to the valve as vegetation; there is no bacterial colonies or fungal organisms identified (hematoxylin and eosin, 20X).

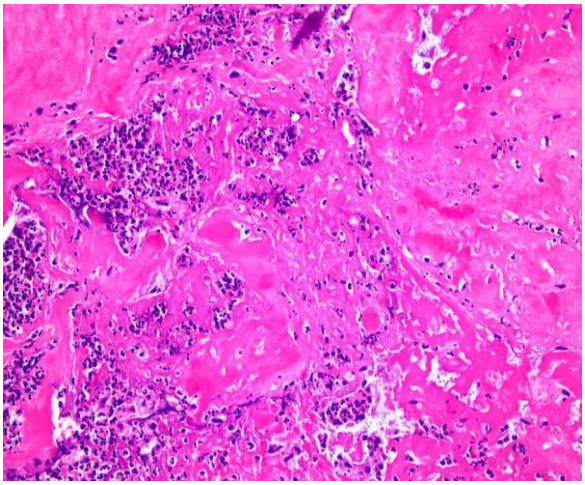

Figure 3: Neutrophils and nuclear remnants are seen focally (hematoxylin and eosin, 40X).

DISCUSSION

APS is a multi-system disorder of autoimmune aetiology. This syndrome is defined clinically by recurrent arterial and venous thrombotic events as well as recurrent pregnancy loss, with serologically positive testing of antiphospholipid antibodies including lupus anticoagulant (LA) and anticardiolipin antibodies (aCL). Clinically, the index of suspicion for APS should be raised if activated partial thromboplastin time is raised, with positive corresponding serum antibody markers. APS comprises a wide array of clinical features such as venous and arterial thromboses, recurrent pregnancy loss and even thrombocytopenia. Heart valve disease is a common cardiac manifestation in patients with APS, and it is defined in the absence of rheumatic and infective endocarditis. It was reported as high as 32-38% prevalence of valvular lesion occur in patients with APS by transthoracic echocardiography.[1,2] When transo-esophageal echocardiography is used, the incidence may increase to 75%.[3] Patients with APS often suffer from valvular heart disease which is defined by its morphological pattern of valvular thickening and valvular vegetation, also known as Libman-Sacks endocarditis.[1] Libman-Sacks endocarditis has a predilection for mitral valve disease, followed by aortic valve although mitral valve is relatively spared in this case. The predominant functional abnormalities ranging from valvular thickening to valvular regurgitation, but stenosis is rarely seen. In this case, the negative infective parameters and cultures with the finding of sterile fibrin fibrinous and verrucous vegetations confirm the diagnosis of Libman-Sacks endocarditis.

The role of antiphospholipid antibodies in the pathogenesis of Libman-Sacks endocarditis remained unclear, probably the result of autoimmune antibodies being directed against the negatively charged phospholipids on the endothelial membranes, or induc-tion of autoantibodies by molecular mimicry caused by infectious agents, leading to subendocardial inflammation and subsequent thrombosis and fibrosis.[4] Grossly, Libman-Sacks valvular lesions are typically small sessile and wart-like growth which forms a fibrous plaque with focal calcification. This process is accompanied by marked scarring and fibrosis, which organize and coalesce leading to thickening and distortion of the valve, and subsequent valvular dysfunction, findings which are evident in this case study.[5]

Patients with APS often first presented with thromboembolic events from other systems rather than cardiac manifestation, most commonly cerebrovascular ischemic events, which is apparent in this case where patient had transient ischemic attack years ago. These thromboembolic episodes might be due to direct effect of antiphospholipid antibodies or intermittent dislodgement of Libman-Sacks vegetations. Majority of valvular impairment associated with Libman-Sacks endocarditis is mild with minor haemodynamic disturbance without clinically overt significance, and only 4-6% of APS patients with heart valve disease develop severe valvular dysfunction that requires surgical intervention.[6]

Diagnosing Libman-Sacks endocarditis often necessitate exclusion of rheumatic valve disease and infective endocarditis. However, it must be remembered that this valve lesion can also predispose to infective endocarditis. Unlike infective endocarditis where the valve needs to be completely excised to remove infected tissue, repair and preservation of the valve is possible in selected patients with Libman-Sacks endocarditis although there is only limited data comparing valve repair and replacement. The indications for surgery remain dispute, and the outcomes of surgical valvular replacement have been limited to case reports or series, however, we agreed on the clear indications for surgical intervention, which include severe valvular dysfunction, large vegetations and recurrent embolization despite therapeutic systemic anticoagulation. Furthermore, non-bacterial thrombotic endocarditis may have much greater risk for vegetation embolization than infective endocarditis.[7] To date, there are still conflicting data regarding the most suitable types of valve used for surgical replacement. The selection of mechanical valve in this case was based on the existing unavoidable requirement for lifelong anticoagulation therapy. A mechanical valve may be theoretically more advantageous over a tissue valve considering the younger age of patients at the time of surgery and the need for lifelong anticoagulation. However, the use of tissue valve has increased progressively over the years to allow for easier and safer management of anticoagulation therapy, compounded by the complex monitoring of anti-coagulation due to presence of antibodies, and the possible coexisting thrombocytopenia.[8] Further studies need to be done to study the outcomes of both types of valve, and if tissue valve is used, the possible immunological deterioration of the valve.

Perioperative management of APS patients undergoing cardiac surgery with cardiopulmonary bypass is a major concern and remains challenging due to the significant risk of thrombosis with the cessation of anticoagulation therapy, as well as bleeding secondary to excessive anticoagulation intraoperatively or coagulation factor deficiency. Preoperatively, these patients may already be on anticoagulation therapy, and discontinuation of such anticoagulation therapy perioperatively exposes them to the risk of thrombolic and vaso-occlusive complications. Furthermore, the stress associated with surgery, systemic inflammatory response syndrome (SIRS) and sepsis, or a minor alteration in anticoagulation regime can trigger catastrophic APS, which in term can cause thrombotic occlusion in multiple organs resulting in mortality as high as 50%.[9,10] In our patient, enoxaparin was used instead of unfractionated heparin to avoid the associated complication of heparin-induced-thrombocytopenia, and therapeutic dose of enoxaparin was started preoperatively prior to surgery and continued postoperatively as bridging

therapy to reduce the risk of thromboembolic event while minimizing hemorrhagic complication.

CONCLUSION

Libman-Sacks endocarditis is common but often underestimated in patients with APS, and it can affect isolated aortic valve causing significant valvular dysfunction. Earlier diagnosis allows for prompt initiation of therapeutic anticoagulation to prevent further thromboembolic complications. Surgical replacement of the affected valve is indicated especially in patients with severe valvular dysfunction or systemic embolization, with mechanical valve being the valve of choice in view of the lifelong anticoagulation therapy requirement. It is hoped that this case report will increase awareness of Libman-Sacks endocarditis as a cause of valvular heart disease in patients with APS, as perioperative management of these patients remains challenging.

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