

RIGHT ATRIAL THROMBUS, AORTIC REGURGITATION, CORONARY ARTERY STENOSIS, AND CHYLOUS PLURAL EFFUSION IN ANTI PHOSPHOLIPIDSYNDROME: A CASE REPORT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

The anti phospholipids syndrome (APS) is a complex autoimmune disease that manifested by arterial and venous thrombosis, repeated abortion, and presence of antiphospholipid antibodies. History of miscarriage, aortic regurgitation, right atrial thrombosis, coronary artery disease, and post-operative chylous plural effusion is an exceedingly rare combination in systemic lupus erythematosus (SLE) patients. We describe a case report of a 35-year-old woman, admitted with a 10-year history of SLE with dyspnea, and typical chest pain. The patient had history of arthralgia, fatigue, and intermittent fever that treated by corticosteroids for the past three years. Subsequent transthoracic echocardiography (TTE) revealed the presence of a large mass in the right atrium that did not attach to tricuspid apparatus. TTE also revealed severe aortic regurgitation. Screening laboratory evaluation for thrombophilia confirmed the diagnosis of secondary APS. The coronary angiography showed, severe three-vessel stenosis. Cardiac surgery with combined coronary artery bypass grafting, aortic valve replacement and right atrial clot resection were performed. The post-operative course was complicated with an exceptional complication of chylothorax which responded to a short period of corticosteroid therapy. Histological examination of clot demonstrated it to be composed entirely of fresh thrombus.

Key words: Antiphospholipid syndrome, Lupus erythematosus, complication.

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Introduction

Antiphospholipid syndrome (APS) is an autoimmune disorder. About 50% of the patients with Systemic Lupus Erythematosus (SLE) have APS. Primary APS is a thrombophilic state associated with wide range of events such as venous or arterial thrombosis, recurrent miscarriage, thrombocytopenia, mitral or aortic valve dysfunction, intra cardiac thrombosis, and increased level of antiphospholipid antibodies^(1,2,3).

Secondary APS is defined when it occurs in the presence of predisposed condition such as known autoimmune disease (e.g. SLE), infection, and tumor or in drug-induced temporary APS. The range of clinical manifestations occurred in secondary APS is, however, much wider and more diverse, including neurologic involvement, gynecologic complications, cardiac-valvular heart disease, and skin involvement. Increased levels of antibody are common in viral and bacterial infections, trauma and chemotherapy or malignancy but are not certainly associated with this syndrome^(4,5,6). Three important sequels of APS in SLE are discussed in following paragraphs. These include, structural valvular deformity, thrombosis in coronary artery and cardiac chambers, and atherosclerosis.

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Case report

A 35-year-old woman with a known case of SLE and history of repeated abortion, acute dyspnea, atypical chest pain, constitutional signs and symptoms of arthralgia, fatigue, and skin changes, since eight months ago was admitted. In exam, her blood pressure was 100/78 mm/Hg, heart rate was

89/min, body temperature was 37°C, and respiratory rate was 21 breaths per minute. A physical examination also showed no evidence of skinormucosalpallor, and normal body mass index. There was no evidence of lip or finger tips cyanosis, finger clubbing, lower extremity pitting oedema, typical skin rash of SLE or joints malformation. Abdominal examwas-normal and no hepatosplenomegaly was detected. The cardiovascular and neurological examinations were normal with no remarkable signs and symptoms. The chest X-ray was normal. Human immunodeficiency virus, HBS, HCVHBS and tuberculin skin tests were negative. Initial laboratory finding including, anemia (hemoglobin, 10.5 g/dl), leucocytosis (17000 / μ l), high serum blood urea nitrogen (65 g/dl) and high serum creatinine (2.5g/dl). Transthoracic echocardiograms (TTE) was performed and showed a large thrombosis in the right atrium and severe aortic regurgitation (Figure 1) Angiography also revealed severe coronary artery disease (CAD).



Figure 1: TTE image showing a large clot in right atrium.

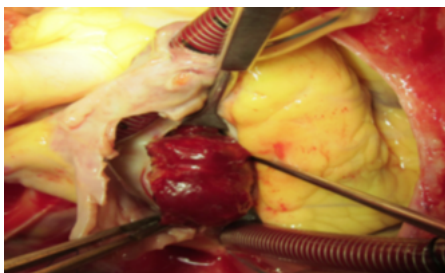


Figure 2: Intra operative view of right atrial clot.

Further laboratory evaluation (doctor Sammie laboratory) for thrombophilia states confirmed the diagnosis of secondary SLE with raised titers of antiphospholipidIgG antibodies of 26 u/ml (positive > 18), lupus anticoagulant 53 (negative, 31-34 second), antinuclear antibodies IgG 3(negative <1.5) and anti-double-stranded DNA antibodies of 43 (positive> 25). Urine analysis revealed evidence of cell cast and proteinuria.

Sedimentation rate and C - reactive protein were also raised. Cardiac surgery was performed with complete removal of right atrial clot and aortic valve replacement with carbomedic number 21 sorinegroup (Figure 2).

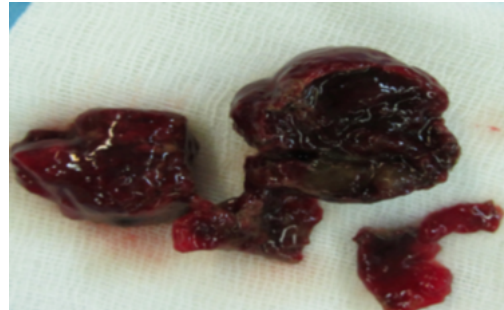


Figure 3: Gross view of resected thrombus.

The gross and histopathology of clot were exhibited in Figure 3 and 4. The histology of clot revealed degenerated fibrin, with focal chronic inflammation in periphery of tissue (Figure 4).

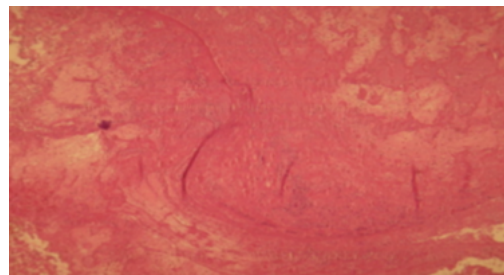


Figure 4: Histopathology view of degenerated fibrin with focal chronic inflammation in periphery of tissue.

The gross pathology of respected aortic valve showed verrucose nodules in rim of aortic valve leaflets or verrucose endocarditic thatnegative bacterial culture of leaflets confirmed its nature (Figure 5).

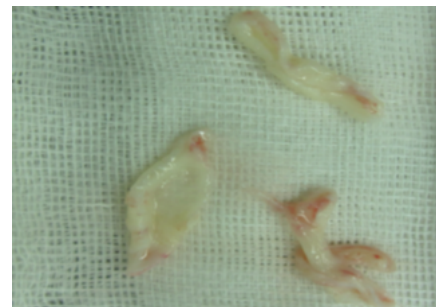


Figure 5: The gross pathology of resected aortic valve showed verucose small nodule in edge of resected aortic valve leaflets.

The aortic wall has been thickened and had fibrotic consistency in intra operative view (Figure 6).

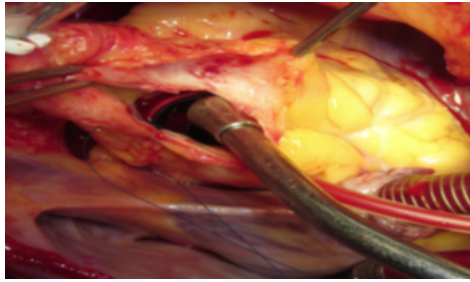


Figure 6: Thickness and inflammation of aortic wall in aortotomy site near aorto-pulmonary groove.

The coronary artery bypass grafting (left anterior descending, left circumflex and right coronary artery) was performed using saphenous vein graft (left internal mammary artery was damaged during harvesting). The post-operative course was complicated by daily voluminous drainage of 800 ml of chyle bilaterally. Analysis of plural fluids revealed its chylous nature (high triglyceride content of 260 mg/dl). Chylothorax treated with limitation of lipid intake, high protein diet and short course of corticosteroid. The chylous drainage was completely recovered in 13th day of operation. The chylothorax is an exceedingly rare post coronary artery bypass event in lupus cases that their internal mammary artery was not harvested. We think that this exceptional complication related to SLE-induced inflammation of lymph ducts that exacerbated by trauma of surgery and with increasing their intraluminal pressure led to chylothorax. Long-term oral anticoagulation with corticosteroid was initiated and echocardiographic follow-up showed no recurrence of right atrial thrombosis or plural effusion.

Discussion

Endothelial cell activation and accelerated atheroma formation has become recognized as a feature of APS. The formation of atheroma is considered as an inflammatory process in the arterial wall, involving the accumulation of macrophages and activation of T-lymphocytes. Atherogenesis begins with endothelial cell activation (ECA). Viral or bacterial infection caused formation of immune complex integrated to low density lipoproteins (LDL). This complex probably has a major role in endothelial cell activation in atherogenesis and become especially effective when its LDL component is oxidized. This complex penetrates to arterial wall and by the trapping of monocytes in the endothelial wall subsequently transformed them to macrophages. These macrophages expose specific receptors which by increasing uptake of oxidized LDL into the cell,

results in foam cell formation^(7,8). Activation of inflammatory results in the release of a cascade of cytokines, and growth factors with subsequent smooth muscle wall proliferation and plaque formation and leading to vessel occlusion and local ischemia and CAD.

Another aspect of this syndrome related to valvar involvement as observed in our patient. A specific noninfectious, inflammatory endocarditis of the heart valves usually limited on the mitral or aortic valves is known in patients with SLE as in our patient. This endocarditis named as verrucous endocarditis. The overlying endocardium, particularly on mitral or aortic valve leaflet, is vulnerable to injuries by shear stress, jet effect and flow turbulence. Micro injuries expose phospholipids on superficial valve structures or on endothelial cells of intravalvular-capillaries, and subsequent binding, of auto antibodies to the phospholipids -antigen complexes causing a endocardial cell activation and microscopic spots of thrombosis⁽⁹⁾.

These micro clots by natural healing mechanism switching into fibrotic tissue on valve. The gross fibrotic valve changes includes, severe thickening and inflammatory commissural adhesion and resulting in valve stenosis. Sometimes valve fibrosis caused distortion of mitral valve apparatus into regurgitation or mitral stenosis. Apart of shear stress, infective agents not only cause the induction of auto antibodies by their similarity in membrane phospholipids but also damage on the surface of a heart valve and exaggerates valvular injury. Approximately 30% of patients with primary APS exhibit valvular abnormalities, which is considerably more than to the general population. Data on the prevalence of APS in patients with isolated valvulopathy are limited^(10,11,12).

A cohort of 87 patients presenting with thermodynamically important mitral or aortic regurgitation due to valvular causes were examined for the presence of IgG and IgM. Increased IgG and IgM were detected in 30% of the patients and none of the normal control subjects. Inflammation of the arterial wall and infiltration of activated immune cells into the arterial intimal are basic features of atherosclerosis. The predominant functional abnormality is regurgitation and stenosis is rare⁽¹³⁾. Mitral valve is mainly affected, followed by the aortic valve. The presences of valvular verrucous nodule further increase the risk for thrombo-embolic complications, mainly cerebrovascular, posed by valve lesions. Superadded bacterial endocarditis is rare.

Thrombosis forms on the plaque. Inflammation of the arterial wall and infiltration of activated immune cells into the arterial intima are basic features of atherosclerosis⁽¹⁴⁾. Although no study has prospectively confirmed the association of APS with the long term development of atherosclerosis it would appear that APS are an independent risk factor for atherosclerosis.

Vaarala et al. (1995) found that a high APS level was an independent risk factor for myocardial infarction or cardiac death. The prevalence of APS in patients presenting with myocardial infarction is between 5 and 15%; and in patients younger than 45 years old, the prevalence rises to 21% or roughly one in five⁽¹⁵⁾. The prevalence of 'antiphospholipid' antibodies in normal population is rare (3 %) and valvular involvement is very rare but about 30% of patients with primary APLS and about 60% of patients with SLE have involvement of one or more valves most often on mitral and aortic valve. So far only few valve operations in APLS patients are reported in literature emphasizing the complex problems which can arise during the surgical treatment⁽¹⁶⁾. Ciocca(1995), reported opposite results in a retrospective analysis of 19 patients with 'anti phospholipids' antibodies and cardiovascular procedures, 8 of them underwent heart valve operations. Twelve of the 19 patients (63%) died of complications related to surgical intervention^(17,18).

Conclusions

Clinical and immune pathological studies support an association between APS and heart valve lesions thrombosis and arthrosclerosis. They also confirmed that APS play a pathogenetic role in endocardial damage.

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