Radiology Forum

# Bone Scintigraphy in Pulmonary Alveolar Microlithiasis

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## CLINICAL SUMMARY

A 33-year-old woman, recently diagnosed to have cholelithiasis and advised cholecystectomy, was referred for evaluation of chest radiograph abnormality detected during pre-operative evaluation. She had no present or past history of any major respiratory illness. Physical examination revealed bilateral basal crackles on auscultation.

## INVESTIGATIONS

Haemogram parameters and serum biochemistry, including calcium, phosphorous and alkaline phosphatase levels were within normal limits. The chest radiograph (Figure 1) showed bilateral middle-zone and lower-zone dense reticulonodular opacities. High resolution computed tomography (HRCT) of the chest (Figures 2 and 3) showed bilateral intra-lobular interstitial and septal thickening with a perivascular distribution patter and dense calcification along with the presence of small subpleural cysts on both sides.

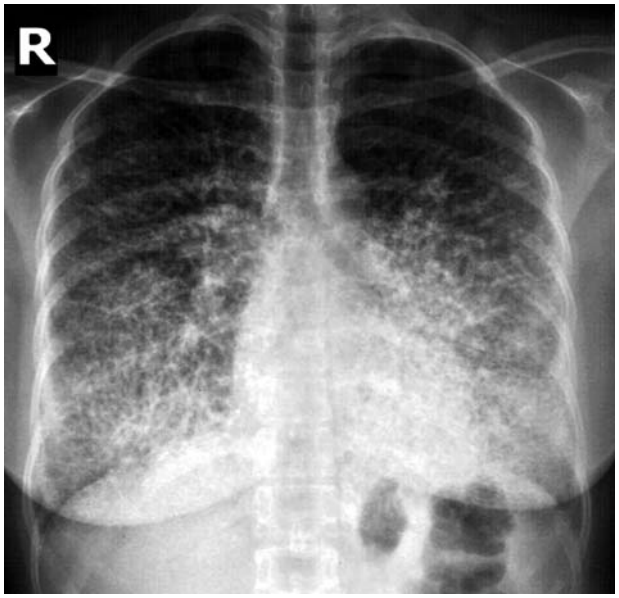


**Figure 1. Chest radiograph (postero-anterior view) showing bilateral dense reticulonodular opacities.**

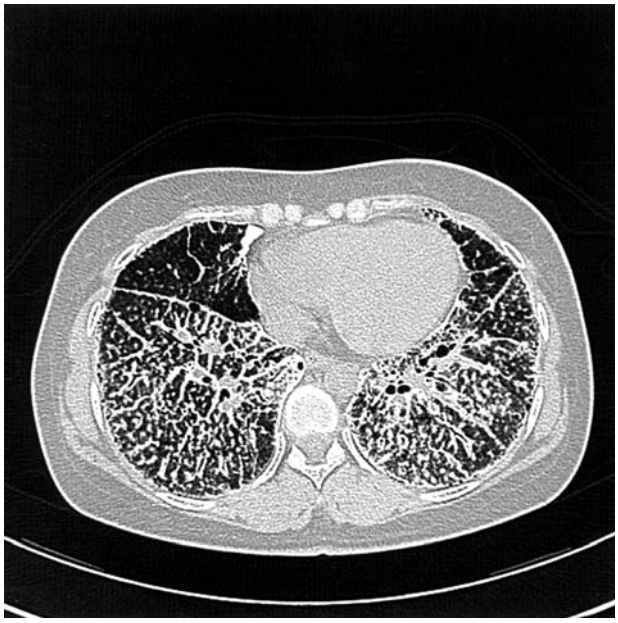

**Figure 2. Coronal section of high resolution computed tomography of chest showing bilateral intra-lobular interstitial and septal thickening with dense calcification. Also note small subpleural cysts on both sides.**

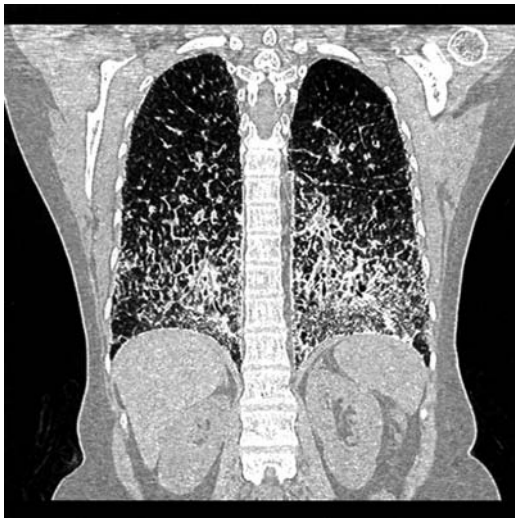

**Figure 3. Axial section of high resolution computed tomography of chest showing the predominant involvement of lower portions of the lungs with extensive calcification.**

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Technetium-99m methylene diphosphonate (Tc-99m MDP) whole body bone scintigraphy (Figure 4) showed diffusely increased radiotracer uptake in both the lungs. Whole body 18-fluorodeoxyglucose positron emission tomography (FDG-PET) did not show any significant uptake in the lungs. Microscopic examination of sputum and bronchial washings did not show presence of "calcospherites".

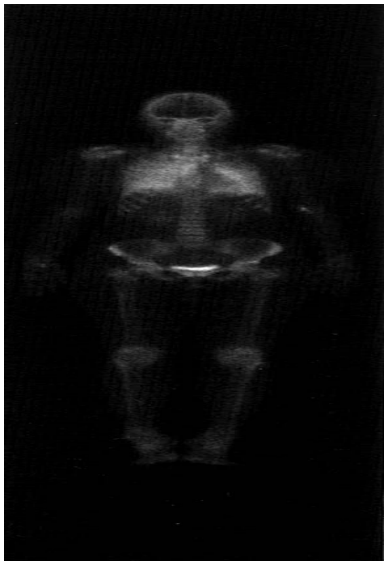

**Figure 4. Technetium-99m methylene diphosphonate whole body bone scintigraphy showing diffusely increased radiotracer uptake in both lungs.**

Arterial blood gas analysis showed a mild increase in the alveolar-arterial gradient. Lung function testing showed a mild restrictive ventilatory defect with a forced vital capacity (FVC) of 64% (1.99L) and a forced expiratory volume in one second ($FEV_1$) of 65% (1.76L) and a decrease in the diffusion capacity of lung for carbon monoxide DLCO (56%).

## DIAGNOSIS

Pulmonary alveolar microlithiasis confirmed by bone scintigraphy.

## DISCUSSION

Pulmonary alveolar microlithiasis (PAM) is a rare idiopathic disorder characterised by intra-alveolar accumulation of spherical calcified concretions which are known as calcospherites or microliths. Most patients are asymptomatic at the time of diagnosis and the disease is found incidentally, as was the case with our patient. The disorder may affect people of any age ranging from early childhood to elderly. However, they usually become symptomatic between the third and fourth decades of life.[1-3] The occurrence may be sporadic or hereditary with an autosomal recessive inheritance.[1]

The hallmark of this disorder is a clinico-radiological dissociation, *i.e.* there is paucity of symptoms in contrast to imaging findings. The predominant symptom is dyspnoea followed by cough and occasionally chest pain. Though various hypotheses for the pathogenesis of this disorder have been proposed, it is now believed that a mutation in the type IIb sodium-phosphate cotransporter gene (SLC34A2 gene), that is involved in phosphate homeostasis in various organs including lungs and prevents excessive phosphate accumulation that may later act as a *nidus* for formation of microliths, is responsible for the pathology.[4]

The chest radiographs usually show diffuse, bilateral areas of micronodular calcifications, resembling a "sandstorm", that predominate in the middle and lower zones of lungs.[1, 2, 5] The calcification may be so dense that it may obliterate the heart borders and the diaphragm. A black pleural line is another typical finding that appears as an area of hyperlucency, caused by the water density of pleura, between the calcified lung parenchyma and the ribs.[5] The characteristic HRCT chest findings include ground-glass opacities probably due to small calculi in alveoli, subpleural linear calcifications, confluent and diffuse calcified nodules, calcification along bronchovascular bundles and small thin-walled subpleural cysts.[5] The inter-lobular septa are of calcium density due to the deposition of calcospherites within the peripheral lobular parenchyma adjacent to the septa.[5] Rarely, multiple calcified plaques may be seen along the costal pleura.[6]

Bone scintigraphy using technetium-99m labelled diphosphonate compounds, that have a natural affinity for calcification foci at soft tissue level, may detect early pulmonary calcification in PAM.[7] Some cases may also show a high FDG uptake in both lungs on FDG-PET examination.[8] Other investigations include demonstration of microliths in sputum and fluid of bronchoalveolar lavage or on histological examination of lung biopsies.[3]

The disease may progress with chronic alveolar calcification causing interstitial inflammation and fibrosis leading to decreased lung volumes and eventually right heart failure.[9] Currently, the only effective therapy is lung transplantation especially when it is performed before the disease progresses to an advanced stage.[3] Disodium etidronate, which acts by inhibiting microcrystal growth of hydroxyapatite, and thus, presenting ectopic calcification, has been used to treat PAM with mixed results. Some reports have shown little or no benefit while a recent study[10] has demonstrated an improvement in lung functions and radiological changes.

In our patient, though the FDG-PET examination did not show any significant uptake in the lungs, the characteristic CT and bone scintigraphy findings were

consistent with the diagnosis of PAM. The parenchymal calcification was not extensive enough to give rise to the black pleural line. Since she had no respiratory symptoms and her spirometry showed only a mild restrictive abnormality, a decision was made to keep her under observation with periodic reassessments. She remains stable over a six-month follow-up period.

## ACKNOWLEDGEMENTS

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