A Rare Case of Asymptomatic Diffuse Pulmonary Ossification Detected during a Routine Health Examination

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Abstract

A 26-year-old man presented at our hospital in 2008 to undergo detailed investigations as part of a routine health examination. Chest computed tomography (CT) showed linear and reticular opacities with, in part, diffuse calcification in the lung fields bilaterally. A surgical lung biopsy was performed and the histological findings were compatible with a diagnosis of diffuse pulmonary ossification (DPO) of the dendriform type. DPO usually occurs as a secondary disease. As the histological changes in interstitial fibrosis were minimal rather than diffuse and not significant enough to be regarded as interstitial pneumonia, we considered this to be an idiopathic case. However, the findings appear to suggest that inflammation and fibrosis were associated with ossification.

Key words: pulmonary ossification, ectopic bone formation


Introduction

Diffuse pulmonary ossification (DPO) is a rare disease characterized by ectopic bone formation within pulmonary tissue. Living cases are rarely encountered; most are diagnosed at autopsy. DPO is usually associated with cardiovascular or respiratory disease. Therefore, the number of idiopathic cases is very small (1-4). We herein present an idiopathic case of DPO detected during a routine health examination.

Case Report

A 26-year-old man presented at our hospital in 2008 to undergo detailed investigations as part of a routine annual health examination. An abnormality on chest radiograph had been noted during the previous annual check-up in 2007. The patient was almost asymptomatic. His medical history included a cleft lip and palate (surgically repaired at 6 years of age) and chronic sinusitis (surgically treated at 10 years of age). He did not smoke until 20 years of age; his Brinkman index was 80. His grandmother had suffered from pulmonary tuberculosis; however, there was no other significant family medical history, including genetic diseases or consanguineous marriage. The patient worked in an office-based job as a forwarding agent and had no past or present exposure to any relevant environmental factors.

A physical examination revealed no respiratory or cardiovascular abnormalities. The patient’s blood pressure was 126/80 mmHg, his heart rate was 80 bpm, his respiratory rate was 20/min and his percutaneous oxygen saturation was 98% (on room air). No murmurs were detected and normal vesicular sounds (without rales) were heard on auscultation.

Peripheral blood and urinary tests showed slight elevations of urinary deoxypyridinoline (8.7 nmol/mmol · creatinine, normal range is below 7.7) and serum cross-linked carboxyterminal telopeptide of type I collagen (I-CTP) (4.6 ng/mL). The results of pulmonary function tests were normal and electrocardiogram and echocardiogram showed no...
Figure 1. Chest radiographs taken in 2005 (a), 2007 (b) and on admission in 2008 (c) (these chest radiographs were taken under different conditions). A chest radiograph taken on admission showed small, diffuse linear opacities in the lung fields bilaterally. The images showed almost normal findings in 2005. The abnormalities first appeared in 2007 and had become apparent in 2008.

abnormalities.

Chest radiography performed on admission showed small, diffuse linear opacities in the lung fields bilaterally (Fig. 1c). Chest X-ray performed in 2005 showed almost normal findings (Fig. 1a); however, abnormalities appeared in 2007 (Fig. 1b) and became exacerbated by 2008 (Fig. 1c). Computed tomography (CT) demonstrated linear and reticular opacities with diffuse calcification in all lung fields bilaterally (Fig. 2a, b). The distribution was partly posterior dominant. The CT opacities were similar to bone (Fig. 2c). Bone scanning with Tc-99m hydroxymethylene disphosphonate showed increased tracer uptake in the lung fields bilaterally (Fig. 3).

Bronchoalveolar lavage fluid (BALF) testing and a transbronchial lung biopsy (TBLB) showed no significant findings. Therefore, we performed a video-assisted thoracoscopic surgery (VATS) lung biopsy.

The histological findings obtained from the VATS-biopsy of rts2 (Fig. 4) showed dendriform mature bone formations with marrow in the alveolar spaces. Although there was some evidence of interstitial fibrosis, the fibrosis was minimal rather than diffuse and not significant enough to be regarded as interstitial pneumonia. Consequently, we diagnosed the patient with idiopathic DPO of the dendriform type.

Discussion

We herein report an asymptomatic case of idiopathic DPO diagnosed on VATS-biopsy that was detected during a routine, annual health examination. DPO is characterized by ectopic bone formation. Living cases are rarely encountered; most are diagnosed at autopsy (1-4). DPO was first reported by Luschka in 1856 (5), and Tseung and Duflou defined DPO as the presence of disseminated, widespread or extensive bone formation in the lungs (1). The etiology of this disease remains uncertain. However, DPO is thought to be associated with inflammation and resulting anoxia, which produces an acidemic environment leading to free radical initiation and propagation (4).

We performed a VATS biopsy on our patient, and a histological pattern of dendriform mature bone formation with marrow was seen in the alveolar spaces. DPO is categorized into two different types: namely, dendriform and nodular. Dendriform ossification is characterized by branching bony spicules in the alveolar septa that usually contain fat marrow (2, 4). Dendriform ossification is seen in patients with chronic pulmonary disease, idiopathic pulmonary fibrosis (6), acute respiratory distress syndrome, chronic obstructive pulmonary disease, organizing pneumonia, rare earth pneumoconiosis or asbestosis or heavy metal exposure (1).

Although we could not completely exclude the possibility of secondary DPO following interstitial pneumonia, the histological changes in interstitial fibrosis were minimal rather than diffuse and not significant enough to be regarded as interstitial pneumonia. Therefore, we diagnosed the patient with idiopathic DPO of the dendriform type.

This case involves a very young patient, a 26-year-old
Figure 2. Computed tomography (CT) performed on admission. CT images demonstrated linear and reticular opacities with, in part, diffuse calcification in all the lung fields bilaterally (a, b). The CT opacities were similar to bone (c).

Figure 3. Bone scanning with Tc-99m hydroxymethylene disphosphate. An increased tracer uptake is visible in the lung fields bilaterally.

man. Most reported cases of dendriform ossification have occurred in older men with an average of 67 years of age (7). Azuma et al. reported the phenomenon of familial clustering of dendriform ossification, which suggests a genetic predisposition for the pathogenesis of this disease (7). The clinical course of dendriform ossification is consid-
Figure 4. Histological findings from a video-assisted thoracoscopic surgery (VATS) biopsy of rt.S² (Hematoxylin and Eosin staining). Dendriform mature bone formations with marrow were seen in the alveolar spaces. Only minimal interstitial fibrosis was observed in the alveolar septum and hemosiderin-laden macrophages were present in the alveolar spaces. In addition, the fibrosis was not diffuse.

Considered to be indolent or slowly progressive (2). Fortunately, the patient’s annual check-ups provided us with a rare opportunity to track the progression of the DPO on chest radiographs from the time when the images had shown almost normal findings. Linear and reticular opacities were seen on high resolution computed tomography (HRCT), some of which appeared to have branching forms. This case also showed increased Tc-99m hydroxymethylene tracer uptake in the lung fields bilaterally. In dendriform ossification, HRCT shows a coral-like dendritic pattern (2). Saks et al. reported a case of DPO detected using bone scanning with Tc-99m hydroxymethylene in 1984 (8). However, it has also been reported that Tc-99m hydroxymethylene is less sensitive in the nonextensive stage (2). In this case, the laboratory findings showed slight elevations of urinary deoxypyridinoline and serum I-CTP, which usually imply the predominance of bone resorption. Previous reports of DPO show no diagnostic value in laboratory findings (2). Therefore, at present, we are unable to explain the significance of the laboratory findings in this case.

Although this case was diagnosed clinically as idiopathic, there might be indirect evidence and scientific scenarios to explain inflammation mediated heterotopic ossification. In heterotopic ossification, osteoblasts demonstrate the coexpression of endothelial and osteogenic markers (9). Endothelial cells transdifferentiate into the mesenchymal stem cells (MSCs) that subsequently form ectopic bone in a process called endothelial-to-mesenchymal transition (EndoMT) (9). Transforming growth factor (TGF) β-1 and β-2 induce EndoMT. Myofibroblasts in fibrotic tissues are derived from the expansion and activation of resident tissue fibroblasts, epithelial-mesenchymal transition (EMT) and tissue migration of bone marrow-derived circulating fibrocytes (10). Recently, EndoMT has emerged as another possible source of tissue myofibroblasts. Both EMT and EndoMT can be induced by TGF-β (10). EndoMT has been reported to be an important mechanism underlying the process of pulmonary fibrosis (10). EndoMT becomes a common pathway between heterotopic ossification and pulmonary fibrosis. This might explain the evidence of minimal interstitial fibrosis.

In conclusion, we herein presented a case of idiopathic DPO that was detected during a routine annual health examination. The patient’s progression was followed over the preceding four years using chest radiographs.

The authors state that they have no Conflict of Interest (COI).

References
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