



Case report

Pulmonary capillary haemangiomatosis – An unusual cause of hypoxia

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ABSTRACT

We describe the case of a 58-year-old man who presented with progressive dyspnoea on exertion and severe exertional hypoxia. There was a paucity of radiological findings, mild pulmonary hypertension, and no demonstrable anatomical shunt. Post mortem examination of lung tissue suggested a diagnosis of pulmonary capillary haemangiomatosis. The case is unusual in displaying few radiological findings. We postulate that the severe hypoxia was due to shunting through the abnormal capillary proliferations.

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1. Case report

A 58-year-old man presented with a 2-year history of progressive exertional dyspnoea. He had smoked 30 cigarettes daily, but had ceased smoking 10 years before presentation. There was a history of systemic hypertension treated with an angiotensin converting enzyme inhibitor. There was no other medical history of note and in particular no history of chronic liver disease or hereditary haemorrhagic telangiectasia. Physical examination was unremarkable with no signs of cardiac defeat, no cardiac murmurs and no adventitious sounds on auscultation of the chest. Chest X-ray showed no abnormality. Spirometry showed an FEV₁ of 3.52 l (110% predicted), and an FVC of 4.36 l (105% predicted), (FEV₁/FVC 81%). Carbon monoxide diffusing capacity was 49% predicted. High resolution CT scans showed no significant lung parenchymal abnormality. A CT pulmonary angiogram showed no thromboembolic disease. An isotope ventilation perfusion scan was unremarkable. A cardiopulmonary exercise test showed slightly reduced exercise tolerance with maximum oxygen consumption of 23.2 ml kg⁻¹ min⁻¹ (81% predicted). The exercise test also showed marked desaturation measured by pulse oximetry (95% at rest to 77% at peak exercise), low end-tidal partial pressure of carbon dioxide (maximum value of 32 mmHg) and high ventilatory equivalent for CO₂ (nadir value of 39), all suggesting ventilation perfusion mismatch or shunt. Contrast echocardiography showed no intra cardiac shunt and otherwise normal appearances. Cardiac

catheterisation showed a mean right atrial pressure of 5 mmHg, a mild increase in pulmonary artery pressure with mean of 26 mmHg, normal pulmonary capillary wedge pressure of 10 mmHg, cardiac output of 4.7 l min⁻¹, and cardiac index of 4.13 l min⁻¹ m⁻². Pulmonary vascular resistance was slightly elevated at 3.4 Wood Units.

He continued to deteriorate symptomatically. Twelve months later, spirometry was unchanged but transfer factor was 38% predicted. Arterial blood sampling breathing room air at rest showed p_aO₂ of 56 and p_aCO₂ of 34 mmHg. After 30 min breathing 98% O₂, the values were 128 and 34 mmHg respectively, giving a calculated shunt of approximately 27%.¹ A microaggregate study showed no intrapulmonary shunt. Repeat echocardiography showed normal left and right ventricular appearances and function. There was mild tricuspid regurgitation with an estimated right ventricular systolic pressure of 30 mmHg by Doppler. Magnetic resonance imaging of the heart was normal. Repeat high-resolution CT scan showed the impression of very subtle diffuse nodular opacities. Open lung biopsy showed scanty small foci of interstitial fibrosis, but no widespread pulmonary fibrosis. There were focal areas of capillary congestion within lobules, but no actual double layer of capillaries, or extension of capillaries into the interstitium, interlobular septa or bronchioles. Haemosiderin laden macrophages were prominent in alveolar spaces. Occasional small veins showed evidence of sclerosis, but there was no definite occlusion of veins and these changes were felt to be insufficient to make a diagnosis of pulmonary veno-occlusive disease (PVOD). There were some regions of increased cellularity in the alveolar walls, reminiscent of pulmonary capillary haemangiomatosis (PCH), but again, insufficient to confirm this diagnosis. Overall, there was some suspicion of

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PVOD or PCH from the biopsy, but the changes were subtle and felt to be non-diagnostic. A vasculitic process was also considered possible.

Warfarin and long-term oxygen therapy were commenced. On the basis that a vasculitic process was possible, a trial of methylprednisolone and pulsed cyclophosphamide was started. However, further deterioration occurred and he died approximately 3 years after initial presentation.

Post mortem examination of the heart and lungs was performed. There was biventricular hypertrophy. Sections of the heart demonstrated intraventricular septal hypertrophy with thickness of 20–22 mm. The circumferential thickness of the left ventricle was 16 mm (normal 13–15 mm). Right ventricular thickness was 6 mm (normal 3–5 mm). Histology of the lungs showed mild pulmonary arterial medial hypertrophy and congestion in the lower lobes. There were multiple focal capillary proliferations within alveolar and bronchiolar walls throughout all areas examined (Fig. 1). There was associated fresh haemorrhage but little evidence of old haemorrhage. Venous occlusive lesions were not identified. The capillary proliferations were felt to be sufficient to diagnose PCH.

PCH was first described by Wagenvoort² in 1978. It is a rare disorder of alveolar capillary proliferation and presents with features similar to idiopathic pulmonary hypertension or PVOD.³ There are fewer than 40 reported cases. The typical patient is aged 20–40 years and there is an equal sex incidence.⁴ Prognosis is poor and median survival is 3 years,⁵ with a typical clinical course of progressive, unrelenting symptoms of pulmonary hypertension.⁶ The hallmark of histology is proliferation of small capillaries within the interstitium and alveolar walls.² One report suggested considerable overlap histologically between PVOD and PCH with features of PCH present in cases of PVOD and vice versa.⁶

Common clinical features of PCH are dyspnoea and right heart failure. Haemoptysis, pleural effusion and acropachy occur less commonly.⁵ Clinically, PCH is difficult to distinguish from PVOD. Progressive dyspnoea and fatigue are common to both.⁸ Haemoptysis and haemorrhagic pleural effusions occur in 30% of PCH but not with PVOD.⁹

Our case was unusual in the paucity of radiological abnormalities. Only when the disease was very advanced did very subtle CT abnormalities become evident. Characteristic CT findings in PCH include diffuse bilateral thickening of the interlobular septae and small centrilobular, poorly circumscribed nodular opacities. Septal lines are present in both PCH and PVOD, but are more numerous in PVOD than PCH. Conversely, the presence of visible, better circumscribed ground glass opacities is more suggestive of PCH than PVOD.¹⁰

Hypoxia is not uncommon in PCH. In our patient, the cardiopulmonary exercise test and the high F_iO_2 study were physiologically in keeping with significant right to left shunt, but no shunt could be identified anatomically. A patent foramen ovale is unlikely to have been responsible as pulmonary hypertension was mild. We postulate that a small-vessel intrapulmonary shunt was responsible, with shunting occurring through the capillary proliferation present as part of the disease. In PCH elevated pulmonary arterial pressures and normal/low pulmonary capillary wedge pressures are seen.⁷ Pulmonary hypertension was unusually mild in our case, and it is possible that shunting through capillary channels resulted in relatively low pulmonary vascular resistance and pulmonary arterial pressures.

The diagnosis in our patient was not made ante-mortem, and empirical therapy proved futile. There are no randomised controlled trials to provide evidence for the safety and efficacy of

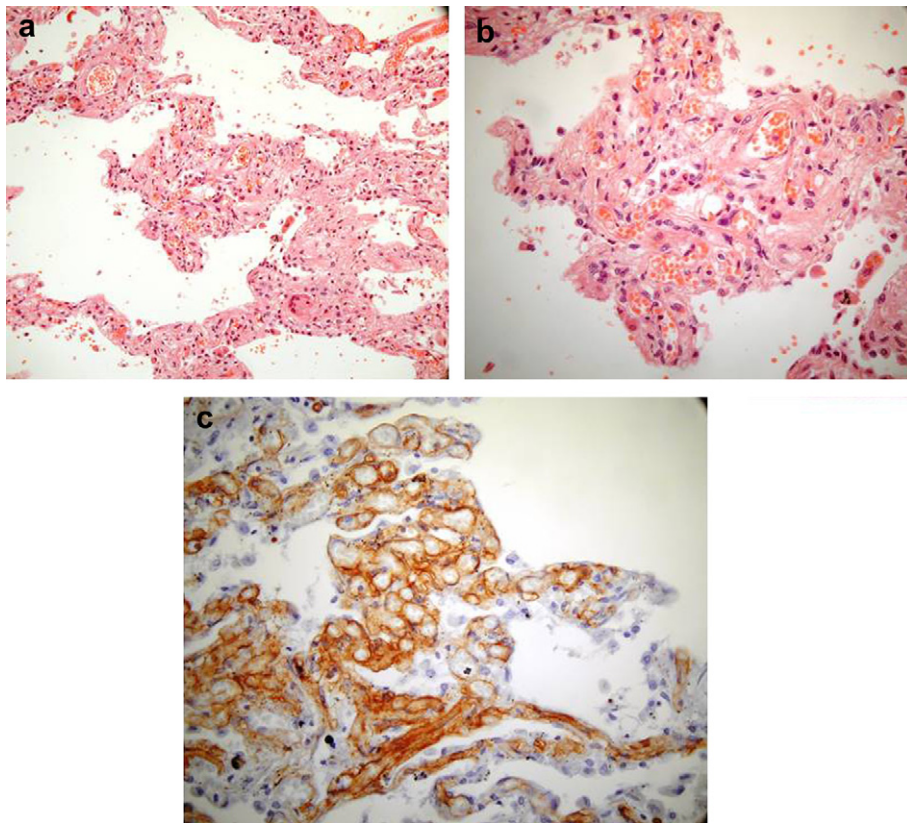


Fig. 1. a) Low power of the lung with expansion by multiple interlacing capillary channels filled with red blood cells. Haematoxylin and eosin $\times 200$ magnification. b) Higher power of the lung with expansion by multiple interlacing capillary channels filled with red blood cells. Haematoxylin and eosin $\times 400$ magnification. c) Lung section showing immunostaining with CD31. Several capillary layers/channels are visible within the lung interstitium.

pharmacological agents to treat PCH.⁸ The use of steroids and cyclophosphamide has proved ineffective in several cases,¹¹ although one case of PCH with atypical endotheliomatosis was successfully treated with doxycycline.¹¹ In contrast to idiopathic pulmonary arterial hypertension, in which epoprostenol therapy is effective, prostanoids show deleterious effects in PCH.⁵

In summary, we present a case of PCH showing no diagnostic radiological features despite otherwise severe disease. Our case illustrates the diagnostic and therapeutic difficulties associated with PCH.

Conflict of interest statement

None of the authors has any conflict of interest to declare.

References

1. Nunn JF. *Applied respiratory physiology*. 3rd ed. U.K.: Butterworths; 1993. 170–172.
2. Wagenvoort CA, Beetstra A, Spijker J. Capillary haemangiomas of the lungs. *Histopathology* 1978;**2**:401–6.
3. Kothari SS, Jagia P, Gupta A, Singh N, Ray R. Pulmonary capillary hemangiomas. *Circulation* 2009;**120**:352–4.
4. Eltorky MA, Headley AS, Winer-Muram H, Garrett HE, Griffin JP. Pulmonary capillary hemangiomas: a clinicopathologic review. *Ann Thorac Surg* 1994;**57**:772–6.
5. Almagro P, Julia J, Sanjaume M, Gonzalez G, Casalots J, Heredia JL, et al. Pulmonary capillary hemangiomas associated with primary pulmonary hypertension: report of 2 new cases and review of 35 cases from the literature. *Medicine* 2002;**81**:417–24.
6. Lantuejoul S, Sheppard MN, Corrin B, Burke MM, Nicholson AG. Pulmonary veno-occlusive disease and pulmonary capillary hemangiomas: a clinicopathological study of 35 cases. *Am J Surg Pathol* 2006;**30**:850–7.
7. Fernandez-Alonso J, Zulueta T, Reyes-Ramirez JR, Castillo-Palma MJ, Sanchez-Roman J. Pulmonary capillary hemangiomas as a cause of pulmonary hypertension in a young woman with systemic lupus erythematosus [letter]. *J Rheumatol* 1999;**26**:231–3.
8. Frazier AA, Franks TJ, Mohammed TL, Ozbudak IH, Galvin JR. Pulmonary veno-occlusive disease and pulmonary capillary hemangiomas. *Radiographics* 2007;**27**:867–82.
9. Ito K, Ichiki T, Ohi K, Egashira K, Ohta M, Taguchi K, et al. Pulmonary capillary hemangiomas with severe pulmonary hypertension. *Circ J* 2003;**67**:793–5.
10. Dufour B, Maitre S, Humbert M, Capron F, Simonneau G, Musset D. High resolution CT of the chest in four patients with pulmonary capillary hemangiomas or pulmonary venoocclusive disease. *AJR Am J Roentgenol* 1998;**171**:1321–4.
11. Ginns LC, Roberts DH, Mark EJ, Bruschi JL, Marler JJ. Pulmonary capillary hemangiomas with atypical endotheliomatosis, successful antiangiogenic therapy with doxycycline. *Chest* 2003;**124**:2017–22.