Pulmonary Thromboembolism Presenting as Pulmonary Hypertension

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Abstract

Chronic thromboembolic pulmonary hypertension is one of the leading cause of severe pulmonary hypertension and is associated with considerable mortality and morbidity. It is essential that diagnostic efforts should be pursued vigorously in patients with severe pulmonary hypertension to ensure that no patient with secondary pulmonary hypertension is erroneously classified as having primary pulmonary hypertension. Pulmonary hypertension associated with thromboembolism of pulmonary artery is relatively undiagnosed and is characterized by intraluminal thrombus formation and fibrous stenosis or complete obliteration of pulmonary arteries. We report here a case presenting with signs and symptoms of severe pulmonary hyper tension and predominant right heart failure Echocardiography was suggestive of enlarged right atrium, right ventricle and severe pulmonary hypertension. CT angiography demonstrated evidence of thrombus in left pulmonary artery. Lower limb venous Doppler confirmed presence of deep vein thrombosis.

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) has emerged as one of the leading causes of severe pulmonary hypertension. The disease is relatively underdiagnosed, and the true prevalence is still unclear. CTEPH is characterized by intraluminal thrombus organization and fibrous stenosis or complete obliteration of pulmonary arteries.[1] The consequence is an increased pulmonary vascular resistance resulting in pulmonary hypertension and progressive right heart failure. Recent research has provided evidence suggesting that the mechanistic view of CTEPH as a disease caused solely by obliteration of central pulmonary arteries due to organized thrombi may have been too simplistic. Pulmonary embolism, either as a single episode or as recurrent episodes, is thought to be the initiating event followed by progressive pulmonary vascular remodeling. This concept explains the clinical observation that CTEPH patients may have severe pulmonary hypertension out of proportion to the pulmonary vascular obliteration seen on a pulmonary angiogram. Both the extent of proximal occlusion of pulmonary arteries and secondary small-vessel arteriopathy contribute to the elevated pulmonary vascular resistance. Most patients who present with persistent pulmonary hypertension after pulmonary embolism will have progressive disease despite adequate anticoagulation and these patients also carry a high risk of dying from right heart failure if left untreated.

Treatment of CTEPH often requires a multidisciplinary approach and may involve surgery, medical treatment, or both. We report here a case of pulmonary thromboembolism presenting as severe pulmonary hypertension associated with predominant right heart failure .1

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Case presentation

A 33 year old man presented with history of progressive breathlessness increasing on exersion 3 months prior to admission, edema feet since 2 and a half months and change in voice 15 days prior to admission. Patient w as non smoker and occasional alcoholic .patient was diagnosed to be a case of pulmonary Koch's and received complete treatment 6 years back. On examination, patient had tachycardia (120/min), tachypnea (respiratory rate32/min),raised JVP with prominent CV complexes and edema over feet. Patient also had cyanosis, suffused conjunctiva and polycythemic tongue. .Grade III clubbing was also noticed. Respiratory system examination revealed

bilateral basal rales. Apex beat was diffuse in character, parasternal heave was present and second heart sound was palpable in left 2nd intercostal space. Systolic murmur could be appreciated in pulmonary area and second heart sound was widely split in pulmonary area.. Pulmonary component of second heart sound was very loud (banging) and Right ventricular S3 gallop could be appreciated. Abdominal examination revealed hepatomegaly.

Patient's haemoglobin was 15.5 gm%, and PCV was 55 Total and differential counts were normal and solubility test for sickling was negative. Liver and kidney function tests were reported as normal.ECG revealed P pulmonale, Right axis deviation ,S till V6 and incomplete RBBB pattern.. X- Ray chest demonstated cardiomegaly, enlarged right heart border, prominent pulmonary conus. Prominent bronchovascular markings and increased upper lobe perfusion was also observed.

Patient was clinically diagnosed to be a case of pulmonary hypertension with congestive heart failure . However there was no middiastolic murmur suggestive of mitral stenosis, patient was non smoker and though he is a treated case of pulmonary Koch's in the past, patient did not have any signs and symptoms of bronchiactasis or suppurative lung disease. Split of second heart sound was wide but variable, indicating ASD to be unlikely diagnosis. In order to know the cause of pulmonary hypertension patient was subjected for Echocardiography, which demonstrated severe pulmonary hypertension, enlarged right atrium as well as right ventricle and moderate right ventricular systolic dysfunction. However, cardiac valves were structurally normal and interatrial as well as inerventricular septum was found to be intact. Left ventricular systolic functions were normal with EF of 62% and mild pericardial effusion was noted. Estimated pulmonary artery pressure was 85 mm Hg and severe tricuspid regurgitation was noticed. Possibility of thromboembolic pulmonary vascular disease was entertained. D-dimer estimation was reported to be raised(850ng/ml FEU)

Patient was subjected to CT angiography and CT thorax for confirmation of throbmoembolic pulmonary vascular disease. which revealed **Chronic thrombosis of left main pulmonary artery with 70% luminal narrowing of Pulmonary trunk** and right pulmonary artery showed normal enhancement. However, bilateral lower lobe pulmonary arteries were chronically thrombosed revealing pulmonary oligemia. Upper lobe pulmonary arteries were mildly dialated and showed normal enhancement . Pulmonary trunk was found to be dialated (3.7 cm in diameter) Bilateral upper lobe ground glass opacities were suggestive of pulmonary edema. There was evidence of chronic fibrotic and cystic changes in both lower lobes CT angiography confirmed the diagnosis of chronic pulmonary thromboembolism predominantly involving left main branch and bilateral lower lobe arteries suggestive of pulmonary hypertension.

To find out the primary source of pulmonary thromboembolism, venous Doppler was performed which demonstrated evidence of **thrombosis of lower 1/3rd of right deep femoral vein .Popliteal as well as posterior tibial vein also demonstrated absence of Doppler detectable** flow and did not show augmentation in distal compression suggestive of thrombus formation .

With clinical signs and symptoms of pulmonary hypertension, Echocardiographic evidence of severe pulmonary hypertension, CT angiographic evidence of thrombus in pulmonary artery and findings of deep venous thrombosis on Doppler evaluation patient is diagnosed to be a case of **chronic pulmonary thromboembolism** presenting as pulmonary hypertension and was treated with low molecular weight heparin followed by warfarin with INR monitoring patient was advised to attend cardiology and CVTS center as these facilities are not available at our centre. Patient's ANA and antiphospholipid antibody titres were within normal limits. pretein C, pretein S deficiency and other tests to know the cause of hypercoagulable tests could not be performed because of financial constraints. Patient's clinical condition improved, and heart failure could be controlled with diuretics and ACE inhibitors and other conventional therapy.

Discussion

Pulmonary hypertension is categorized as -

1) pulmonary arterial hypertension 2)pulmonary venous hypertension 3)pulmonary hypertension associated with hypoxemic lung disease, 4)pulmonary hypertension due to chronic thromboembolic disease and 5) miscellaneous causes like sarcoidosis, chronic

anaemias, histiocytosis X ,lymphangiomatosis and schistosomiasis. Pulmonary arterial hypertension can be idiopathic , or is associated with conditions like collagen vascular diseases, congenital systemic to pulmonary shunts, portal hypertension and HIV infection[2]. It is essential that diagnostic efforts should be pursued vigorously in patients with severe pulmonary hypertension to ensure that no patient with secondary pulmonary hypertension is erroneously classified as having primary pulmonary hypertension. Mitral stenosis, pulmonary parenchymal disease, congenital cardiac defects, pulmonary thromboemboliosm, and pulmonary venous obstruction are important causes. Sickle cell disease can also cause in situ thrombosis of pulmonary vessels and collagen vascular diseases are also associated with development pulmonary thromboembolism and pulmonary hypertension. Mitral stenosis and congenital cardiac defects causing Eissenmenger's syndrome can be ruled out by echocardiography, pulmonary parenchymal disease can be recognized by characteristic physical findings, chest radiograph, pulmonary function tests, and high resolution chest CT .Collagen vascular disease is suggested by involvement of other organ systems or the presence of antinuclear antibodies or antiphospholipid antibodies.[3]

Pulmonary hypertension due to chronic thromboembolic disease is characterized by elevation of pulmonary artery pressure with documentation of pulmonary arterial obstruction for 3 months and includes chronic pulmonary thromboembolism and nonthrombotic pulmonary embolism associated with tumor or foreign material. Most patients diagnosed as acute pulmonary embolism and treated with intravenous heparin and chronic oral warfarin do not develop chronic pulmonary hypertension. However, some patients have impaired fibrinolytic resolution of thromboembolism, which leads to organization and incomplete recanalisation and chronic obstruction of pulmonary vascular bed. Because the initial pulmonary thromboembolism may go undetected, or untreated, many patients are misdiagnosed as having idiopathic pulmonary arterial hypertension. These patients may have underlying thrombophilic disorders, such as lupus anticoagulant/anticardiolipil antibody syndrome, prothrombin gene mutation, or factor V . leiden.

Patients with CTEPH typically present in either of 2 scenarios: patients may complain of progressive dyspnea on exertion, hemoptysis, and/or signs of right heart dysfunction including fatigue, palpitations, syncope, or edema after a single episode or recurrent episodes of overt pulmonary embolism. A "honeymoon period" between the acute event and the development of clinical signs of CTEPH is common and may last from a few months to many years. However, up to 63% of patients have no history of acute pulmonary embolism. In these patients, progressive dyspnea on exertion, rapid exhaustion, and fatigue are the most common symptoms, and the clinical course is often indistinguishable from other forms of severe pulmonary hypertension, especially idiopathic pulmonary arterial hypertension. Physical findings are often subtle and may include a left parasternal heave, a prominent pulmonary component of S2, and a systolic murmur of tricuspid regurgitation. Signs of right heart failure, ie, raised JVP edema, ascites, and acrocyanosis, occur late in the course of the disease and may signal a life-threatening situation. A rare clinical finding that is virtually pathognomonic for CTEPH is bruits over peripheral lung fields,typically over the lower lobes, which result from turbulent blood flow in partially occluded areas. [4]

Our patient also presented with signs of right heart failure and signs of pulmonary hypertension. Even if patient has a past history of pulmonary tuberculosis clinical examination as well as radiological findings do not indicate severe lung parenchymal disease, resulting in development severe pulmonary hypertension. Diagnosis of pulmonary throboembolism in the present case is confirmed by Venous Doppler indicating the presence of deep venous thrombosis and demonstration of thrombus and occlusion of left pulmonary artery on CT angiography.

Pulmonary embolism, either as a single episode or as recurrent episodes, is thought to be the initiating event followed by progressive pulmonary vascular remodeling. This concept explains the clinical observation that CTEPH patients may have severe pulmonary hypertension out of proportion to the pulmonary vascular obliteration seen on a pulmonary angiogram. Thus, treatment of CTEPH often requires a multidisciplinary approach and may involve surgery, medical treatment, or both.

Echocardiography is widely used as the initial diagnostic tool when pulmonary hypertension is

suspected, and routine echocardiography 6 weeks after pulmonary embolism has been suggested to identify patients at risk for developing CTEPH. Imaging technologies including ventilation-perfusion scanning, computed tomography (CT), MRI, and pulmonary angiography are a fundamental part of the diagnostic workup of patients with suspected CTEPH. Nevertheless, ventilation-perfusion scanning is a useful tool to start searching for possible CTEPH. There is consensus among experts that a normal ventilation-perfusion scintigram practically rules out the presence of CTEPH If scintigraphy shows indeterminate results, ie, whenever the perfusion scan is not completely normal or reveals findings suggestive of CTEPH, the next diagnostic step is usually CT angiography, which may reveal eccentric thrombotic material within the pulmonary arteries, subpleural densities, and a characteristic mosaic attenuation of the pulmonary parenchyma .It is important to note that patients with pulmonary arterial hypertension can develop secondary thrombosis of the central pulmonary arteries, a condition mimicking CTEPH In addition, neoplasms involving the pulmonary arteries or pulmonary large-vessel vasculitis may present with a similar CT picture. In these cases, ventilation-perfusion scanning usually does not show the typical bilateral segmental and subsegmental perfusion defects but rather normal findings, an inhomogeneous perfusion pattern, or unilateral abnormalities. Large bronchial artery collaterals are typically visible in patients with CTEPH . MRI may also provide a clear diagnosis of CTEPH, but this technique is infrequently used for this indication.[4,5]

Pulmonary angiography remains a standard diagnostic tool in the assessment of patients with probable or definite CTEPH both to establish the diagnosis and to assess operability. Pulmonary angiography is often performed in conjunction with a diagnostic right heart catheterization, which is required to confirm the diagnosis of pulmonary hypertension, rule out pulmonary venous hypertension, and establish the degree of hemodynamic impairment. As Facilities for ventilation perfusion scanning, MRI, Cardiac catheterization and Cardio thoracic surgery are not available at our centre, we had to refer our patient for further investigations and management.

CTEPH patients should receive lifelong anticoagulation adjusted to a target international normalized ratio between 2.0 and 3.0. The rationale for anticoagulation is the prevention of recurrent thromboembolic events; once CTEPH is fully established, one should not expect significant regression of pulmonary hypertension from anticoagulation. Thrombolytic therapy is rarely helpful in patients with chronic pulmonary hypertension and may expose them to increased risk of bleeding without potential benefit.

Pulmonary thromboendarterectomy is an established surgical treatment in patients whose thrombi are accessible to to surgical removal. The operative mortality is <10% in experienced centres.postoperative survivors can expect an improvement in functional class and exercise tolerance [4,5]

In a comprehensive review of 1500 PEA procedures performed at University of California at San Diego, Jamieson et al stated that "there is no degree of embolic occlusion within the pulmonary vascular tree that is inaccessible and no degree of right ventricular impairment or any level of pulmonary vascular resistance that is inoperable." However, there is an almost linear relationship between preoperative pulmonary vascular resistance and perioperative mortality.[4,6]

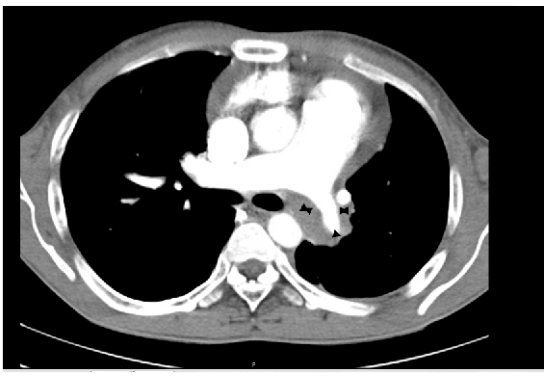
On the basis of pathophysiological considerations, medical treatment is now being studied for CTEPH patients. Intravenous epoprostenol has been used with varying results to achieve hemodynamic stabilization before surgery, but at least some patients seemed to have had significant hemodynamic and clinical improvement. Uncontrolled studies suggest a potential role of both the phosphodiesterase-5 inhibitor sildenafil and the endothelin receptor antagonist bosentan for inoperable CTEPH patients. In 12 patients with inoperable CTEPH, 6 months of sildenafil treatment resulted in an average increase of 6-minute walk distance of 54 m and a drop in pulmonary vascular resistance of 30% from baseline. Comparable results were achieved with 3 months of bosentan therapy in 18 patients, which resulted in a mean increase of 6-minute walk distance of 73 m and a fall in pulmonary vascular resistance of 33%. The only controlled clinical trial thus far to include CTEPH patients was the Aerosolized Iloprost Randomization (AIR) study This study included 57 patients with CTEPH, but subgroup analysis failed to show a significant benefit of inhaled iloprost on hemodynamics or exercise capacity. A

randomized, placebo-controlled trial is currently under way to determine the safety and efficacy of bosentan in patients with inoperable CTEP .To define the exact role of medical management, further studies are needed.4,6

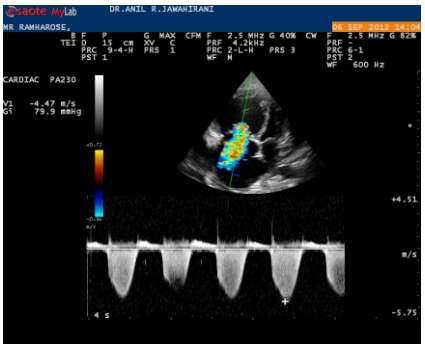
Conclusions

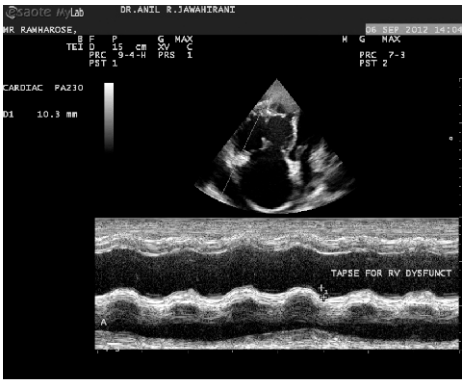
Pulmonary thromboembolism is an important cause of severe pulmonary hypertension. High index of suspicion , proper diagnostic and therapeutic strategies and facilities and expertise for surgical management is absolutely essential in improving the outcome of patients with thromboembolic pulmonary hypertension. Lifelong anticoagulation is mandatory - however, exact role of newer drugs recommended for pulmonary hypertension in managing cases with CTEPH needs to be studied further.

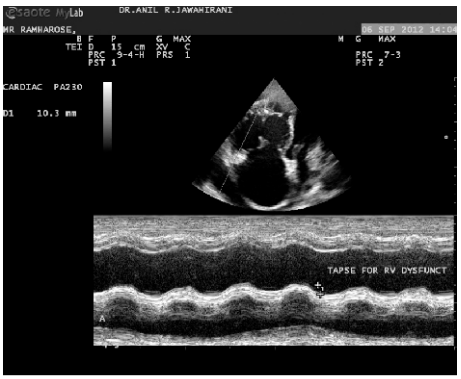
CT angiography; thrombus in left pulmonary artery causing occlusion



Echocardiography : Dialated Righr Atrium, Right ventricle, TR JET and pulmonary hypertension







Bibilography

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