CASE REPORT

Pulmonary alveolar microlithiasis: report of two brothers with the same illness and review of literature

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SUMMARY

Pulmonary alveolar microlithiasis (PAM) is a rare lung disease characterised by extensive deposition of calpospherites within the alveoli. The disease is caused by mutations in the gene SLC34A2 encoding sodium-dependent phosphate co-transporter. It is an autosomal recessive disease with sporadic cases worldwide. Most patients are asymptomatic at the time of diagnosis. It may progress slowly over years to respiratory failure and cor pulmonale.

BACKGROUND

This is a very rare occasion to have two brothers affected by this illness. It will contribute to the understanding of the general as well as chest physicians of the genetics, pathophysiology, prognosis and current treatment of this condition.

CASE PRESENTATION

Case 1

A 45-year-old male patient presented with 10-day history of dry cough and mild shortness of breath not responding to empirical course of antibiotics. Clinical examination was unremarkable. His full blood counts and biochemistry results were normal. However, his chest X-ray showed bilateral micronodular calcifications mainly in mid and lower zones, typical for pulmonary alveolar microlithiasis (PAM; [figure 1](#)). High resolution CT scan of the chest showed the classical features of PAM ([figure 2](#)). Pulmonary function tests showed mildly restrictive pattern, with normal O₂ saturation. The ECG was normal. Bronchoscopy did not show any intrabronchial lesion. Bronchial lavage and brush cytology revealed shedded bronchial epithelium, mixed with inflammatory cells and occasional metaplastic bronchial epithelium. He was given a course of inhalers with open clinic appointments.

Case 2

A 49-year-old man, the older brother of the first patient, was previously diagnosed as PAM at the age of 29 years during a routine chest X-ray survey for military personnels. He presented with cough productive of greenish sputum and dyspnoea. He was a long-term smoker. He looked plethoric with mild cyanosis.

Chest auscultation revealed bibasal coarse crackles. The breath sounds were of vesicular breathing with prolonged expiratory phase. His haemoglobin was high at 20 g/dL with raised

haematocrit of 56.6%. His inflammatory markers and biochemistry results were normal. The pulmonary function tests showed restrictive ventilatory defect and low O₂ saturation at 91%. Arterial blood gas showed type 2 respiratory failure with mild CO₂ retention.

The chest X-ray showed bilateral calcific reticulo-nodular shadowing more prominent in the lower and middle zone, typical of PAM ([figure 3](#)). Echocardiogram revealed elevated pulmonary pressure. He was diagnosed with chronic obstructive pulmonary disease due to longstanding smoking. He was given a course of antibiotics, a short course of oral steroids with inhalers. He was strongly advised to stop smoking.

DISCUSSION

PAM is a rare autosomal recessive disease characterised by widespread deposition of microliths in the alveoli.¹ It is caused by mutations of the solute carrier, the gene SLC34A2 which encodes a type IIb sodium-dependent phosphate co-transporter² which is only found in the surfactant secreting cells, type II pneumocytes.³ It is also expressed in other tissues where it plays a major role in the homeostasis of inorganic phosphate.⁴ The mutations lead to reduced uptake of phosphates by these cells and the deposition of innumerable calpospherites in the alveolar spaces, a process aided by the chelating action of calcium in the extracellular fluid.⁵ Despite heavy calcific depositions, no abnormalities of calcium metabolism have been reported.⁶

Figure 1 Chest X-ray showing diffuse nodular calcifications in both lung fields with pleural involvement.

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Figure 2 High-resolution CT scan of the chest showing the classical crazy-paving appearance of pulmonary alveolar microlithiasis.

The disease can be found worldwide⁷ as sporadic as well as inherited cases, however, the familial pattern was noted predominantly in Mediterranean countries.⁸ While men

Figure 3 Chest X-ray showing bilateral calcified reticulonodular shadows more prominent in middle and lower zones.

predominate in sporadic cases,⁹ there is no sex predilection in the familial type of the disease.^{9,10}

Most cases are asymptomatic at the time of diagnosis and are usually found incidentally during routine chest X-ray examinations for other purposes.^{10–12} Symptoms if present, are mainly dry cough, shortness of breath and non-specific chest pains.¹¹ Clinical examination is usually unremarkable early in the disease. The results of bloods and biochemistry are usually normal. Pulmonary function tests vary from normal-to-mild restrictive pattern¹¹ as shown in our cases. The chest X-ray is characteristic, revealing a sandstorm appearance; a picture of sand-like calcific micronodulation bilaterally predominant in middle and lower zones.^{1,9–11} The high-resolution CT scan of the chest shows crazy-paving pattern with ground glass appearance, pleural and subpleural calcification, interseptal thickening and classical calcific micronodules.^{13–15} Open lung biopsy is not feasible in all cases, however, the bronchoalveolar lavage¹⁶ and/or transbronchial biopsy¹⁷ are less invasive and can be performed to confirm the diagnosis. Occasionally microliths can be found in the sputum.¹⁸ The course of the disease is variable. In

some patients it remains static, while others develop progressive deterioration of the lung functions with an end-stage respiratory failure and cor pulmonale¹⁹ and may end up with palliative treatment in the absence of donors. Generally, smokers have more severe clinical manifestations than non-smokers.² Disease progression can be monitored by serial measurements of serum levels of surfactant which is elevated in an active disease and the levels tend to rise with the progression of the illness. Surfactant proteins A and D can be used to monitor the activity as well as the progression of the disease.²⁰ Various therapies have been tried including steroids, hydroxychloroquine, disodium etidronate^{21–23} without significant effects on the course of the disease. The only definitive treatment at present is lung transplantation.^{24–26}

Learning points

- Pulmonary alveolar microlithiasis is an autosomal recessive disease.
- It is usually diagnosed incidentally during a routine chest X-ray examination.
- It may take decades before the symptoms appear.
- It may end up in respiratory failure and cor pulmonale.
- Other causes of multiple micronodular shadowing must be investigated.

Contributors All authors contributed in writing and reviewing the cases.

Competing interests None.

Patient consent Obtained.

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