

Calcified pulmonary consolidations in pulmonary alveolar microlithiasis: Uncommon computed tomographic appearance of a rare disease

Sir,

Pulmonary alveolar microlithiasis (PAM) is a rare disease of unknown etiology that affects young adults and is characterized by intra-alveolar accumulation of microliths consisting of calcium phosphate.^[1,2] Although the etiology remains unclear, PAM is considered an autosomal recessive disease caused by mutations of SLC34A2 gene, which encodes a sodium-dependent phosphate cotransporter.^[3] Familial occurrence has been described.^[4] It is characterized by a clinical-radiological dissociation. The disease is usually slowly progressive and may worsen over time with the development of respiratory failure and cor-pulmonale. The classical radiographic picture is one of the numerous symmetrical micronodular shadows obliterating the pulmonary vasculature, heart, and the diaphragm, described as a “sand-storm” appearance along with a thin area of linear hyperlucency along the ribs, the “black pleura” sign. This radiological picture is considered virtually diagnostic precluding the need for a biopsy.^[5-9] Calcified pleural has been described in addition to the characteristic parenchymal involvement.^[10] Dense confluent calcifications causing consolidation of the lungs in the lower lobes are however unusual. We recently observed this uncommon radiological manifestation of PAM on high-resolution computed tomographic (HRCT) scan in a 27-year-old nonsmoker female patient.

The patient presented with the complaints of exertional shortness of breath and dry cough of 1-year duration. There was no history of fever, chest pain, hemoptysis, or weight loss. Examination revealed clubbing and bilateral basal end-inspiratory crackles. Blood counts, serum biochemistry, and urine analysis were within normal limits. Chest radiograph (posteroanterior view [Figure 1]) revealed bilateral symmetrical reticulonodular shadows with a relative sparing of the upper zones and without any obvious loss of lung volume. The nodular shadows were confluent at places with density suggesting calcification with ill-defined cardiac borders and diaphragm (“sand-storm appearance”). Contrast-enhanced HRCT of the thorax showed the presence of bilateral upper lobe ground glass attenuation with diffuse calcification along the interlobular and intralobular septae, and in the mediastinal pleura. The pulmonary artery was enlarged [Figure 2]. The lower lobes showed symmetrical, dense confluent calcified opacities, more so in the posterior regions causing a complete consolidation. A thin area of linear hyperlucency along the ribs, the “black pleura” sign was visible [Figure 3]. Serology for HIV was nonreactive.

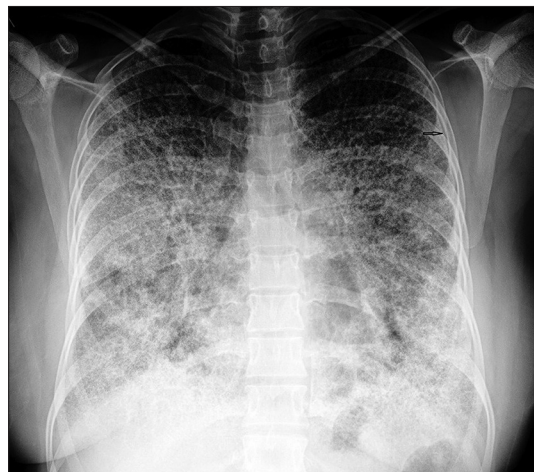


Figure 1: Chest radiograph (postero-anterior view) showing bilateral symmetrical reticulonodular shadows with a relative sparing of the upper zones and without any obvious loss of lung volume. The nodular shadows were confluent at places with density suggesting calcification obliterating the cardiac borders and diaphragm (“sand-storm” appearance). A thin area of linear hyperlucency along the ribs, the “black pleura” sign is seen on the left side (arrow)

Mantoux test was negative. Pulmonary function test studies revealed severe restrictive lung disease with a forced vital capacity (FVC) of 1.4 L (43% predicted) and a forced expiratory volume in 1 s (FEV₁) of 1.3 L (46% predicted). The FEV₁/FVC ratio was 93%. The total lung capacity was 2.25 L (51% predicted). Diffusing capacity of the lung for carbon monoxide was 29%. The patient desaturated on a 6-minute walk test with the pulse oximetry showing a fall in arterial oxygen saturation from 94% at rest to 86% on walking. The 6-minute walk distance was 60 m. Serum Angiotensin-converting enzyme was elevated (99 U/ml). Fiberoptic bronchoscopic examination revealed a normal appearing tracheobronchial tree. Bronchoalveolar lavage (BAL) fluid was negative for acid-fast bacilli and other pathogens with an unremarkable cytology. A transbronchial lung biopsy from the right lower lobe was noncontributory due to inadequate tissue. Two-dimensional and color Doppler echocardiography showed normal wall motion, chamber sizes, and cardiac valves, a left ventricular ejection fraction of 61% and an estimated high mean pulmonary artery pressure of 39 mm Hg.

The radiological appearance narrowed down the differential diagnosis to PAM and metastatic pulmonary calcification. Calcium metabolism indices were investigated that showed normal serum calcium and phosphorus levels. Serum



Figure 2: Contrast-enhanced high-resolution computed tomography of the thorax (mediastinal window) showing the presence of bilateral upper lobes ground glass attenuation with diffuse calcification along the interlobular and intralobular septae, and in the mediastinal pleura (arrow). The pulmonary artery is enlarged. The “black pleura” sign is seen on the right side (arrow)

Vitamin D 25-hydroxy levels were reduced (17 ng/ml), and parathormone level was elevated (121.70 pg/ml). The absence of any obvious etiology and hypercalcemia and a radiological picture on plain chest radiograph and HRCT scan that was pathognomonic for PAM ruled out metastatic calcification in the present case. The hyperparathyroidism observed in our case was likely secondary to hypovitaminosis D. A diagnosis of PAM was thus established on clinical and radiological grounds.

PAM is a rare autosomal-recessive pulmonary disease characterized by intra-alveolar accumulation of microliths consisting of calcium phosphate.^[1] It is found worldwide though it predominates in Italy, Turkey, and the USA.^[7] The hallmark of this disease is a clinical-radiological dissociation with few symptoms at least in the initial stages. The disease may be discovered at any age from childhood to middle age and is most often diagnosed incidentally during radiography of the chest for other reasons.^[6] In symptomatic patients, the usual presentation is with exertional dyspnea, nonproductive cough, and chest pain. The disease is usually slowly progressive. Chest radiographic findings in PAM are a bilateral diffuse, sand-like micronodular infiltration, particularly in the middle and lower lung zones that may be confluent leaving a thin area of linear hyperlucency along the ribs or mediastinum caused by small, thin-walled subpleural cysts, the “black pleura” sign.^[1] Described as a “sand-storm” appearance obliterating the heart and the diaphragms, this picture is highly characteristic and together with the clinical picture is sufficient for a diagnosis. Common HRCT findings are ground-glass opacities, subpleural linear calcifications, subpleural cysts, parenchymal nodules, and calcification along the interlobular septa.^[6] Dense and confluent calcification to form consolidations as seen in the present case is uncommon.^[9] As calcium metabolism is normal, serum calcium, phosphate, and parathyroid hormone remain within normal range.^[11]



Figure 3: Contrast-enhanced high-resolution computed tomography of the thorax (mediastinal window) showing symmetrical, dense calcified consolidation in the posterior basal segments of both lower lobes. The “black pleura” sign is seen at the lung bases on both sides (arrows)

The differential diagnosis of PAM includes metastatic pulmonary calcification related to chronically elevated calcium levels that may occur in chronic renal failure, primary hyperparathyroidism, hypervitaminosis D, and milk-alkali syndrome.^[12] Metastatic pulmonary calcification usually occurs in normal pulmonary parenchyma and is secondary to abnormal calcium metabolism without any prior soft tissue damage. Calcium deposits can be found in interstitium of the alveolar septae, bronchiolar walls, in the large airways and in the walls of the pulmonary vessels.^[13] The most common imaging features are poorly marginated nodular opacities in the upper lobes of lungs. Ground-glass opacities, subpleural linear calcifications, and calcification along the interlobular septa that are the most frequent HRCT findings in PAM^[6] are not seen in metastatic calcification. The absence of a known cause, normal calcium levels, and the radiological appearance ruled out metastatic calcification in the present case.

The radiographic appearance of a sand-storm with a “black pleura” sign is pathognomonic of PAM. Fiberoptic bronchoscopy with BAL showing microliths or histological examination of a lung biopsy is only occasionally required to confirm the diagnosis.^[7] In the present case, fiberoptic bronchoscopy was done but was inconclusive. However, the diagnosis of PAM was confirmed by the characteristic radiological findings. The dense and confluent calcifications to form consolidations seen in the present case are distinctly uncommon and add to the known radiological manifestations of PAM. Currently, the only effective therapy is lung transplantation. Systemic glucocorticoids, whole lung BAL, or disodium etidronate have been tried but are not effective to prevent the progression of PAM.^[1] Long-term oxygen therapy is necessary for the patients with hypoxemia and chronic respiratory failure.

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Conflicts of interest

There are no conflicts of interest.

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