Pulmonary Artery Thrombosis in ASD with Eisenmenger syndrome - A Case Report

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Abstract:
A 55 year old man presented with progressively worsening breathlessness for 1 month and was diagnosed to be having atrial septal defect ostium secondum type Eisenmenger syndrome for the first time. The Echocardiogram showed dilated pulmonary arteries and large thrombi in main, right and left pulmonary arteries. The possibility of in situ thrombus formation was considered more likely than thromboembolism, as there were none of the acute symptoms expected with the embolisation of such thrombi. Patient was not a known case of ASD and for the first time presented as ASD with Eisenmenger syndrome with pulmonary thrombosis.

Keyword: Atrial septal defect, Eisenmenger syndrome, pulmonary artery thrombosis. Pulmonary artery hypertension (PAH) due to chronic thromboembolism is well known. A pulmonary artery thrombus can also develop in situ as described in primary PAH as well as PAH due to chronic obstructive pulmonary disease.

There are few reports regarding the occurrence of thrombi in the main pulmonary arteries in Eisenmenger syndrome. This case is presented because of the unusual occurrence of large thrombi in a case of atrial septal defect-Eisenmenger syndrome. A 55 year old male was having symptoms of breathlessness for the past 6 years and the patient did not seek any medical attention for the same. The patient got admitted due to progressive aggravation of his symptoms for the past 1 month. Patient was also having bilateral leg swelling for the past 15 days. No H/o any acute chest pain, palpitation, giddiness or loss of consciousness. He did not give any history of abdominal pain, oliguria, facial puffiness or prolonged fever. No history of previous surgery or prolonged immobilisation. Clinically he had mild cyanosis, pan digital clubbing grade 1, bilateral pitting pedal edema, prominent ‘a’ waves in JVP, cardiomegaly, prominent pulmonary artery pulsations, left parasternal heave and epigastric pulsations. The first heart sound was normal and second heart sound was wide and with fixed split and the pulmonary component of
second heart sound was accentuated. Tricuspid regurgitation murmur was present. The respiratory system was clear and other systems were normal.

![Fig 1: ECG](image1)

The haemoglobin and packed cell volume were above normal. Routine biochemical and other haematological investigations were within normal limits. The electrocardiogram showed sinus rhythm, right axis deviation, right ventricular hypertrophy with pressure overload pattern. There is also negative terminal p wave force in V1. The initial descending portion of p wave in V1 is less than 30 msec. This reflects the presence of right atrial anomaly rather than left atrial anomaly. Chest X-ray revealed cardiomegaly with dilated main and right pulmonary arteries with peripheral pruning.

The 2D echocardiogram showed a large atrial septal defect – ostium secundum type of size 31 mm, dilated main, right and left pulmonary arteries. There was a large thrombus seen in main pulmonary artery (MPA) measuring 44 X 19 mm in size and another large thrombus in MPA at its bifurcation which extends into both Right Pulmonary Artery (RPA) and Left Pulmonary Artery (LPA). Doppler evaluation showed bidirectional shunt across ASD and presence of pulmonary hypertension evidenced by severe tricuspid regurgitation with peak gradient of 95 mm Hg. Contrast injection showed prominent right to left shunt across ASD.

Right ventricular function was normal by echocardiography. Patient was not thrombolysed as the blood pressure was normal and increased bleeding risk in these type of patients. Patient was treated with Heparin infusion 70 units/kg loading dose followed by 17 units/kg infusion. Patient died of respiratory failure 24 hours after admission.

![Fig 2: Echo A4C](image2)

![Fig 3: Echo - Colour Doppler](image3)
DISCUSSION:
Eisenmenger syndrome is the clinical phenotype of an extreme form of pulmonary arterial hypertension (PAH) associated with congenital heart disease. Chronic increasing pulmonary blood flow eventually reverses the original left-to-right shunts to right-to-left or bidirectional shunts through the original lesions. Thrombi in the distal pulmonary circulation are known to occur in Eisenmenger syndrome. However, the occurrence of large thrombi in the proximal pulmonary arteries is unusual. Patients with Eisenmenger syndrome have a substantial risk for pulmonary artery thrombus formation.\(^1\,^2\) Several studies have found women and patients with...
lower oxygen saturation,\(^{(1)}\) low pulmonary artery velocity,\(^{(2)}\) and biventricular dysfunction, who are at the highest risk for developing a thrombosis.\(^{(2)}\)

Hemostatic abnormalities are common and complex in cyanotic patients. They are attributed to abnormalities in platelets, coagulation pathways and other coagulation mechanisms.

**Platelets:**
Platelet abnormalities include both thrombocytopenia and thrombasthenia. There is a positive correlation between platelet count and oxygen saturation or an inverse relationship with hemoglobin/hematocrit level. Platelet counts are usually in the lower range of normal or reduced due to decreased production because of ineffective thrombopoiesis. In addition, platelet survival is reduced, and platelet function is decreased in patients with elevated hematocrit.

**Abnormal coagulation parameters:**
Vitamin K dependent clotting factors (factors II, VII, IX, X) and factor V are reduced. Increased fibrinolytic activity and depletion of the largest von Willebrand multimers contribute to the bleeding tendency in these patients. In this process, cyanosis, pulmonary vascular disease, and turbulent blood flow are major determinants of the von Willebrand abnormality, which appears to be acquired and may contribute to the bleeding diathesis.

**Vascular factors:**
Increased tissue vascularity in ES patients. Endothelial derived nitric oxide and other vasodilators are released by the increased shear stress and results in arteriolar dilatation. Bleeding and Thrombotic Diathesis Patients with ES are at risk for both bleeding and thrombosis. The coagulation abnormalities increase the risk of spontaneous bleeding, which is usually mild, self-limited and not life-threatening in Eisenmenger patients. Hemoptysis is the most common and life-threatening bleeding complication, the others are less common.

In situ thrombi can be the source of artery-to-artery intrapulmonary emboli resulting in pulmonary infarction and intrapulmonary hemorrhage. Female gender and low oxygen saturation were identified as risk factors for thrombus formation in the proximal pulmonary arteries.

There are no clinical data to show effectiveness and benefit of routine anticoagulation or aspirin therapy in this population in the absence of any other strong indication (e.g. persistent atrial fibrillation/flutter). Anticoagulation may be offered to patients with thrombus material in the central pulmonary artery or in case of pulmonary artery-to-pulmonary artery embolism. However, meticulous monitoring is needed if an Eisenmenger patient is on anticoagulants. Although anticoagulation has been shown to reduce morbidity and mortality in patients with idiopathic PAH, there are no data to support this approach and recommendations for routine anticoagulation cannot be given to patients with ES.

Strategies to reduce the risk of bleeding include:

- Limitation of anticoagulation to urgent indications for anticoagulation such as atrial fibrillation, recurrent thromboembolic events, mechanical heart valve prostheses
- Meticulous surveillance of anticoagulation; the optimal range of the INR or aPTT has not been evaluated. Recommendations for therapeutic anticoagulation are a target INR between 2.0 and 2.5 (in the absence of a mechanical valve) or a
therapeutic aPTT of 1.5 times of the normal value;

Prompt therapy of respiratory tract infections.

Strategies to reduce the risk of ischemic events include:

Avoidance and treatment of volume depletion;

Iron supplementation in patients with iron deficiency or those undergoing repeated phlebotomies;

Use of air filters in all intravenous lines.

Proximal pulmonary artery thrombosis has been reported in patients with ASD and PAH,\(^3\) and in a patient with ventricular septal defect and Eisenmenger syndrome.\(^4\) Thrombotic lesions have been reported in the RPA in a patient with a history of corrected ASD.\(^5\) Thrombotic lesions have also been described in the central elastic pulmonary arteries of patients with primary PAH.\(^6,7\) The presence of central pulmonary artery lesions suggestive of thrombi has been reported in patients with chronic obstructive pulmonary disease with PAH and dilated pulmonary arteries.\(^8\) In the present case, the thrombi were considered to have formed in situ as there were no symptoms suggesting embolisation of such large thrombi. The aggravation of symptoms could be due to the added obstruction to flow by the thrombi and minute embolisations from the large thrombi to the peripheral pulmonary circulation. Endothelial dysfunction induced by PAH, abnormal coagulation factors and platelet dysfunction have been implicated as the causes of thrombosis in secondary PAH.

\(^9\) The relatively sluggish flow in the dilated pulmonary arteries and polycythemia might have contributed to the formation of such large thrombi in this patient. Chronic endothelial damage can be caused by increasing shear stress on the vessel walls, increasing blood volume, viscosity, and chronic hypoxemia.\(^10, 11\) These observations imply that structural and functional damage to the pulmonary artery endothelium may play a critical role during the development of pulmonary thrombosis.\(^12\) The natural history of large in situ thrombi in the pulmonary arteries is not known, as only a few case reports are available. In patients with PAH and pulmonary embolism due to such large thrombi, acute worsening of symptoms with right heart failure leading to death in weeks to months, or occasionally sudden death, may occur. Worsening of symptoms could also be due to progression of the PAH in non-occluded vessels because of relatively increased flow through these vessels. The outcome depends on the size of the thrombus or the degree of PAH. Management depends on the symptoms, hemodynamic status, whether the thrombus is considered acute or chronic and the basic disease. Anticoagulation is the traditional method of treatment to prevent further thrombus formation and embolisation. It should also be given following measures to remove the thrombus and continued for at least 6 months or, in some cases, lifelong. If there is a hemodynamic disturbance or worsening of symptoms, especially in the acute phase, the thrombus has to be removed. Options for removal of the thrombus are thrombolytic therapy\(^13\) with streptokinase/tissue plasminogen activator (t-PA) or mechanical removal.
Thrombolytic therapy may be considered up to 2 weeks after the onset or on worsening of symptoms. The major complication is bleeding and the advantage is the ease of therapy. Thrombolytic therapy may be given in lesser dosage if it is administered locally by a catheter; but since the requisite infrastructure is needed, the therapy is not popular. Mechanical means are more effective in removing the thrombus than lytic therapy. The former may also be considered in patients with a chronic pulmonary thrombus with significant symptoms and those in whom thrombolytic therapy is contraindicated. The available options are surgical removal by thromboendarterectomy and percutaneous removal using a hydrolyzer thrombectomy catheter or other devices. Surgical thrombectomy carries the risks of any major surgery and requires cardiopulmonary bypass in a sick patient. The percutaneous catheter technique is safer and equally effective in removing the thrombus but is not readily available.

In conclusion, we report an uncommon case that presented with huge pulmonary thrombi accompanied by pulmonary hypertension with dilated pulmonary arteries. ASD with Eisenmengersyndrome combined with pulmonary artery thrombosis was diagnosed. The importance of this case report is that the patient was not a known case of ASD previously and for the first time presented as ASD with Eisenmenger syndrome with pulmonary thrombosis which is a rare presentation.

REFERENCES:


