Pulmonary Capillary Haemangiomatosis: A Rare Cause of Pulmonary Hypertension

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Abstract

Pulmonary capillary haemangiomatosis (PCH) is a rare disorder of unknown aetiology, characterised by proliferating capillaries that invade the pulmonary interstitium, alveolar septae and the pulmonary vasculature. It is often mis-diagnosed as primary pulmonary hypertension and pulmonary veno-occlusive disease. Pulmonary capillary haemangiomatosis is a locally aggressive benign vascular neoplasm of the lung. We report the case of a 19-year-old female who was referred to us in the early post-partum period with severe pulmonary artery hypertension, which was diagnosed as PCH by open lung biopsy. [Indian J Chest Dis Allied Sci 2014;56:259-262]

Key words: Pulmonary capillary haemangiomatosis, Pulmonary hypertension.

Introduction

Pulmonary capillary haemangiomatosis (PCH) is a rare cause of pulmonary hypertension of unknown aetiology and is characterised by a slow progressive clinical course with signs and symptoms of pulmonary hypertension, haemoptysis and right heart failure (RHF). A reticulonodular pattern with dilated main pulmonary artery is evident on chest radiograph.¹ On histopathological examination, there is proliferation of capillary channels within the alveolar wall, pulmonary interstitium, pulmonary blood vessels and pleura. The clinical, radiographic, and histopathologic features are similar and often confused with other causes of unexplained pulmonary hypertension, usually pulmonary venoocclusive disease (PVOD).² To the best of our knowledge, 37 cases have been reported in medical literature till date.³ Most of these³ were diagnosed at autopsy. We report the case of a young female, who presented three months postdelivery with progressive breathlessness and RHF due to severe pulmonary artery hypertension, diagnosed as pulmonary capillary haemangiomatosis by videoassisted thoracoscopic (VATS) lung biopsy.

Case Report

A 19-year-old female presented with progressive exertional dyspnoea for the past four years, which significantly worsened three months after delivery. She also gave history of abdominal distension, and swelling of both lower limbs. Physical examination revealed cyanosis, pedal oedema, tachycardia, hepatomegaly, ascites and loud pulmonary component of second sound (P2) with S3 gallop on cardiac auscultation. Her temperature was 98.6 °F, blood pressure 80/50 mmHg, heart rate 130 beats/ min; and arterial oxygen tension (PaO₂) was 38mmHg. The

electrocardiogram (ECG) showed right ventricular strain pattern with sinus tachycardia. The chest radiograph showed a dilated main pulmonary artery (Figure 1). Twodimensional echocardiography demonstrated markedly dilated right heart chambers with right ventricular peak pressure of 71mmHg and an ejection fraction of 75% that was suggestive of severe pulmonary hypertension; there was no evidence of left-to-right shunt.



Figure 1. Chest radiograph (postero-anterior view) showing enlarged main pulmonary artery.

High resolution computed tomography of the chest with contrast showed dilated central pulmonary arteries, bilaterally diffuse ill-defined centrilobular nodules with ground-glass opacities and no mediastinal adenopathy or pleural effusion (Figure 2). Complete blood counts, as well as liver and renal function tests were normal.

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Serological testing for human immunodeficiency virus (HIV), rheumatoid factor, anti-nuclear antibody, antineutrophil cytoplasmic antibody, anti-cardiolipin antibody, serological testing for hepatitis B and C viruses, thyroid profile, troponin I were all negative.



Figure 2. CT chest showing enlarged main pulmonary artery, bilateral diffuse centrilobular nodules with ground-glass opacity.

After stabilising her condition with supplemental oxygen, vasopressors, heparin and furosemide, VATS lung biopsy was performed. Microscopic examination of the lung biopsy specimen showed multifocal proliferation of capillaries in the alveolar walls, pulmonary interstitium and interlobar septa. Pulmonary arteries and arterioles showed medial hypertrophy. There are focal areas of fresh and old haemorrhages with haemosiderophages and also some focal intimal fibrosis (Figure 3A). Capillary proliferation was well demonstrated by reticulin stain (Figure 3B) and immunohistochemistry for CD31, CD34 was positive in the endothelial cells of the proliferating capillaries (Figure 3C and 3D). The above features were consistent with a diagnosis of PCH. She was discharged with home oxygen therapy.

Discussion

Pulmonary capillary haemangiomatosis is a rare cause of pulmonary hypertension.⁴ It is characterised by uncontrolled proliferation of the pulmonary capillaries, resulting in infiltration of pulmonary vessels, bronchi, interstitium and alveoli causing pulmonary hypertension, haemoptysis, alveolar



Figure 3. (A) Photomicrograph showing numerous proliferation of capillary channels within alveolar walls with haemosiderophages (PAS x 400); (B) Photomicrograph showing numerous capillary proliferation in the alveolar walls (Reticulin x 400); (C) Photomicrograph showing endothelial cells lining the proliferating capillaries and without cytologic atypia (Immunohistochemistry staining by CD31 x 400); and (D) Photomicrograph showing endothelial cells lining the proliferating capillaries and without cytologic atypia (Immunohistochemistry staining by CD31 x 400); and (D) Photomicrograph showing endothelial cells lining the proliferating capillaries and without cytologic atypia (Immunohistochemistry staining by CD34 x 400).

haemorrhage, fibrosis and haemosiderosis.⁴ It is not gender specific and mainly affects young adults; although case reports involving individuals from newborn to elderly have been documented.^{5,6} A genetic basis for the disease is not yet known, although there is a report of a family with three affected children in an autosomal recessive pattern^{6,7} and three cases of congenital PCH diagnosed at early infancy.⁵ Recently, mutation in eukaryotic translation initiation factor-2 alpha kinase 4 (EIF2AK4) has been reported to be one of the cause for autosomal recessive PCH in both familial and sporadic origin.⁸ Pathologically, in PCH there will be an increased expression of vascular endothelial growth factor (VEGF), platelet-derived growth factor-B, platelet-derived growth factor receptor á and â, angiopoetin 1 and CD-117. Decreased nitric oxide synthase III expression has been reported in PCH patients with severe pulmonary hypertension versus those with normal pulmonary artery pressure.9-13

Pulmonary capillary haemangiomatosis is considered a disease of unknown aetiology, but it can in association with occur systemic lupus erythematosus, scleroderma, takayasu arteritis and hypertrophic cardiomyopathy.14-18 The clinical manifestations of PCH include progressive dyspnoea on exertion, haemoptysis, haemorrhagic pleural effusion, signs and symptoms of pulmonary hypertension and finally cor-pulmonale. All patients with PCH have elevated pulmonary arterial pressures measured by right heart catheterisation with normal or low pulmonary capillary wedge pressure. Pulmonary function test most commonly shows restriction with a decreased diffusion capacity for carbon monoxide. The chest radiograph reveals enlarged central pulmonary arteries, accompanied by diffuse or bibasilar recticulonodular or micronodular areas of opacity,² as in our case the patient had enlarged central pulmonary artery. High resolution computed tomography shows dilated central pulmonary arteries, diffuse, ill-defined centrilobular nodules of ground glass opacity with basal predominance, which was demonstrated in our case. However, septal thickening, lymphadenopathy, pleural effusion, pericardial effusion can also be seen.² Pulmonary arteriogram usually appears normal in pulmonary capillary haemangiomatosis. Definitive diagnosis is established by histopathological examination. PCH is rarely diagnosed ante-mortem and the diagnosis is made on autopsy. In a series of 37cases,³ only 9 cases were diagnosed ante-mortem.

The histological hallmark of PCH is the proliferation of capillary channels within the alveolar walls and interlobar septa. These proliferating capillaries surround and compress the walls of pulmonary venules and veins, causing intimal fibrosis and secondary veno-occlusion, resulting in compensatory muscularisation of arterioles and medial hypertrophy of muscular pulmonary arteries. The endothelial cell that lining the proliferating capillary do not show cytologic atypia and mitotic activity.^{2,4} Pulmonary capillary haemangiomatosis should always be differentiated from PVOD, which presents as widespread venous occlusion by intimal fibrous tissue that resembles organising thrombi and also with patchy areas of capillary dilatation.² Although in some cases of PVOD, some foci of PCH will be seen and reverse can also occur, but in PVOD the capillary proliferation is only focal. Pulmonary congestion with atelectasis is another common entity often mis-diagnosed as PCH, which presents as diffuse congestion with prominent capillaries. Another differential is the pulmonary arteriopathy in which the plexiform lesions were seen. The proliferation of the capillary channels was not seen either in PVOD, pulmonary congestion or in pulmonary arteriopathy, which is a histological hallmark for the diagnosis of PCH.1 There are no randomised clinical trials to examine the safety and efficacy of pharmacologic agents in treating patients with PCH, as very few cases have been reported. Treatment with corticosteroids and cyclophosphamide has not been successful; lung transplantation is the only curative therapeutic option and pharmacologic agents serve only as supportive care.^{3,4} Experimental drugs like alpha-interferon were used in one case¹⁹ and doxycycline in another patient with an atypical manifestation of endotheliosis.²⁰ Vasodilators (like intravenous prostacyclin and calcium channel blockers) will induce florid and even fatal pulmonary oedema in patients with PCH.²¹ Untreated PCH is usually fatal due to bleeding or respiratory failure. We did not use any of the above-mentioned therapeutic strategies except for oxygen therapy. The prognosis of PCH is very poor. The mortality is high with median survival approximately three years from the time of initial clinical manifestations.³ In India, one other case report of this condition has been described.22

In conclusion, early recognition of PCH in patients with pulmonary hypertension without an obvious cause is possible based on clinical and radiologic characteristics. The PVOD and PCH are clinically indistinguishable from a primary pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension. This distinction, however, is essential for appropriate pharmacologic intervention as well as for timely evaluation for lung transplantation. There is a no definite pharmacological treatment available for these diseases. Lung or heart lung transplant is the treatment of choice.

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