International Journal of Contemporary Pediatrics
Thapar V et al. Int J Contemp Pediatr. 2023 Jul;10(7):1149-1151
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20231861

Case Report

Pulmonary capillary hemangiomatosis: an unusual cause of primary pulmonary hypertension in pediatric age group

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Received: 04 May 2023
Accepted: 07 June 2023

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ABSTRACT

Pulmonary capillary hemangiomatosis (PCH) is a rare and controversial entity that is known to be a cause of pulmonary hypertension and is microscopically characterized by proliferation of dilated capillary-sized channels along and in the alveolar walls. Clinically, it is mostly seen in adults. PCH's main clinical presentations are progressive dyspnea, fatigue, hemoptysis, palpitations and later irreversible pulmonary hypertension and right-sided heart failure. It is characterized by severe hypoxemia, centrilobular ground-glass opacities on computed tomography and pulmonary congestion triggered by pulmonary vasodilating therapy. The imaging features include diffuse centrilobular ground-glass opacities with features of pulmonary hypertension. We present a case of PCH in a 4-year-old boy who was diagnosed with post-partum hemorrhage (PPH) in echocardiography and computed tomography of the thorax.

Keywords: Pulmonary capillary hemangiomatosis, Pulmonary hypertension, Right-sided heart failure

INTRODUCTION

Pulmonary capillary hemangiomatosis (PCH) is a rare pulmonary disease characterized by numerous capillary-sized blood vessels that proliferate diffusely throughout the pulmonary interstitial tissue, pulmonary blood vessels, and airways.[1] The disease does not have a sexual predilection. Unfortunately, the diagnosis of PCH is usually not made until an autopsy is performed.[2] The condition usually progresses rapidly until severe pulmonary hypertension and resulting right cardiac failure develop.[3] It presents with features similar to idiopathic pulmonary hypertension or pulmonary veno-occlusive disease (PVOD).[4] The distinction of PCH or PVOD from idiopathic pulmonary arterial hypertension (IPAH) is important because pulmonary vasodilators may lead to deleterious complications in patients with PCH and PVOD, resulting it hemoptysis and hemothorax. This is the case of pulmonary capillary hemangiomatosis with classical clinicoradiological findings in very early pediatric age group, which is rarely reported.

CASE REPORT

A 4-year-old boy presented to pediatric emergency department, NIMS Hospital, Jaipur with history of dry cough and difficulty in breathing for last 3 months. He had history of intermittent upper respiratory tract infection in this duration which was relieved by taking oral medications. Now, he had acute exacerbation of difficulty in breathing for last 5 days which was not relieved by outpatient based treatment and referred to us for further evaluation and management. He had no history of weight loss, persistent fever, decreased appetite. General physical examination was unremarkable except grade 2 clubbing over nails. Respiratory system examination shows mild tachypnea, mild sub costal retraction and nasal flaring. Pulse oximetry showed saturation of 85–89% on room air.

Chest auscultation revealed mild tachycardia. There were no signs of cardiac failure, no cardiac murmurs, and no adventitial sounds. Chest X-ray was taken which showed diffuse, fine reticulonodular opacities uniformly distributed in both the lung fields, and dilated main pulmonary artery. The electrocardiography showed the right axis deviation. He underwent echocardiography which showed enlarged Right atrium and right ventricle. Main pulmonary artery was dilated with size of 25 mm. PR gradient was 53.7 mm Hg. The left ventricular systolic function, mitral valve, and pulmonary veins were normal. Above findings were in favor of severe pulmonary hypertension. His laboratory workup showed hemoglobin 9.8 g/dl, total leukocytes count 5200/mm^3 with 79% neutrophils, and platelets 152,000/mm^3. His liver and renal function tests were within normal range.

His markers sepsis as C-reactive protein (CRP), procalcitonin were also in normal range. Respiratory viral panel by PCR for common respiratory viruses and SARS-CoV-2 was done which also came negative. Computed tomography (CT) pulmonary angiogram was taken with arterial and venous phases, along with high-resolution CT of thorax which showed multiple, randomly distributed tiny, and centrilobular ground-glass opacities in bilateral lung parenchyma. These opacities were distributed in all lung fields. The main pulmonary trunk was dilated with a luminal diameter of 2.5 cm. The right and left branches of the pulmonary artery were also enlarged with peripheral pruning of the branches. Concentric hypertrophy of the right ventricle with bulging of the interventricular septum toward the left ventricle was observed along with enlarged right atrium features suggestive of pulmonary artery hypertension. In view of pulmonary hypertension, initially he was started on oral sildenafil which lead to worsening of symptoms in form of increased cough. Sildenafil was stopped after HRCT chest as clinical history and imaging were in favour of pulmonary capillary hemangiomatosis.

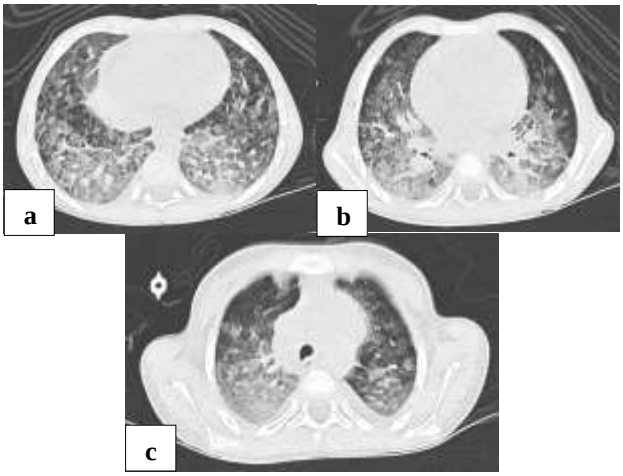

Figure 1: High-resolution computed tomography sections showing many, randomly scattered small, and centrilobular ground-glass nodules in bilateral lung parenchyma.

The patient had no other symptoms other than mild cough and remained clinically stable. Pulmonary biopsy confirmation was suggested; however, the parents refused biopsy. As the patient was clinically stable and the imaging findings were strongly suggesting PCH, histological confirmation was deferred. Regular follow up with pediatric pulmonologist was planned.

DISCUSSION

Pulmonary capillary hemangiomatosis is a rare cause of pulmonary hypertension (PH) that is typically seen in younger adults but can occur in an age range from 2 years to 72 years. PCH is a rare etiology of PH characterized by a widespread proliferation of pulmonary capillaries within the alveolar walls, unlike PVOD which is caused by extensive vascular obstructive process originating from pulmonary venules and small veins.[5] Wagenvoort et al, was the first to describe PCH in a 71-year-old woman complaining of progressive dyspnea and hemoptysis. He discovered a characteristic proliferation of capillary-like channels in lung tissue that appeared to be distinct from the classical findings described in PAH or PVOD, leading to the identification of a new entity, PCH.[6] So far, no identifiable risk factors for PCH are recognized. Best et al identified eukaryotic translation initiation factor 2α kinase 4 (EIF2AK4) mutations in familial PCH in 2 brothers and in 2 of 10 cases with sporadic PCH.[7] Also, Eyries et al discovered 11 of causative EIF2AK4 mutations in patients with familial and sporadic PVOD.[8] So, the current guidelines agreed to advise patients with PVOD and PCH about genetic testing and counseling. The hallmark of PCH is the presence of aberrant proliferation of capillary vessels at least 2 layers thick. Histopathological description shows a patchy parenchymal involvement often forming nodules with capillary proliferation lined by bland-looking endothelium with intra-alveolar hemosiderin-laden macrophages, small areas of acute or old hemorrhage, hemosiderosis. Small pulmonary arteries with in-timal thickening/medial hypertrophy. Rare capillary proliferation into pleura, mediastinal lymph nodes and pericardium were described. The incidence of PCH remains uncertain. El-Gabaly et al reported a frequency of almost 4 cases per million individuals.[9] Progressive dyspnea and fatigue are the principal clinical manifestations of both PVOD and PCH. Chronic cough (dry or productive), chest pain, syncope, digital clubbing, fever, respiratory tract infection, thrombocytopenia and hemorrhagic complications may occur. With further progression of PCH, PH and right-sided heart failure develops.

HRCT chest plays a crucial role in the diagnosis of PCH as it shows a group of characteristic cardiovascular and pulmonary parenchymal findings. The cardiovascular findings include enlarged central pulmonary arteries, dilated right-sided heart, IV contrast reflux into the IVC, normal caliber pulmonary veins and average-sized left atrium. Pulmonary parenchymal findings are diffuse well-defined small centrilobular ground-glass pulmonary nodules with no zonal predominance with or without few

and sparse smooth inter-lobular septal thickening. The associated findings, which may be encountered in PCH patients, include mediastinal lymphadenopathy and pleural effusions. The predominance of the centrilobular ground-glass nodules over the septal lines help to distinguish PCH from PVOD, which shows predominant septal lines, and to a lesser extent cen-trilobular ground-glass nodules. Additionally, the lack of dilated pulmonary veins in PCH patients is particularly important to differentiate PCH/PVOD from other causes of post-capillary pulmonary hypertension, which similarly show smooth septal thickening and ground-glass opacities due to constriction/impedance of the pulmonary venous drainage.[10] Pharmacologic managements of PCH remains uncertain. Pulmonary vasodilator therapies such as calcium channel blockers and prostacyclin analogue have been proposed to improve hemodynamics and clinical course in PAH patients. Yet catastrophic pulmonary oedema has been reported following the initiation of pulmonary vasodilators in PCH patients. This unfavorable outcome can be explained by the increased transcapillary hydrostatic pressure due to dilated pulmonary muscular arteries and arterioles and fixed pulmonary venous resistance leading to massive transudation of fluid into the lung parenchyma. High-resolution CT chest examination is now recommended for PAH patients to exclude unsuspected radiologic evidence of PVOD or PCH before initiation of vasodilator therapy. Favorable responses have been reported to angiogenesis inhibitors such as doxycycline and imatinib. The only definite treatment of PCH is lung transplant or combined heart-lung transplantation in advanced disease.

CONCLUSION

Pulmonary capillary hemangiomatosis is a subclass of PAH group 1. Determining PCH as the underlying cause of pulmonary hypertension is crucial as medications used for PAH are relatively ineffective in cases of PCH. Vasodilator therapy should be avoided due to an increased risk of pulmonary oedema, respiratory distress, and death. So far, no definitive treatment of PCH apart from lung transplantation. To the best of our knowledge, this is the first report of ANEC secondary to dengue infection with a very fulminant course. With the passage of time and more awareness, the outcome of ANEC is improving but it.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Thapar V, Sarthalia M, Kumar GDP, Saini SK, Kumari S, Saini AK. Pulmonary capillary hemangiomatosis: an unusual cause of primary pulmonary hypertension in pediatric age group. Int J Contemp Pediatr 2023;10:1149-51.