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Case report

Unsuspected pulmonary alveolar proteinosis in a patient with a slow resolving pneumonia: A case report

Stephanie Main [a], Vikas Somani [a], Angus Molyneux [b], Milan Bhattacharya [a], Rabinder Randhawa [a], Ajikumar Kavidasan [a,*]

[a] Department of Chest Medicine and Lung Physiology, Milton Keynes Hospital NHS Foundation Trust, Standing Way, Eaglestone, Milton Keynes, Buckinghamshire MK6 5LD, UK
[b] Department of Cellular Pathology, Milton Keynes Hospital NHS Foundation Trust, Buckinghamshire, UK

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ABSTRACT

Pulmonary Alveolar Proteinosis (PAP) is a rare condition with an incidence of one in two million and is classified as primary or secondary. This is the first reported case presenting as a slow resolving pneumonia.

1. Introduction

A 79-year-old lady of Nigerian origin living in the UK presented with a right basal pneumonia. She was in remission from chronic lymphocytic leukaemia, diagnosed in 1999.

She had a slow to resolve right basal consolidation (Fig. 1), despite multiple courses of antibiotics. Her CT scan showed a large area of irregular consolidation in the middle lobe, extending into the upper lobe (Fig. 2).

The patient was further investigated with a bronchoscopy, showing no endobronchial lesion. A blind endobronchial biopsy and bronchoalveolar lavage did not show any features to support the diagnosis of malignancy or atypical infection. She underwent a CT guided biopsy of the middle lobe consolidation. This excluded malignancy, however showed features of Pulmonary Alveolar Proteinosis (PAP) (Fig. 3).

2. Discussion

Rosen et al. first described Pulmonary Alveolar Proteinosis, a rare diffuse lung disease [1,2], in 1958 [3]. There is a large intra-alveolar accumulation of surfactant [4] with lipoproteinaceous material [2,3,5,6], disrupting the transfer of oxygen [1,7].

The epidemiology suggests PAP is as rare as one case in every two million [5] and more common in males by 3:1 [8]. The onset is in the third or fourth decade.

PAP can be primary or secondary, however most cases are primary [5]. The classification includes two congenital forms and there are suggestions that PAP may be part of a syndrome [5,9].

This presentation of a patient with an unresolving pneumonia and diagnosis of PAP is probably the first in the literature. The diagnosis is most likely related to the patient's chronic lymphocytic leukaemia (CLL) and thus is secondary PAP.

The incidence of PAP in a person with a haematological malignancy (usually myeloid) is 5.3% [5] and therefore the case of PAP in this patient is likely to be even less common as the leukaemia is leucocytic.

Patients with PAP usually present with dyspnoea [1,5] and a cough [1,2]. Approximately 75% of patients are smokers at diagnosis [1,2,8]. Blood tests can highlight a high lactate dehydrogenase (LDH) and raised tumour markers. Spirometry shows a restrictive pattern [1,2,8], although can be obstructive in smokers. Blood gases can predict the clinical course, for instance a PaO_2 of over 9.3 kPa can mean a patient is more likely to recover [5].

Imaging shows non-specific bilateral patchy consolidation [1,2,5] and approximately 20% have unilateral abnormalities.

* Corresponding author. Tel.: +44 1908 660033.
E-mail address: Ajikumar.Kavidasan@mkhospital.nhs.uk (A. Kavidasan).

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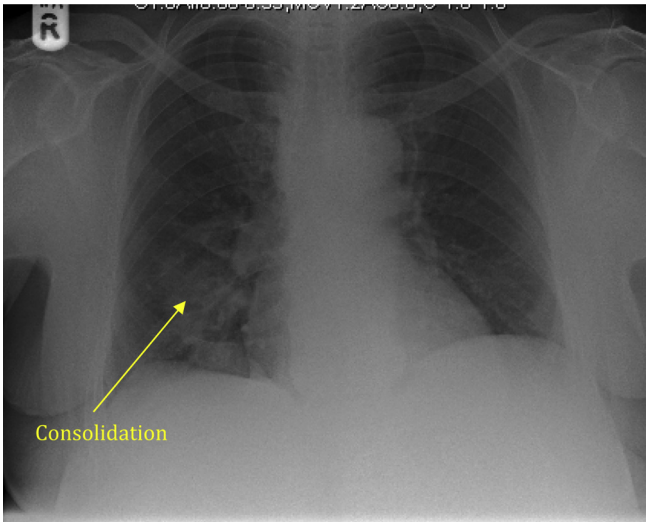

Fig. 1. Chest X-ray illustrating right basal consolidation.

The diagnosis is made from interpreting CT images and lung lavage specimens. A tissue biopsy may not always yield the diagnosis if the consolidation is patchy.

The gold standard for treatment of primary PAP is whole lung lavage [1,4,5]. There have been various treatments used in the past, such as steroids, streptokinase and potassium iodide [5]. There is a report of one patient improving in response to ambroxol, despite this causing an increased production of surfactant [5]. One alternative treatment is aerolsolised trypsin, although this can lead to allergic reactions and proteolytic damage [5,7]. Another is granulocyte-macrophage colony-stimulating factor (GM-CSF), which can clear surfactant and be used in patients resistant to lung lavage [1,4]. However, this can be expensive and the patient may go into cardiac failure. Three trials have also shown that patients can relapse after this treatment, although there is a benefit in some patients [10–13]. Gene therapy may be a potential future treatment in congenital PAP.

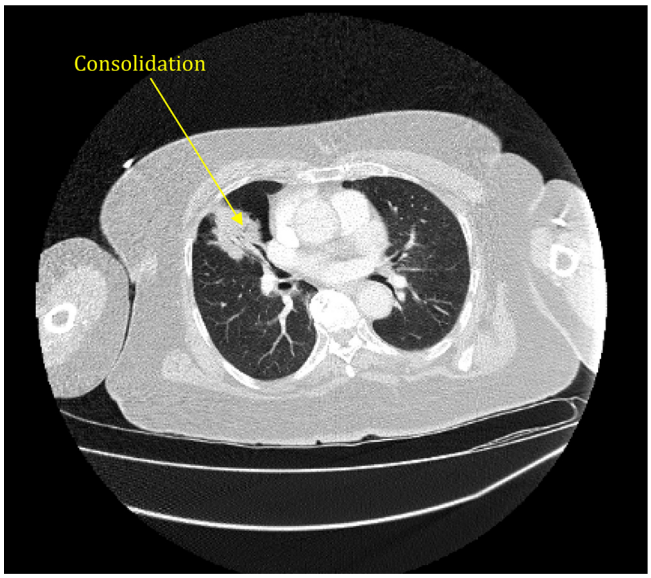

Fig. 2. CT scan showing a large area of irregular consolidation in the middle lobe extending into the upper lobe.

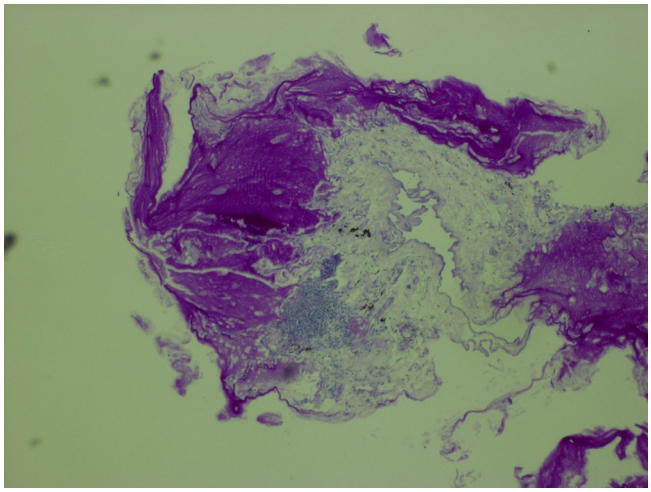

Fig. 3. Lung Biopsy (*Periodic acid Schiff stain*): Alveolar spaces are filled by homogenous faintly eosinophilic material, staining positive on PAS stain and resistant to diastase digestion. The lung interstitium shows lymphatic dilation and a small collection of lymphocytes. The features are those of alveolar proteinosis.

PAP is classified as secondary if related to a medical condition such as a malignancy [2] (particularly myeloid leukaemia) [1,3,6,8,14], pulmonary infection, immunodeficiency or as a result of the inhalation of chemicals [1,2,8,14]. Secondary PAP accounts for 5–10% of all cases [1,2]. One study shows a patient with secondary PAP receiving GM-CSF had no change in their condition, one improved with stem cell transplantation and the other with antifungal treatment [6]. Another did well with no treatment intervention [6].

The pathophysiology of secondary PAP in those with a haematological malignancy is that alveolar macrophages are abnormal [6,8,14] as they originate from the malignant clone and have malfunctioning GM-CSF transduction [6,15]. This therefore leads to a build up of surfactant [16]. The mainstay of treatment is managing the underlying malignancy [1,6,9]. Whole lung lavage and GM-CSF therapy are options.

In conclusion, the literature mainly discusses treatments for primary and congenital PAP. As secondary PAP is extremely rare, there is no specific recommended therapy. Treatment is centred on treating the underlying cause [1,5,6] and providing symptomatic relief.

The prognosis of PAP can be worse with atypical infections such as pneumocystis carinii [2], mycobacterium and viruses [1,5,8]. This leads to increased morbidity [1] and mortality for patients with secondary PAP [6]. The accumulation of surfactant encourages microorganisms to grow and the susceptibility is further increased by abnormal macrophages [6,7]. The use of steroids should therefore not be encouraged [5]. Ultimately, the prognosis of secondary PAP is dependent on the course of the underlying disease.

Conflict of interest statement

There is no conflict of interest.

References

[1] Loachimescu OC, Kavuru MS. Pulmonary alveolar proteinosis. Chronic Respir Dis 2006;3(3):149–59.
[2] Presneill JJ, Nakata K, Inoue Y, Seymour JF. Pulmonary alveolar proteinosis. Clin Chest Med 2004;25:593–613.
[3] Lakshminarayan S, Schwarz MI, Stanford RE. Unsuspected pulmonary alveolar proteinosis complicating acute myelogenous leukemia. Chest 1976;69:433–5.
[4] Beccaria M, Luisetti M, Rodi G, et al. Long-term durable benefit after whole lung lavage in pulmonary alveolar proteinosis. Eur Respir J 2004;23(4):526–31.

[5] Shah PL, Hansell D, Lawson PR, Reid KBM, Morgan C. Pulmonary alveolar proteinosis: clinical aspects and current concepts on pathogenesis. Thorax 2000;55:67–77.
[6] Chung JH, Pipavath SJ, Myerson DH, Godwin JD. Secondary pulmonary alveolar proteinosis: a confusing and potentially serious complication of hematological malignancy (original research). J Thorac Imaging 2009;24(2):115–8.
[7] Cheng SL, Chang HT, Lau HP, Lee LN, Yang PC. Pulmonary alveolar proteinosis: treatment by bronchofiberscopic lobar lavage. Chest 2002;122(4):1480–5.
[8] Seymour JF, Presneill JJ. Pulmonary alveolar proteinosis progress in the first 44 years. Am J Respir Crit Care Med 2002;166:215–35.
[9] Holbert JM, Costello P, Li W, Hoffman RM, Rogers RM. CT features of pulmonary alveolar proteinosis. AJR 2001;176:1287–94.
[10] Moreland A, Kijsirichareanchai K, Alalawi R, Nugent K. Pulmonary alveolar proteinosis in a man with prolonged cotton dust exposure. Respir Med CME 2011;4(3):121–3.
[11] Greenhill SR, Kotton DN. Pulmonary alveolar proteinosis: a bench-to-bedside story of granulocyte-macrophage colony-stimulating factor dysfunction. Chest 2009;136:571–7.
[12] Thind GS. Acute pulmonary alveolar proteinosis due to exposure to cotton dust. Lung India 2009;26:152–4.
[13] Das M, Salzman GA. Pulmonary alveolar proteinosis: an overview for internists and hospital physicians. Hosp Pract (Minneap) 2010;38:43–9.
[14] Ishii H, Trapnell BC, Tazawa R, et al. Comparative study of high-resolution CT findings between autoimmune and secondary pulmonary alveolar proteinosis. Chest 2009;136:1348–55.
[15] Tekgűl S, Bilaceroglu S, Ozkaya S, et al. Pulmonary alveolar proteinosis and superinfection with pulmonary tuberculosis in a case. Respir Med Case Rep 2012;5:25–8.
[16] Yildiz T, Ates G, Bogatekin G, Ozmen CA, Mizrak B. A case of idiopathic pulmonary alveolar proteinosis. Respir Med CME 2010;3(4):267–9.