Dendriform pulmonary ossification (DPO) is a rare condition characterised by branching bony spicules which usually contain marrow and are found in the lung parenchyma associated with pulmonary fibrosis. Rare earth pneumoconiosis is an uncommon occupational disease caused by the inhalation of dust containing rare earth metals. Rare earth metals are commonly encountered in a large number of industrial settings including the manufacture of mirrors, optical lenses, and certain electronic components. Several reports show that rare earth metals cause lung parenchymal inflammation and fibrosis.

We report here a patient with pathologically proven DPO. Analytical transmission electron microscopy of an open lung biopsy specimen confirmed that the patient had underlying rare earth pneumoconiosis. To our knowledge, there have been no previous reports of this association.

**CASE REPORT**

**Clinical history**

A 38 year old man presented with a non-productive cough which had lasted several months. There was nothing significant in his past medical history with no history of smoking or the use of alcohol or illicit drugs. Twenty years previously he had worked for 3 years as a polisher at a crystal factory. His work place was located below ground, with poor ventilation such that the air in the work place was heavily contaminated with greenish polishing powder. He subsequently changed jobs and worked as a frame worker for an electric manufacturer for the following 15 years. There was no history of recent travel, environmental exposure, or a family history of any lung disease.

On physical examination his vital signs were normal but a chest examination revealed a bilateral distant breathing sound. There was no clinical evidence of arthritis or any other physical manifestations of a collagen vascular disease.

Basic laboratory studies, including complete blood count, electrolyte analyses and liver function tests, were normal. Auxiliary studies failed to establish a rheumatological or other specific cause for the lung disease. Microbiological studies including sputum bacterial culture and smear for acid-fast bacilli showed no evidence of active infection.

Pulmonary function tests revealed a mild diffusion defect: forced vital capacity (FVC) 3.63 l (94% predicted); forced expiratory volume in 1 second (FEV1) 3.22 l (100% predicted), and FEV1/FVC 89%. Lung volumes showed total lung capacity (TLC) of 5.16 l (90% predicted) and carbon monoxide transfer factor (TLCO) of 16.18 ml/min/mm Hg (66% predicted). Arterial blood gas analysis on room air was pH 7.40, PaCO2 4.9 kPa and PaO2 13.8 kPa.

**Radiological findings**

A chest radiograph showed diffuse reticulonodular infiltrates in the whole lung fields. Both lungs were overinflated (fig 1). A high resolution CT scan of the lung showed diffuse, tiny, circular or bead-like densities with branching structures in the interlobular septum, including the subpleural region. Intervening cystic radiolucencies suggestive of emphysema were also seen (fig 2). A CT scan with bone setting showed a branching twig-like ossified mass in the right lower lobe and a few dot-like ossifications in both lower lobes.

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**Figure 1** Chest radiograph showing diffuse reticulonodular infiltrates in the whole lung fields. Both lungs are overinflated.

**Figure 2** High resolution CT scan of the chest showing diffuse, tiny circular or bead-like densities with branching structures in the interlobular septum. Intervening cystic radiolucencies are also present, suggesting emphysema.
Pathological findings

An open lung biopsy of the left lung showed that the lung surface was irregular and the lungs appeared emphysematous and mottled with anthracotic pigmentation. The most striking intraoperative finding was the presence of several thorn-like hard materials in the lung parenchyma. Some bony fragments contain fatty marrow. Stain: haematoxylin and eosin; original magnification ×10.

Figure 3 Microscopic appearance consistent with organising pneumonia, interstitial fibrosis, peripheral emphysema with multiple particles. Tubular bone formations are seen in the fibrotic and emphysematous lung parenchyma; the bones occasionally have a branching projection into the alveolar spaces. Some bony fragments contain fatty marrow. Stain: haematoxylin and eosin; original magnification ×10.

Analytical study

To determine the nature of the particles in the lung parenchyma, analytical transmission electron microscopy (H-8000; Hitachi, Japan) with energy dispersive x ray (EDX) analysis (Kevex Co, Japan) was performed. The lung tissue was prepared using the method of Kohyama and Suzuki. The chemical composition of the particles was analysed and the chemicals were quantitatively expressed by an EDX spectrum.

Particles of rare earth metals such as cerium oxide (CeO₂) and phosphates of cerium and lanthanum were detected in the lungs (fig 4). Most of the particles were aggregates of fine particles of about 0.1–0.3 μm in size. Mineral particles other than rare earth metals such as quartz, feldspar, mica, kaolinite, halloysite, talc and TiO₂ were also found in the lungs but were detected only infrequently.

DISCUSSION

This report is the first to present a case of DPO associated with pneumoconiosis caused by the inhalation of industrial rare earth metals. DPO is rarely recognised radiographically during life so it may be more prevalent than is thought, but it is usually mistaken for more serious clinical entities such as interstitial pneumonia or fibrosis, bronchiectasis, lymphangitic tumour spread, or septal thickening. DPO progresses slowly over many years and may remain unchanged; spontaneous regression has not been reported.

The pathogenesis and aetiology of DPO has not been fully elucidated, but there are several pieces of evidence showing a strong relationship between DPO and interstitial fibrosis caused by inflammation. In most cases the bones were confined to the areas of fibrosis, suggesting a link between the bony structures and fibrosis. These observations suggest that dendriform pulmonary ossifications may be regarded as a rare complication or a septal manifestation of chronic interstitial inflammation of the lungs. The osseous structures have been interpreted as being derived from a metaplastic

Figure 4 Analytical transmission electron microscopy and energy dispersive x ray (EDX) spectrum findings. Particles of rare earth metals such as cerium oxide (CeO₂) and phosphates of cerium and lanthanum (La) were detected in the lungs. Most of the particles were aggregation of fine particles of about 0.1–0.3 μm in size.
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Although talc, TiO₂ or mica could have influenced the pathological changes, the main causative agent in this case was thought to be rare earth metals rather than the abovementioned materials because of their low tissue content and the lack of characteristic pathological findings. An in vitro cytotoxicity assay suggested that the fumes of rare earth metals should be considered cytotoxic to lung tissue and therefore potentially fibrogenic.

Less common causes of pneumoconiosis are being increasingly recognised and diagnosed. The fibrogenic potential of a number of respirable inorganic particles is still poorly understood but can be significantly determined by the amount of deposition, the clearance of the particles, the size and solubility of the particles, susceptibility of the host, as well as other factors. Microanalytical techniques can be used to aid the identification of uncommon or unusual biopersistent particles or elements in fibrotic lung tissue.

This case adds support to the belief that rare earth metals are potentially hazardous and can result in the development of DPO in the lungs by causing lung inflammation and fibrosis. This report also emphasises the importance of taking a thorough occupational history of patients with unexplained pulmonary disease, and the benefit of analytical electron microscopy in reaching a correct diagnosis.

LUNG ALERT

Premedication with zolpidem may reduce poor quality polysomnography

The increasing awareness of sleep disordered breathing has resulted in an increased demand for polysomnography (PSG). A number of factors may lead to poor quality studies requiring repeat studies; these factors can prolong waiting times.

Zolpidem is a non-benzodiazepine sedative which has been shown to decrease sleep latency and increase sleep efficiency with minimal side effects on sleep architecture and respiratory events. The authors hypothesised that premedication with zolpidem before PSG might therefore result in a higher diagnostic yield.

They retrospectively reviewed 203 PSGs performed in adults. Two were excluded because they were given 5 mg zolpidem and one was excluded because he was on long term zolpidem treatment. Zolpidem premedication was not standardised and was prescribed at the discretion of the consulting sleep physicians who were unaware of the study. Of the remaining 200 patients, 54 (27%) received 10 mg zolpidem before the PSG. This resulted in a significant reduction in sleep latency (11.8 minutes vs 26.0 minutes, \( p = 0.002 \)) and sleep efficiency was also improved with zolpidem (\( p < 0.0001 \)). There was no difference in the mean (SD) apnoea-hypopnoea index with or without zolpidem (32.4 (12.7) vs 30.1 (11.9), \( p = 0.28 \)). Without zolpidem 33.6% studies were of poor quality compared with 7.4% with zolpidem. Thirty of the 49 PSGs of poor quality were repeated during the study period, 21 with zolpidem premedication all of which were of good quality and nine without zolpidem of which five remained of poor quality.

The authors conclude that premedication with 10 mg zolpidem will enhance the diagnostic yield of PSG, thus saving costs and time. However, this study does not conclusively exclude any effect of zolpidem on the PSG itself. A prospective study is required before this can be generally recommended.

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REFERENCES