

Anti-phospholipid Antibody Syndrome Presenting as Right Sided Endocarditis in a Young Male

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ABSTRACT

A 23-year old male of South-Asian ethnicity, presented with fever and cough of one month duration. Examination revealed pansystolic murmur in tricuspid area, ejection systolic murmur in pulmonary area and a normal second heart sound. Echocardiogram showed tricuspid valve vegetations with mild to moderate Pulmonary artery hypertension (PAH) with non dilated right atrium and right ventricle. Blood Cultures for typical and atypical organisms of endocarditis were sterile. Anti-nuclear antibody (ANA) turned out to be positive but ds-DNA and anti-sm were negative. Lupus anticoagulant and anti cardiolipin antibody were positive in high titers. CECT thorax revealed thrombotic occlusion of left main pulmonary artery (LMPA). Criteria for Systemic lupus erythematosus (SLE), was not met initially, developed subsequently during the course of the disease. He was finally diagnosed as Anti-Phospholipid Antibody Syndrome (APS) secondary to SLE. This is a rare case of APS presenting as right sided endocarditis in a young male. Initially confused for Infective Endocarditis but finally diagnosed as APS secondary to SLE.

Key words: Anti-phospholipid syndrome, Chronic thromboembolic pulmonary hypertension, Endocarditis, Lupus anticoagulant, Tricuspid valve vegetations.

INTRODUCTION

Anti-phospholipid antibody syndrome (APS) manifests as recurrent episodes of fetal loss and/or thrombosis in females of reproductive age along with characteristic auto-antibodies. Cardiac involvement in the form of thickening of the mitral valve, pericardial effusion and non bacterial endocarditis are known to occur. The characteristic endocarditis of APS, the libmannsachs, mostly involves the mitral and aortic valves.

CASE HISTORY

A man in his early 20's consulted us for his cough and fever of 1 month duration. This was his first presentation to the

hospital with no prior antibiotic use. Vitals were stable. Cardiovascular examination revealed a normal jugular venous pulsation with pansystolic murmur in tricuspid area and an ejection systolic murmur in pulmonary area. Second heart sound is of normal intensity and was normally split. Respiratory system examination was normal. There was no history of intravenous drug abuse and no medical complaints in family. Routine biochemical investigations were normal. Initial Hematologic evaluation revealed thrombocytopenia. Chest roentgenogram was normal. Infective endocarditis (IE) was strongly considered. Echocardiogram showed a large valvular vegetations in anterior and septal leaflets of the tricuspid valve (Figure 1), with mild-moderate pulmonary artery hypertension and anon dilated right atrium and right ventricle. Four sets of blood cultures were sterile till 7 days on inoculation. Culture negative IE was considered but again cultures for anaerobic and fungal microbes as well as the agglutination tests for Brucella and Chlamydia were negative. He continued to have fever. His thrombocytopenia worsened and he later

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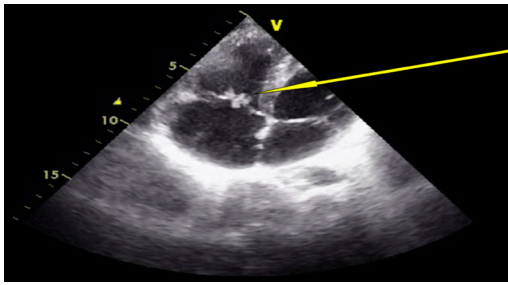


Figure 1: Large valvular vegetations in anterior and septal leaflets of the Tricuspid valve, the largest measuring 10 mm × 6 mm with mild-moderate pulmonary artery hypertension

developed pancytopenia. Non-infective endocarditis was considered. Autoimmune workup was suggestive APS (Table 1 & 2).

He was diagnosed as APS but differentiation of primary from secondary was now a big question.

At presentation he only had thrombocytopenia, but in due course developed pancytopenia and proteinuria. 24 hr urine protein was only 250 mg/dl but urine sediment analysis showed granular casts in urine. He also developed arthritis during his hospital stay, roentgenograms of which showed non erosive joints. His immunologic profile was also atypical. However, he had three of the clinical and 2 of the immunologic features of SLE and was diagnosed to have secondary APS.

He was started on I.V methylprednisolone for 3 successive days in view of his alarming pancytopenia. He was later changed over to oral methylprednisolone at a dose of 40 mg/day. He then complained of having NYHA grade 2 dyspnoe. Repeat ECHO showed disappearance of tricuspid valve vegetations (Figure 2) but with severe PAH and a right ventricular systolic pressure (RVSP) of 72. CT Pulmonary Angiogram (CTPA) was done, for possible occurrence of pulmonary embolism, which showed near complete thrombotic occlusion of left main pulmonary artery (Figure 3). Thrombolysis was deferred in view of thrombocytopenia. He was started on sub-cutaneous enoxaparin. To rule out the possibility of co-existing deep venous thrombosis, a bilateral lower limb venous Doppler was done which was normal study. He was symptomatically better, his blood counts improved and was hence discharged on steroids, warfarin and hydroxychloroquine(HCQ).

Table 2: Serum compliment levels

	Test results	Reference range
c3	54 mg/dl	90-150 mg/dl
c4	14 mg/dl	15-50 mg/dl

Table 1: Auto-immune panel

STANDARD DILUTION	1:100
HEP 2010 NUCLEUS	GRANULAR AND 3+
PRIMATE LIVER	GRANULAR AND 3+
SS-A	3+
Ro-52	3+
SS-B, nRNP/sm, sm, ds DNA	NEGATIVE.
Scl-70, PM-Scl, Jo-1, PCNA, CENP-B, nucleosomes, histones, Rib P-Protein.	NEGATIVE.
ANTI CARDIOLIPIN Ig M	POSITIVE (101.3 PLU/ml)
ANTI CARDIOLIPIN IgG	POSITIVE (>120 PLU/ml)

He was under regular follow, was doing fine and his blood counts normalized. While continuing warfarin and HCQ, dose of Methylprednisolone was gradually tapered by 8 mg at monthly intervals until he was on 8 mg at 5th month. He was advised 4 mg for one more month. At this follow-up, ACA testing was IgG positive and IgM negative. His ACA positivity after 6 months confirmed the diagnosis of APS. LA testing was deferred as he was on anti-coagulation. This patient had one clinical and two immunologic criteria of APS.

Repeat echo showed moderate PAH with RVSP of 58. He was asymptomatic and denied of having dyspnoe, even on exertion. As his clinical picture is of chronic thrombotic pulmonary artery hypertension (CTPH) he is being considered for pulmonary thrombo-endarterectomy. He was advised to continue Methylprednisolone (4 mg), warfarin and HCQ as bridging therapy till surgery.

DISCUSSION

Anti-phospholipid antibody syndrome (APS), an auto-immune disease, manifests as recurrent episodes of fetal loss and/or thrombosis in females of reproductive age along with characteristic auto-antibodies. Primary APS accounts for about 60% of cases where no obvious association was found while the rest test positive for other rheumatic disease specially, SLE. It affects women five times more frequently than men and is typically diagnosed between the ages of 30 and 40.¹ APS is diagnosed by criteria set by Sapporo.² Laboratory evidence of isolated activated prothrombin time (APTT) prolongation serves as a simple hint though should be interpreted clinically in view of numerous other conditions in which results in transient APTT prolongation.

APS keeps an individual at increased risk of cerebro-vascular accidents (CVA) and myocardial infarction (MI). CVA/ MI may either be due to in situ thrombosis or embolization secondary to intra cardiac vegetations. Cardiac involvement



Figure 2: CTPA showing near complete thrombotic occlusion of left main pulmonary artery

in the form of thickening of the mitral valve, pericardial effusion and non bacterial endocarditis are known to occur. The characteristic sterile vegetations in SLE, the Libman-Sacks, have a propensity to involve the left sided valves.³ These vegetations are verrucous near the edge of the valve. Unlike many other manifestations of SLE that are frequent during flares of disease activity, valvular lesions in SLE may occur at any time irrespective of disease activity. The effect of steroids on valve vegetations and other valvulopathies is controversial. Some authorities are in favour of steroids while others say steroids are detrimental. In our patient, steroid treatment given for his life threatening pancytopenia has resulted in dislodgement of vegetations. This has led to the disclosure of his pulmonary artery occlusion. Some suggest anti-platelet and/ or anti-coagulants will help to reduce the size of valve vegetations. It is unusual for APS to present as thrombosis of pulmonary artery and very rarely it involves the main pulmonary artery.

Individuals with SLE will usually test positive for anti-dsDNA and/or anti-sm. Nevertheless a very small number of patients fall under the category of ANA negative lupus. This includes selected patients with anti-phospholipid syndrome, histologically documented lupus nephritis and patients with positive skin biopsies and clinical features of SLE. A significant majority of these patients test positive for anti Ro. Anti-Ro antibodies may be the only auto-antibodies present in more than half of the patients

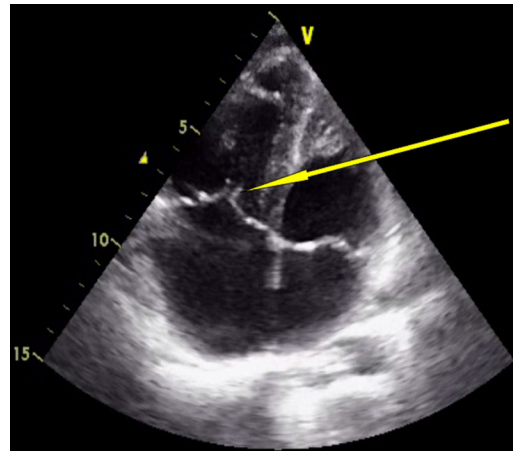


Figure 3: Disappearance of vegetations after treatment with steroids with severe PAH

with “ANA-negative” SLE. Anti-Ro antibodies may also be the first detectable auto-antibodies that precede the development of SLE in asymptomatic individual.⁴⁻⁶

The primary treatment of APS is anti-coagulation, often in association with low-dose aspirin and HCQ.⁷ Lifelong anticoagulation is indicated. In patients with thrombosis of left main pulmonary artery and who come under the category of CTPH, pulmonary thromboendarterectomy is the treatment of choice.⁸ The differentiation from primary and secondary SLE is dictates management as additional steroids and/or immunosuppressants are required in secondary APS.^{9,10}

CONCLUSION

This case is remarkable primarily for its rarity in involving right side valve, for its occurrence as thrombosis of left main pulmonary artery, for its peculiarity of occurrence in a young male, for its atypical clinical and immunologic picture which made differentiation of primary from secondary APS challenging. Differentiating primary from secondary APS is important for it dictates the management.

CONFLICT OF INTEREST

Author declared no conflict of interest.

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