

## Breathless with stones!

**Uma Devaraj, Priya Ramachandran, Uma Maheswari**

Department of Pulmonary Medicine, St. John's Medical College and Hospital, Bengaluru, Karnataka, India

**Address for correspondence:** Dr. Uma Devaraj, 3<sup>rd</sup> Floor, PFT Laboratory, Oncology Block, St. John's Medical College, Sarjapur Road, Bengaluru - 560 034, Karnataka, India. E-mail: druma.devaraj@gmail.com

### CASE REPORT

A 48-year-old male presented with gradual onset of breathlessness and cough, progressing over the past 4 years to symptoms suggestive of respiratory failure for the past 2 months. A farmer by occupation, he had a smoking history of 11 pack-years. On examination, he had a body mass index of 17.4 kg/m<sup>2</sup> and Grade 3 clubbing. He was hemodynamically stable but had tachypnea with oxygen saturation of 78% on room air. Respiratory system examination revealed bilateral fine crackles. He was on antituberculosis therapy for 5 months, started elsewhere based on his chest X-ray (CXR) findings, although sputum was negative for acid-fast bacilli. Laboratory evaluation

showed normal blood counts, serum calcium of 9.1 mg/dl, and serum phosphorous of 3.5 mg/dl. Spirometry showed severe restrictive defect. Abdominal ultrasound was normal. His chest radiographic and high-resolution computed tomographic (HRCT) images are shown in Figures 1 to 3.

### QUESTIONS

1. Question 1: What is the classical radiological finding seen on the CXR?
2. Question 2: What is the named radiological sign seen in the HRCT?
3. Question 3: What is the diagnosis?

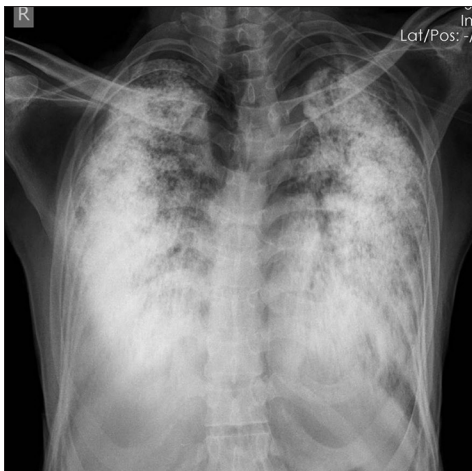


Figure 1: Chest X-ray



Figure 2: Computed tomography showing chest, lung window

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**Figure 3:** Computed tomography showing chest, mediastinal window

## ANSWERS

1. The CXR shows bilateral, profuse, 1–5 mm, calcified micronodules in all the lung zones described as “sandstorm” appearance [Figure 1]
2. The sharp contrast between the dense alveolar calcification of the lung on one side of the radiolucent pleura and the rib cage on the other side gives rise to the characteristic “black pleura sign.” The HRCT also shows dense calcified mediastinal lymphadenopathy [Figure 3], thickened intra- and inter-lobular septae, and dense calcifications [Figure 2]
3. A diagnosis of pulmonary alveolar microlithiasis (PAM) was made based on the classical calcified micronodules and black pleura sign.<sup>[1]</sup>

Apart from few pleural calcifications, the patient did not have any other organ involvement. Although familial pattern of disease is known, none of the five sisters of the patient had the similar illness. Fiber-optic bronchoscopy with bronchoalveolar lavage showed cloudy solution with grainy particles, and transbronchial lung biopsy revealed alveoli filled with calcific microspherules. He was discharged on domiciliary oxygen and was advised to enlist for lung transplantation.

## DISCUSSION

PAM is an autosomal recessive heritable disorder, due to mutation in the SLC34A2 (solute carrier family 34 member 2) gene.<sup>[2]</sup> There are 13 exons in the SLC34A2 gene; the first exon is noncoding and the other 12 exons code for a Type 2 sodium phosphate cotransporter, a 690-amino acid protein. This cotransporter controls the uptake of phosphate released from phospholipids in antequated surfactant. Mutations of the SLC34A2 gene result in altered Type IIb cotransporter function, leading to reduced cellular uptake of phosphate. This inability to clear phosphate from the alveolar space results in the formation of intra-alveolar microliths.

This is a rare disorder, with <1100 cases reported worldwide.<sup>[3]</sup> Most cases have been reported from Asia, Europe, and America with highest number of cases from Turkey. As of 2015, eighty cases of PAM have been reported from India. Although PAM has been reported in all age groups from newborns to elderly, the most frequent reports are in the second and third decades. Although no sex predilection is seen in the distribution of PAM,<sup>[4]</sup> a slight male predominance has been reported.<sup>[3]</sup>

The clinical symptomatology and course is variable, from some patients being asymptomatic, with minimal progression of the disease, to some patients proceeding to develop pulmonary fibrosis and respiratory failure. Some patients are incidentally detected on the chest radiograph. Many patients are misdiagnosed with pulmonary tuberculosis or sarcoidosis.<sup>[5]</sup>

The alveoli filled with immeasurable diffuse calcospherites (microliths made of calcium and phosphorus) are seen as classic sandstorm appearance in the chest radiograph.<sup>[6,7]</sup> Profuse calcified micronodules, ground-glass opacities, intra- and inter-lobular septal thickening, pleural and subpleural calcification, and enlarged calcified mediastinal lymph nodes are typical radiological findings seen in HRCT.<sup>[8,9]</sup>

Larger calcifications have been reported in the extrapulmonary organs such as pericardium, gall bladder, medullary nephrocalcinosis, prostate, and testicles.<sup>[3]</sup>

There are few differential diagnoses when such micronodular calcification is seen in the CXR. Occupational lung diseases such as silicosis, coal workers’ pneumoconiosis, stannosis, and baritosis and infectious causes such as healed varicella pneumonia are to be considered, but none of the conditions are known to cause such extensive calcification as that seen in PAM.

Till date, there are no curative treatment options available for this illness. Systemic steroids, etidronate (bisphosphonate), and repeated bronchopulmonary lavage have been tried and shown to be ineffective treatment options.<sup>[4]</sup> Domiciliary oxygen supplementation is required with onset of respiratory failure, and patients may benefit from single or double lung transplant.<sup>[5,10]</sup>

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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