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Case report

Antiphospholipid Antibody Syndrome with Fatal Multiple Thrombi in the Right Atrium Complicated with Massive Pulmonary Embolism

Azza Al-Afify MSC MD[1,2*], Mubarak A[1].Dossari[1] SBIM, SBAC

[1]*King Saud Medical City,*

[2]*Cardiology department, Faculty of Medicine Tanta University*

**Corresponding author: Dr. Azza Al-Afify,Kingdom of Saudi Arabia, Riyadh 11373 po box 331135, Tel: +966530827974;*

Email: alafifiazza@hotmail.com

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Abstract

Catastrophic antiphospholipid syndrome (APS) is a severe manifestation of antiphospholipid syndrome. An emergency surgical intervention might be lifesaving in catastrophic antiphospholipid antibody syndrome. We are reporting a young lady with APS who died with life threatening massive pulmonary emboli (PE) and multiple large right atrial (RA) thrombi. Conservative treatment by thrombolytic therapy and anticoagulant has no role in the management of multiple intercardiac thrombi due to risk of recurrent embolization from these mobile large thrombi.

Keywords: Antiphospholipid antibody ; Lupus anticoagulant; Mobile right atrial thrombi; Pulmonary embolism

Abbreviations:

APS: Antiphospholipid antibody syndrome ;

LAC: Lupus anticoagulant;

ACA: Anticardiolipin antibodies ;

PE: Pulmonary embolism;

RA: Right atrium

Introduction

Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by arterial and venous thrombosis, and raised levels of antiphospholipid antibodies [1]. There is an alteration in hemostatic process in APS and the mechanisms of thrombosis are undefined [2,3].

The proposed mechanisms of recurrent arterial and venous thrombosis are complement activation, production of antibodies against coagulation factors (including prothrombin, protein C, protein S), activation of platelets, activation of vascular endothelium, and a reaction of antibodies to oxidized low-density lipoprotein [1,2]. APS occurs most commonly in young women of fertile age - male: female 1:3.5.

The condition accounts for about 20% of recurrent thrombosis in young people and 15% of cases of recurrent fetal loss [2].

Beside the well-recognized arterial and venous thrombotic events APS, these patients can also present with a variety of

manifestations such as thrombocytopenia, nephropathy, cardiac valve disease, skin ulcers, diffuse pulmonary hemorrhage and neurological manifestations [4,5].

In-situ right atrial thrombi are usually immobile, attached to the atrial wall with occasional calcification. Secondary right atrial thrombi are often mobile as they have propagated from the peripheral veins [6]. Mobile thrombi in the right atrium tend to transit and embolize the pulmonary arteries. Thus, these mobile right atrial thrombi have often been referred as "emboli in transit" [6].

Case Report

42 years old Saudi lady known case of hypertension due to pre-eclmpsia accepted to king Saud medical city (KSMC) by fax from a peripheral hospital. She was presented to the Emergency and Accident department with history of chest tightness, palpitation, shortness of breath NYHA class IV. She had history of cough with haempytsis one week before transfer to KSMC. She gave history of two miscarriages, and history of using oral contraceptive pills two months ago. She did not smoke and there was no personal or family history of thrombosis.

By examination patient was conscious oriented lying flat, dyspneic tachypenic with respiratory rate 34/min, blood pressure was 180/100 mmHg, pulse rate 120 beat per minute, she was afebrile and O_2 saturation was 88% on 9 liter of O_2. Jugular venous pressure was 8 cm above the sternal angle, cardiac examination revealed palpable left parasternal pulsation with audible first heart sound loud P_2 and a holosystolic murmur grade 4/6 at the lower sternal border increasing in intensity with inspiration. Chest examination revealed harsh vesicular breath sounds. Her electrocardiogram showed sinus tachycardia 120 BPM with S_1, Q_3, T_3, and inverted T wave from V_1-V_3. Arterial blood gases showed PH 7.46, PCO_2 22.7, PO_2 59.7, HCO_3 31 and O_2 sat 87.9.

Blood biochemical evaluation disclosed a serum lactic dehydrogenase LDH of 512 U/L (normal 81-243 U/L), AST 32.72 U/L (0-32), ALT 13 U/L (0-3) and complete blood picture showed white blood cell count 14.34 10^3/uL, hemoglobin 13.53 g/dL, platelet 126, D-dimer 4.4, prothrombin time PT 13.9 second, partial thromboplastin time PTT 34.7, INR International Normalized Ratio 1.2, Cardiac Trponin I 5.49(0.00-0.06) Blood urea 10, serum creatinin level 143(53-88).

Echocardiography revealed dilated right ventricle (RV) 56 mm with impaired RV systolic function, right atrium (RA) was dilated measuring 45x 57 mm, paradoxical septal motion. There were three large mobile echogenic masses in the right atrium. The largest one was measuring 38x12 mm and it was protruding from the RA to RV across the tricuspid valve. There were moderately severe tricuspid regurgitation and estimated systolic pulmonary artery pressure was 89-94 mmHg. The left ventricle was normal in size and systolic function and showed the D-shaped sign in short axis view due to the acute RV pressure overload (Figure 1).

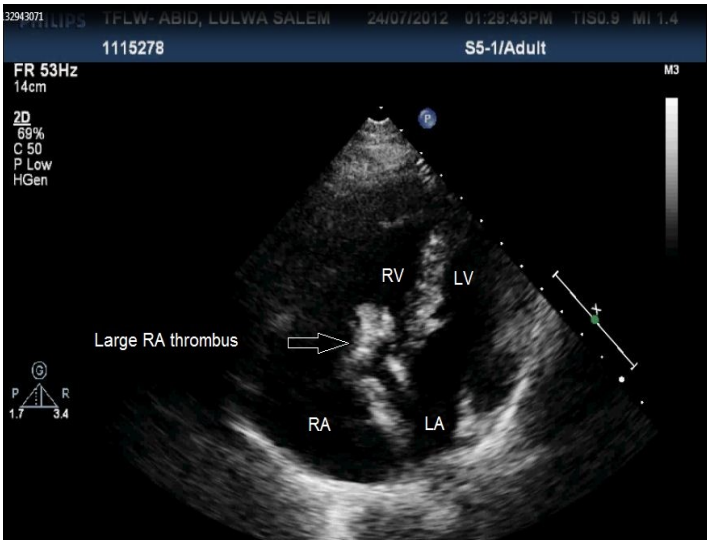

Figure 1. Four chamber view showing a large right atrial thrombus protruding across the tricuspid valve.

The patient was shifted immediately to intensive care unit with a ventilator support using the Biphasic Positive Airway Pressure BIPAP and she received intravenous heparin (1000 units/hour), warfarin and amlodopin 5 mg. She was de-saturated on BIPAP O_2 sat was 94% arterial blood gases after BIPAP, PH 7.4, PO_2 73.5, PCO_2 32, HCO_3 22.5 O_2 sat. 93.1%.

The spiral computed scan of the thorax showed pulmonary trunk, right pulmonary artery, and right upper lobar branch were patent, right middle, lower lobar arteries showed segmental thrombosis, left pulmonary artery was totally occluded and there was no evidence of pulmonary infarction (Figure2).

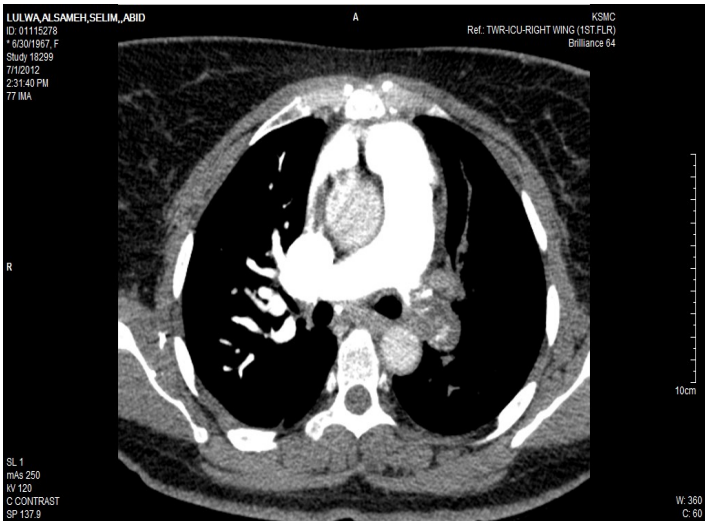

Figure 2. Spiral CT scan showed totally occluded left pulmonary artery

Antiphospholipid antibody syndrome was suspected as the patient gave history of two miscarriages beside these multiple thrombi in the RA. So we sent the antinuclear antibodies ANA was found to be positive, antiphospholipid Ab IgM 3.7 (normal range 0-11) Gplu/ml, antiphospholipid Ab IgG was 5(0-11) Gplu/ml, and the anticardiolipin Ab IgG was high 39.7 (0-11) Gplu/ml, and lupus anticoagulant (LAC) was found to be positive.

Patient was transferred to a higher center King Faisal Specialist hospital and research center for emergency cardiac surgery but her family refused the surgical intervention for her and she died after 24 hours.

Discussion

Antiphospholipid antibody syndrome is a hypercoagulable disorder that increases the risk of recurrent vascular thrombosis. Catastrophic APS is the most dangerous form it presents with fatal manifestation.

It causes multiple organ infarctions over a period of days to weeks with potentially lethal problems such as massive pulmonary embolism PE, stroke and myocardial infarction [1].

Besides PE, other pulmonary manifestations of APS include pulmonary hypertension, adult respiratory distress syndrome, intraalveolar hemorrhage and primary thrombosis of lung vessels [7].

We are presenting a case of APS with massive pulmonary emboli. The thrombosis in our patient seems to be multifactorial.

It could be due to obesity, her use of oral contraceptives, hyperlipidemia, and hypertension along with the existence of LAC lupus anticoagulant. All of these factors might have led to a massive thrombotic event.

The most common manifestation of the APS is pulmonary thromboembolic disease. Esen et al [8] reported that pulmonary embolism could be the first manifestation of the disease. This is coinciding with our case as she was presenting with massive pulmonary embolism.

It was suggested that oral contraceptives may trigger the formation of thrombosis in patients with LAC [9,10]. Our patient was using oral contraceptives which might contribute as procoagulant factors.

Tajender et al reported a case of APS who developed massive bilateral pulmonary emboli after being started on oral contraceptive pills [11].

Our patient had positive lupus anticoagulant and elevated levels of anticardiolipin It was confirmed that persistent presence of lupus anticoagulant fulfill the diagnostic and classification criteria of antiphospholipid syndrome [12].

The presence of antiphospholipid antibodies can be proved either by a solid phase assay (anticardiolipin) or by a test for an inhibitor of phospholipid-dependent clotting (lupus anticoagulant) [13] .

Because of a lack of prospective trial, the optimal management of antiphospholipid syndrome-associated thrombosis or pregnancy loss is controversial. Overall, Acute management of arterial or venous thrombosis in APL syndrome is by using anticoagulants as in other patients with similar problems.

Patients with recurrent thrombotic episodes require lifelong anti-coagulation therapy [14].

In our patient a large RA thrombus precipitates a lethal massive PE. It was reported that catastrophic APS is associated with high morbidity and mortality a finding concordant with our case report [15]. Therefore, an aggressive multidisciplinary treatment strategy is indicated. Anticoagulation, immunosuppression, plasma exchange, intravenous immunoglobulins, and anti-platelet agents, used in various combinations, have resulted in improved patient outcome [15].

Recently Kazzaz et al reported that all patients with antiphospholipid antibody syndrome should be treated with anticoagulants, corticosteroids, and possibly plasma exchange. New therapies, such as rituximab and possibly eculizumab, may be options in catastrophic APS, but need further study [16].

However, the management of mobile right atrial thrombi is a therapeutic dilemma; therapeutic alternatives include systemic heparinization, systemic or local thrombolysis, catheter embolectomy and surgical removal [17,18].

It was reported that mobile thrombus in the right atrium is an unusual echocardiographic finding; it portends a poor prognosis with death due to pulmonary embolism [19].

Data from limited experiences suggest that thrombolytic therapy might be considered in patients with right heart thrombi with pulmonary embolism.

Hung et al [19] reported two patients who developed large right atrial thrombi with pulmonary embolism. One of them was treated with recombinant tissue plasminogen activator survived with uneventful results, whereas the second patient died after 15 days of operative thrombectomy.

Bradly et al [20] reported that one option to consider for the treatment of giant right atrial thrombus is catheter-directed, continuous, prolonged infusion of thrombolysis.

Although the presence of right heart thrombi in patients with PE is associated with increased mortality, little is known about optimal management of this difficult clinical situation. The treatment of choice remains controversial with limited data to compare the various options [21].

There were multiple large, mobile thrombi in our patient so the choice of the decision of surgical thromboectomy was appropriate. In a meta-analysis that included 177 cases, the overall mortality rate was 27% [22]. The mortality rate associated with no therapy, anticoagulation therapy, embolectomy, and thrombolysis were 100%, 29%, 24%, and 11%, respectively [22]. These findings suggest that anticoagulation by itself appears insufficient to treat patients with mobile right heart thrombi, this finding explain the fatal end of our patient when surgical intervention was interrupted by the family of the patient.

Embolectomy is typically limited to large medical centers since it requires an experienced surgeon and cardiopulmonary bypass. Surgical pulmonary embolectomy could have acceptable results, if it is performed early in patients with acute massive PE who have not reached the profound cardiogenic shock or cardiac arrest [23].

In conclusion, catastrophic antiphospholipid syndrome APS associated with high morbidity and mortality. The presence of mobile right atrial thrombi in patients with APS and pulmonary embolism portends poor prognosis with cardiopulmonary collapse due to PE. Therefore, treatment should be started immediately as any delay might be lethal. The optimal therapy remains controversial given absence of randomized trials.

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