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AUTOPSY FINDINGS IN A CASE OF SEVERE IDIOPATHIC PULMONARY ARTERY HYPERTENSION COMPLICATED BY PULMONARY ARTERIAL THROMBOEMBOLUS

Pathology

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ABSTRACT

Objective: We report post-mortem findings of a sudden death case of severe idiopathic pulmonary arterial hypertension complicated by thromboembolism and review the relevant literature. Methods. A 36 years old man was brought to Accident and Emergency ward of a 492 bedded zonal level hospital with history of sudden collapse. The patient was a known case of Idiopathic pulmonary arterial hypertension and was under treatment. On arrival, he was unresponsive to therapy, and died suddenly. Results. Autopsy revealed presence of pulmonary arterial endoluminal thromboembolism grossly completely blocking the pulmonary arterial trunk, with features of pulmonary hypertension in the both lungs. The main pulmonary artery trunk wall show features of perivascular mononuclear inflammatory infiltrate. Conclusion. This appears to be rare reported case of pulmonary arterial hypertension complicated by thromboembolism of main pulmonary artery in association with large vessel perivascular inflammatory infiltrate.

KEYWORDS

Idiopathic pulmonary arterial hypertension; thromboembolism; perivascular infiltrate

Introduction:

Pulmonary hypertension (PH) is defined as a clinical condition presented with mean resting pulmonary artery pressure ≥ 25 mm Hg [1]. Ernst von Romberg first identified this clinical entity in 1891 [2]. The causes and classification of pulmonary hypertension evolved through years till in 2008, the Dana Point 4th World Symposium on Pulmonary Arterial Hypertension modified the classification based on recent pathophysiological understandings of disease mechanisms [3-4]. According to most recent classification based on World Symposium on PH in 2013 [5], PH can be one of six different clinical types based on haemodynamics and pathophysiology-

1. Pulmonary arterial hypertension (PAH)
2. Pulmonary veno-occlusive disease (PVOD) and or pulmonary capillary haemangiomatosis (PCH)
3. PH due to disease of left heart,
4. PH due to lung diseases and/or hypoxia
5. Chronic thromboembolic PH (CTEPH)
6. PH with unclear and/or multifactorial mechanisms

The recent consensus defined PAH (group 1) as a clinical condition characterised by the presence of pre-capillary PH characterised by mean pulmonary arterial pressure ≥ 25 mmHg, pulmonary capillary wedge pressure ≤15 mmHg and normal /reduced cardiac output provided this pre-capillary PH is not due to other causes, such as PH due to lung diseases, chronic thromboembolic PH, or other rare diseases. PAH can be of different forms as mentioned below:

1. Idiopathic
2. Heritable
3. Drug and toxin induced
4. Associated with- Connective tissue disease, HIV infection, Portal hypertension, Congenital heart diseases, Schistosomiasis, Chronic haemolytic anaemia
5. Persistent PH of newborn

We describe here rare reported case of a patient who was clinically diagnosed as idiopathic PAH, in whom thromboembolus developed in main pulmonary trunk resulting in sudden death and post mortem findings exhibit association with large arterial perivascular inflammatory infiltrate**.**

Case History:

The deceased, a 36 years old working individual was brought to Accident and Emergency (A&E) ward of 492 bedded zonal level hospital with history of sudden unresponsiveness for one hour before admission. Patient was having lunch when he suddenly become unresponsive and was immediately brought by his colleagues .. He was a known case of IPAH and was diagnosed during evaluation for dyspnoea on exertion (DOE) NYHA class II 07 years before the incidence. There was no history of drug abuse or positive family history. During initial evaluation he was found to have ECG abnormalities exhibiting right axis deviation (RAD), right bundle branch block (RBBB), right ventricular hypertrophy (RVH), right atrial enlargement (RAE) and mild tricuspid regurgitation (TR). His right ventricular systolic pressure (RVSP) was 84 mm Hg. 2D ECHO during evaluation 06 months before revealed normal ventricular function, grossly dilated right atrium (RA) and right ventricle (RV). (RA-52 mm, RV-64 mm), severe TR, RVSP-90 mm Hg with RAE, dilated main pulmonary artery (MPA- 30 mm). Patient was kept on conservative management with review on regular interval. He was on regular treatment with restriction in physical activities alongwith Oral anticoagulants, Diuretics, Digoxin, Endothelin receptor antagonists and Phosphodiesterase type-5 inhibitors. During his last three monthly review by cardiologist his chest X ray was reported showing cardiomegaly with prominence of pulmonary arteries and 2D ECHO left ventricular ejection fraction (LVEF) was 60% with features of severe PAH. Clinically he was symptomatic with DOE NHYA class I with late ejection systolic murmur in pulmonary area and pan-systoloic grade III/IV murmur in tricuspid area.

On the day of the incidence patient was apparently asymptomatic in view of his underlying illness. On quick assessment in A&E ward patient was unresponsive and unconscious. His pulse was feeble with low volume, respiratory rate 22/min and irregular, blood pressure was 108/72 mm of Hg. ECG was found to have features of RVH. No obvious injury marks was seen over body and no frothing from mouth. After 05 mins of arrival patient was evaluated and found to have un-recordable blood pressure, un-recordable pulse, and no active respiration with occasional gasping. Urgent resuscitative measures were initiated. Despite all possible measures he could not be revived.

Salient features of gross autopsy were as follows: **1)** Cardiomegaly (heart weighing 480gm) with right atrial enlargement and biventricular hypertrophy. The left and right ventricle wall thicknesses were 02 cm (N= 1.0-1.5cm) and 1.9 cm (N=0.25-0.5 cm) respectively. Mitral valve Tricuspid valve and Aortic valve circumference was of 10cm (N=9-11cm),, 14 cm (11-13cm) and 6.5 cm (6.7 cm) respectively. The chordae tendinae were delicate, pliable and overall normal free of

lesion. No commissural fusion is observed. Pulmonary trunk appeared grossly enlarged with semi-lunar valves circumference 9.5 cm (N=6.6 cm).There was presence of endoluminal atheromatous thromboembolus grossly completely blocking the pulmonary arterial trunk (Approx 05 cm in length). The thrombi seen over both sides cusps. Epicardium and endocardium were normal. The myocardium appeared hypertrophied. The coronary arteries arise from normal positions. The vessel wall lumens were patent. The aortic and pulmonary arteries arise from normal anatomical position. The aortic wall showed focal atheromatous streaks. The major branches of aorta were patent and showed mild atherosclerosis. 2) Lungs showed congestion , edema and petechial haemorrhages over areas. Cut surface of the lungs appeared haemorrhagic. (Fig 1) 3) Liver showed mild hepatomegaly. External surface was smooth and shiny. Cut surface appeared congested, homogenous, without any nodularity.

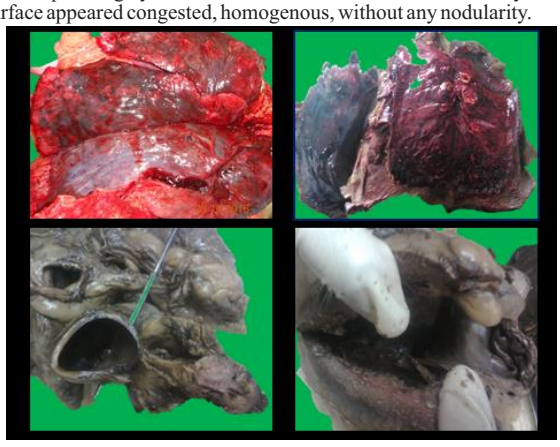

Figure1. Gross features of the lungs and heart at postmortem examination. A. Lungs showed congestion , edema and petechial haemorrhages. B. Cut surface of the lungs appeared haemorrhagic. C. Endoluminal atheromatous thromboembolus grossly completely blocking the pulmonary arterial trunk. D Hypertrophy of the right ventricle.

Relevant features of histopathological examination were as follows: 1)Sections from heart showed features of cardiac hypertrophy. Sections from pulmonary artery show distended artery with organizing endoluminal thromboembolus with lysed RBCs along with recent thromboembolus consisting mostly of fibrin and red blood cells completely occluding the main trunk of pulmonary artery. Vascular wall of pulmonary artery showed foci of adventitial mononuclear infiltrate with perivascular cuffing of the vasa vasorum. 2) Sections from both lungs show features of variable degree of interstitial fibrosis along with vascular changes. There is features of pulmonary hypertension with variable degree of mascularization and medial hypertrophy alongwith intimal hyperplasia of small to medium pulmonary arteries which narrowed the vascular lumina. Areas showed subintimal fibrosis with onion ring appearance. The arterial branches are dilated and many of which contain platelet plugs. There is presence of plexiform lesion within lumen of dilated pulmonary artery which consists of plexus of small–caliber vascular channels. These dilated vessels show marked thinning of tunica media. Evidence of recent pulmonary infarction and previous microinfarct seen. (Fig 2 & 3)

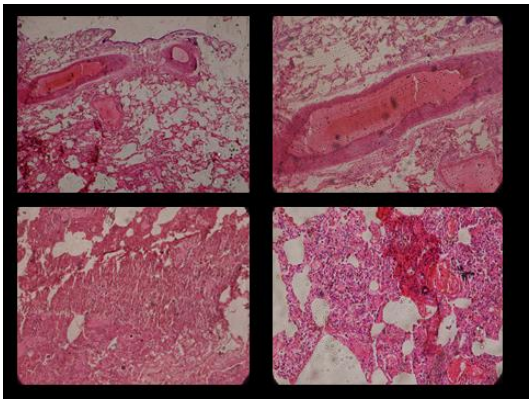

Figure 2 : . A. (10x) B. (40x)Hematoxylin and eosin-stained section of lung tissue, showing a typical medial hypertrophy, intimal fibrosis and luminal narrowing. C.(10x)D.(40x) Hematoxylin and eosin-stained section of lung tissue, showing features of variable degree of interstitial fibrosis.

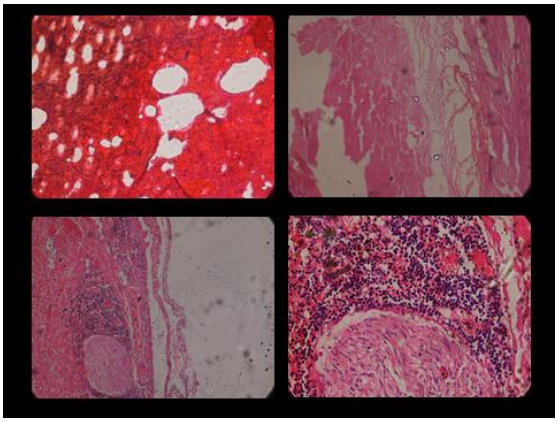

Figure 3. A. (10x) Hematoxylin and eosin-stained section of lung tissue, showing features of recent pulmonary infarction. B (10x) Hematoxylin and eosin-stained section of pulmonary artery show arterial wall with organizing endoluminal thromboembolus. C. (10x) D (40x) Hematoxylin and eosin-stained section of pulmonary artery showed foci of adventitial mononuclear infiltrate.

3) Kidneys showed features of acute tubular necrosis and liver showed features of microvesicular steatosis.

Discussion:

Most recent data from a French registry advocates that prevalence of PAH is approximately 15 per million and of which IPAH prevalence of about 06 per million. IPAH is commoner in females than males (2-9:1) [6]. According to recent modifications, IPAH refers to sporadic PAH with no family history of PAH or any other identifiable risk factors. In the new classification “familial PAH” is now replaced with the term “heritable PAH.”. “Heritable PAH” diagnosis does not mandate genetic testing as it is not going to change clinical management. Therefore in resource constraint countries like India genetic testing, should be performed weighing limitations of such testing. Our patient clearly had no reported family history or any other identifiable risk factors during his initial and subsequent evaluation and genetic testing was not done.

PAH comprises of heterogeneous conditions but its share virtually identical clinical and pathological changes of lung circulation. Many pathobiological mechanisms have been demonstrated , but the exact cellular interactions leading to initiation and progression of the pathological processes are yet to be revealed [7-8]. While perivascular inflammation has limited value in pathological work up of cases of PH, it is presently one of the most promising areas of investigation. Inflammatory cells may interact with viral factors, which have emerged as potential etiological/pathogenetic agents [9-10]. Studies showed evidences of immunological alterations in IPAH patients [11]. Our patient clearly had no clinical features of vasculitis recorded or any suggestive features of ongoing chronic thromboembolic phenomenon on repeated evaluations. The histopathological examination of the lungs showed grade I to V changes according to Heath Edwards grading system signifying severe PAH[12]. The condition was complicated by development of a large thromboembolus in the main pulmonary trunk which may be related to the vasculitis induced events. Here is the rarest reported case of clinically diagnosed severe IPAH complicated by thromboembolism of main pulmonary trunk in association with large vessel perivascular inflammatory infiltrate.

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