ORIGINAL RESEARCH PAPER

Pulmonary Medicine

RECURRENT PULMONARY THROMBOEMBOLISM IN A CASE OF COMBINED ANTITHROMBIN III AND PROTEIN C DEFIECIENCY

KEY WORDS: Chronic Thromboembolism, Protein C Deficiency, Anti Thrombin III, Pah

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ABSTRACT

Venous thromboembolism (VTE) and PE is the third most common cause of cardiovascular death after myocardial infarction (MI) and cerebrovascular accidents (CVA) worldwide . Most clinically significant PEs originate from the deep leg or pelvic veins. Inherited risk factors include antithrombin III deficiency, protein C, protein S deficiency, factor V Leiden mutation .Prompt recognition of a PE is crucial because of the high associated mortality and morbidity. Recent studies have showed that protein C deficiency is also associated with arterial thrombosis.

Antithrombin (AT) is a serine protease inhibitor which inactivates many activated coagulation factor in the coagulation cascade, mainly thrombin and factor Xa. AT deficiency occurs in 1 in 500 to 1 in 5000 overall populations. Patients with low levels of Anti Thrombin III possess an increased risk of thromboembolic disorders . Homozygous anti thrombin III deficiencies are rare as compared to heterozygous type.

Combined inherited thrombophilia are rare cause of PE with an incidence of approximately 1 in 40,000.

INTRODUCTION:

26 year old male patient was admitted with complaints of breathlessness, right sided chest pain, jaundice and swelling of bilateral lower limbs since the past one week. Patient was an occasional tobacco chewer and social drinker. On Examination patient was found to have tachycardia with bilateral lower limb edema (right > Left) ,non pitting in nature and jaundice and raised Jugular Venous pressure .Patient was tachypnoeic with bilateral normal vesicular Breath sounds and Per Abdomen showed evidence of Ascites .Patient also gave history of similar complaints in the past and had reports showing evidence of Pulmonary Thromboembolism.

Initially Patient underwent the basic **blood investigations** which showed the following results :

Blood Investigations

Routine Blood Counts : normal

Liver Function Tests :
S.Bilirubin total -6.93 (Direct-4.13) ,SGOT-32,SGPT – 40,

Renal Function Tests :
Creatinine- 2.2 ,Urea- 48

Since the Patient had evidence of **recurrent thromboembolism,** further investigations were done to find out any rare causes .The reports are as follows :

Protein C Levels: **40.80 %** (65-140 %)

Anti Thrombin III Levels: **79.1 %** (83-128 %)

Protein S Levels: 110 (89 to 128.5)

ANA :Negative (0.29)

Lupus Anticoagulant :Negative

PT/INR:17.1/1.42

Bilateral Lower Limb Doppler:

USG Abdomen :
Moderate Ascites with congestive hepatomegaly

2D Echo :
Severe PAH with Mild pericardial effusion,LVEF- 60 %

CT Pulmonary Angiography:
Chronic Pulmonary Thromboembolism in the Right Distal Pulmonary Artery and its ascending branches

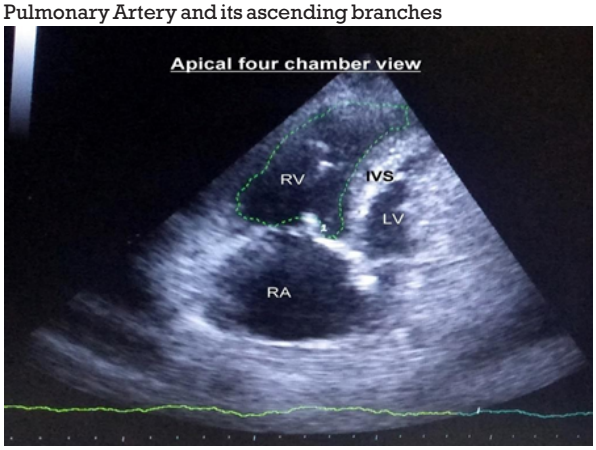

Figure 1 : 2D Echo Showing Enlarged Right Ventricle

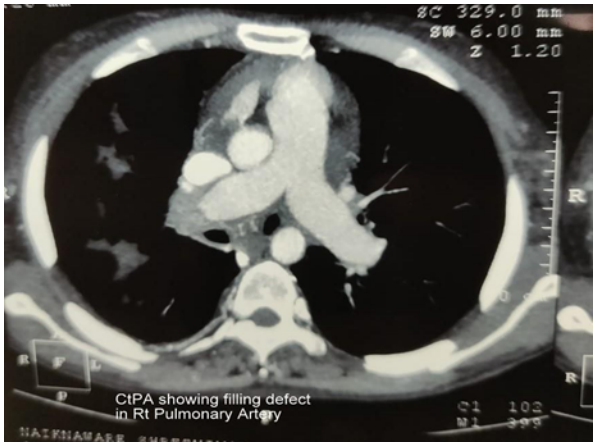

Figure 2 :CT Pulmonary Angiography Showing Filling Defect In Right Main Pulmonary Artery

Patient was found to have low levels of Protein C and Anti Thrombin III, which was identified as the cause of Recurrent Thromboembolism.

DISCUSSION :

Pulmonary Thromboembolism is commonly caused due to emboli arising from deep veins of the legs. Whenever , a definitive cause for Thromboembolism could not be obtained ,a diagnosis of Clotting factor and Other mutations like protein C, Protein S ,Anti thrombin IIIand like wise should be kept in mind and Coagulation Profile Analysis should be done

to get an accurate diagnosis.

AT deficiency is a rare autosomal dominant inheritance, affecting men and women equally. There are 2 types of AT III deficiency which are classified as type I and type II deficiencies. Type I causes reduction in both functional activity and antigenic levels of AT proportionately (quantitative deficiency). In contrast, type II deficiency shows low AT activity despite normal antigen levels due to a dysfunctional protein (qualitative deficiency). Type II deficiency is further subdivided into IIa, IIb, and IIc, based on the location of the mutations. Patients with type I AT deficiency is commonly symptomatic, often representing 80% of all thromboembolic events. Before a patient is diagnosed as having hereditary AT deficiency, acquired causes of protein deficiency should be considered.

Similarly Protein C defieciency is a rare cause of Pulmonary Embolism.Even it can be inherited or acquired.Protein C takes part in coagulation cascade only when it is activated.The most common manifestation of Protein C Deficiency is recurrent thromboembolism .

But however Combined inherited thrombophilia are rare cause of PE with an incidence of approximately 1 in 40,000. Since the above subject has both the deficiencies, it is a rare case.

Pulmonary Thromboembolism is the most common manifestation of patients with such deficiencies. In the present case patient had combined anti thrombin III and Protein Cdeficiency. Patient was advised life long anti coagulation with warfarin for the same. However the patient presented with recurrent thromboembolism and deranged LFT's. Viral markers and autoimmune workup were negative. Deranged LFT was contributed due to congestive hepatopathy. Hence, patient was started on Low Molecular Weight Heparin along with low dose warfarin for management.

CONCLUSION :

Pulmonary Thromboembolism is a medical emergency. Inherited disorders should always be considered in recurrent thromboembolism. As such patients have high associated mortality and morbidity and will require life long anti coagulation. Different thrombophilias require specific management which needs consideration while management of such cases.

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