

Pulmonary alveolar proteinosis — a case report and review

J Ker

MB ChB, MMed (Internal Medicine)

Department of Physiology
University of Pretoria and Pretoria Heart Hospital

Introduction

The radiological detection of pulmonary air space consolidation opens up a broad differential diagnosis.¹ In various pathological conditions alveoli may be filled with fluid, pus, blood, tumour, gastric contents or a phospholipoproteinaceous material.^{1,2} The latter condition is known as pulmonary alveolar proteinosis.² I report on a case of acquired pulmonary alveolar proteinosis and give a short review of this fascinating disorder.

Case report

A 51-year-old caucasian male patient presented with a 2-year history of progressive dyspnoea with a cough, productive of a yellow sputum. The patient had smoked 20 cigarettes a day for the past 30 years. One year ago the patient underwent a lung biopsy and a histological diagnosis of pneumonia was made. Both his occupational and recreational history did not reveal any risk factors for pulmonary disease. Clinical examination revealed cyanosis and bilateral inspiratory crackles.

The chest radiograph demonstrated extensive, bilateral alveolar consoli-

ation. A high-resolution computed tomography (HRCT) scan confirmed widespread, bilateral air space consolidation, with thickened interlobular septae, producing the so called 'crazy paving' pattern (Fig. 1). The patient was subjected to another thoracoscopic lung biopsy and this time the histological examination revealed alveoli and terminal bronchioles filled with granular, eosinophilic, proteinaceous material (Fig. 2) with preservation of the alveolar architecture. The

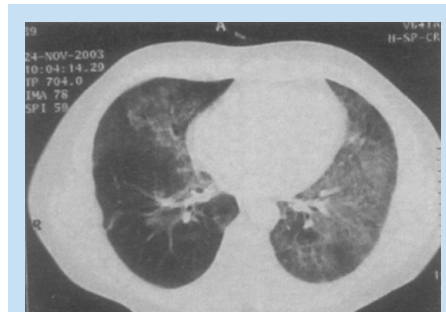


Fig. 1. Widespread, bilateral areas of ground glass opacities with inter- and intralobular septal thickening leading to a 'crazy paving' pattern.

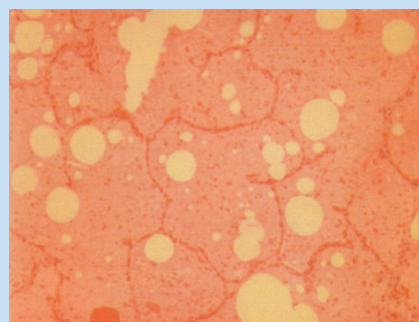


Fig. 2. Alveoli filled with an eosinophilic, granular material, staining with periodic acid Schiff (PAS). Note the preservation of the alveolar architecture.

patient was treated by whole-lung lavage, followed by a 4-week trial of subcutaneous granulocyte-macrophage colony-stimulating factor (GM-CSF). The trial of GM-CSF failed, however, and the patient is currently being treated by monthly whole-lung lavages.

Discussion

Pulmonary alveolar proteinosis (PAP) is a rare syndrome that was first described by Rosen *et al.* in 1958.³ This disorder is characterised by abnormal intra-alveolar surfactant accumulation⁴ with a variable clinical course, ranging from respiratory failure to spontaneous resolution.⁵

Three distinct clinical forms of PAP can be distinguished:³⁻⁵ congenital, secondary, and primary (idiopathic) pulmonary alveolar proteinosis.

Congenital PAP is a heterogeneous group of disorders caused by mutations in surfactant proteins B or C, or the receptor for GM-CSF.^{3,6,7} Secondary PAP can develop in association with various conditions, such as immunodeficiency states, acute silicosis and other inhalational syndromes, haematologic malignancies and myelodysplastic syndromes.^{4,5} In all of these conditions there is a reduction in the number and/or functional impairment of alveolar macrophages.⁵ More than 90% of all cases of PAP occur as the primary (idiopathic) form.⁴ Recent studies have led to the current concept that primary PAP is an autoimmune disease, which produces neutralising immunoglobulin G (IgG) antibodies against GM-CSF.⁸

Surfactant is normally cleared by uptake into alveolar macrophages and GM-CSF is critical for this process, as it is a cytokine stimulating the production of alveolar macrophages by

the bone marrow. Therefore, all three forms of PAP share the feature of an impairment in the number and/or activity of alveolar macrophages leading to the alveolar accumulation of surfactant.¹⁻⁸

The most common symptoms are dyspnoea and cough, and because of the impaired alveolar macrophage function these patients are susceptible to pneumonia.^{2,4,5} Pulmonary function tests usually reveal a restrictive defect with a reduction in lung volume and diffusion capacity.²

The radiological feature is that of a non-specific pattern of air space consolidation, which is usually bilateral and patchy and can be very extensive.² It has been reported that in up to 50% of cases this patchy consolidation is peri-hilar, giving a 'bat's wing' pattern.² However, the consolidation may also be predominantly peripheral or basal in distribution.² HRCT demonstrates patchy, ground-glass opacifica-

tions with superimposed inter, and intralobular septal thickening, and this pattern is commonly referred to as 'crazy paving'.⁵

Open-lung biopsy is the gold standard for the diagnosis and reveals alveoli filled with granular, eosinophilic material that stains with periodic acid Schiff (PAS)⁵ with preservation of the alveolar architecture.²

In secondary PAP treatment depends on the underlying cause. Successful lung transplantation has been reported in cases of congenital PAP.⁵ Whole-lung lavage remains the standard of care for primary PAP, although some patients may respond to subcutaneous GM-CSF at a dose of 5 µg/kg of body weight per day for 6-12 weeks.⁵

The natural history of PAP can follow one of three pathways: spontaneous improvement, stable with persistent symptoms, or progressive deterioration.⁵

References

1. Manheimer E. Chest roentgenography for cardiovascular evaluation. In: Walker HK, Hall WD, Hurst JW, eds. *Clinical Methods. The History, Physical and Laboratory Examinations*. New York: Butterworth, 1990: 188.
2. 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.
3. Rosen SH, Castleman B, Liebow AA. Pulmonary alveolar proteinosis. *N Engl J Med* 1958; **258**: 1123-1142.
4. Seymour JF, Presneill JJ. Pulmonary alveolar proteinosis. Progress in the first 44 years. *Am J Respir Crit Care Med* 2002; **166**: 215-235.
5. Trapnell BC, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. *N Engl J Med* 2003; **349**: 2527-2539.
6. Teja K, Cooper PH, Squires JE, Schnatterly PT. Pulmonary alveolar proteinosis in four siblings. *N Engl J Med* 1981; **305**: 1390-1392.
7. Noguee LM, deMello DE, Dehner LP, Colten HR. Deficiency of pulmonary surfactant protein B in congenital alveolar proteinosis. *N Engl J Med* 1993; **328**: 406-410.
8. Kitamura T, Tanaka N, Watanabe J. Idiopathic pulmonary alveolar proteinosis as an autoimmune disease with neutralizing antibody against granulocyte-macrophage colony-stimulating factor. *J Exp Med* 1999; **190**: 875-880.