Dendriform Pulmonary Ossification

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Dendriform pulmonary ossification is a rare condition often diagnosed by either surgery or postmortem examination. We report a 43-y-old man with a history of nonproductive cough for 1 y. His physical examination was unremarkable. Chest computed tomography showed multiple bilateral micronodules in both lower lobes; however, the patient's pulmonary function was normal. Flexible bronchoscopy with transbronchial biopsies revealed branching ossification. Pulmonary ossification is a chronic process characterized by progressive metaplastic ossification. We reviewed a total of 42 cases of dendriform pulmonary ossification reported in the medical literature: most of these cases were diagnosed by autopsy. Despite its rarity, dendriform pulmonary ossification should be considered in the differential diagnosis of diffuse lung disease. Bronchoscopy with transbronchial biopsies must be considered as a potential diagnostic procedure. *Key words: bronchoscopy; diffuse lung disease; lung disease; ossification.* [Respir Care 2015;60(4):e64–e67. © 2015 Daedalus Enterprises]

Introduction

Dendriform pulmonary ossification is a rare condition with an incidence of 1.63 cases/1,000 autopsies. It is a chronic process characterized by progressive metaplastic ossification and is found primarily in men.[1,2] Dendriform pulmonary ossification may be either idiopathic or associated with pre-existing disorders such as idiopathic pulmonary fibrosis, ARDS, COPD, organizing pneumonia, rare earth pneumoconiosis, asbestosis, and heavy metal exposure.[1] Patients may be asymptomatic or present with chronic cough. There have been cases of spontaneous pneumothorax. Dendriform pulmonary ossification may be diagnosed by radiologic testing, surgical biopsy, or autopsy.[1]

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The authors have declared no conflicts of interest.

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We present the only reported case of a patient with dendriform pulmonary ossification diagnosed by bronchoscopy with transbronchial biopsies. A search of the literature using MEDLINE, Google Scholar, and the LILACS Database using the key words dendriform pulmonary ossification both alone and in conjunction with various terms such as diffuse ossification was carried out. We included articles in either Spanish or English. After excluding other causes of ossification such as nodular ossification, a total of 42 cases were identified for this review.

Case Report

A 43-y-old Hispanic man with a history of chronic gastroesophageal reflux presented with the complaint of nonproductive cough for 1 y. He reported being a non-smoker and noted no previous exposure to environmental allergens. On physical examination, he appeared to be in no acute distress and exhibited normal vital signs, as well as a P_{aO_2} of 97% (environmental oxygen). Chest auscultation was unremarkable. A complete blood count and serum chemistry were within normal limits. A chest x-ray was normal, but chest computed tomography (CT) showed multiple bilateral irregular micronodules in both lower lobes, as well as a 6-mm calcified high-density nodule in the left lower lobe (Figs. 1 and 2).

Pulmonary function tests showed an FVC of 99% and an FEV_1 of 92%, as well as a total lung capacity of 113%,

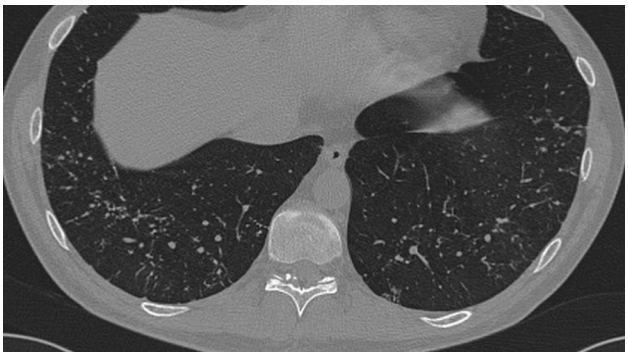

Fig. 1. Chest computed tomography shows multiple bilateral irregular micronodules in the lower lobes and a 6-mm calcified high-density nodule in the left lower lobe.

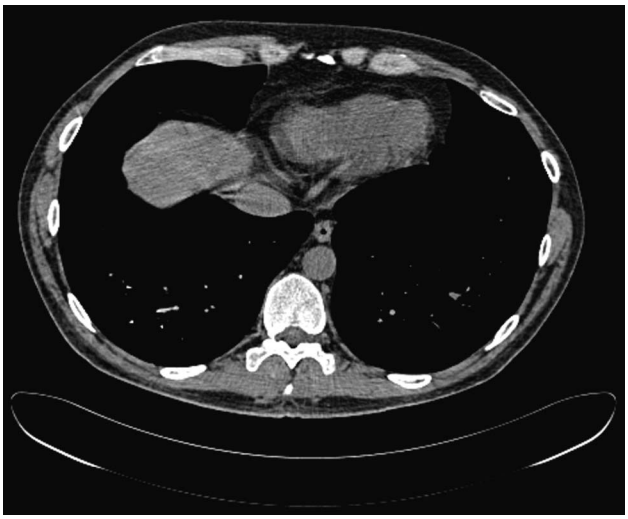

Fig. 2. Mediastinal window computed tomography together with the pulmonary micronodules.

a residual volume of 130%, a vital capacity of 110%, and a diffusing capacity of 71%.

Other lab results were as follows: human immunodeficiency virus and venereal disease research VDRL laboratory findings were both negative, and thyroid function, calcium, and parathyroid hormone were normal. Rheumatologic studies were as follows: antinuclear antibody, Scl-70, Jo-1, DNA, neutrophil cytoplasmic antibody, rapid plasma reagin (RPR), and rheumatoid factor were negative.

A flexible bronchoscopy (BF Q180 videobronchoscope, Olympus, Miami, Florida) with bronchoalveolar lavage and transbronchial biopsies was performed. Bronchoalveolar lavage revealed 79% macrophages, 15% neutrophils, and 6% lymphocytes. Microbiologic studies were negative. Bronchoscopy showed no macroscopic abnormalities. Ten transbronchial lung biopsies were performed in the right lower lobe; biopsies were obtained by conventional transbronchial biopsy, without cryoprobe.

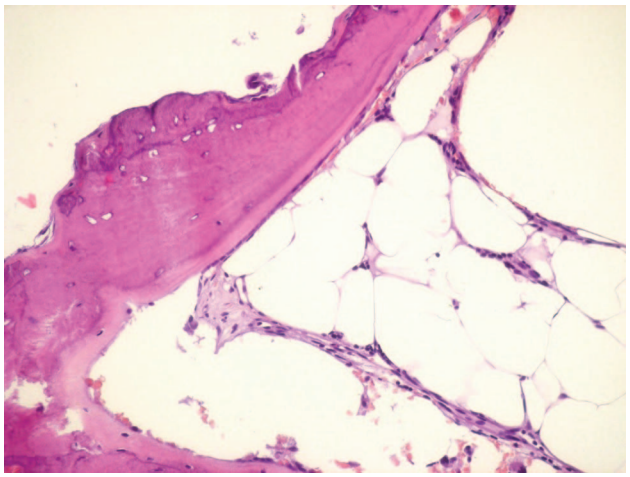

Fig. 3. Mature bone trabeculae with osteocytes and osteoblastic lining without cellular atypia and cartilage tissue (hematoxylin and eosin stain, × 100).

Histopathologic lung samples revealed branching ossification, mature bone trabeculae with osteocytes, and osteoblastic lining without cellular atypia and cartilage (Fig. 3). Transbronchial biopsy consisted of tissue fragments measuring 1–2 mm. The specimen was then formalin-fixed and paraffin-embedded, and 2-μm-thick serial sections were obtained. Once deparaffinized, the tissue sections were stained with hematoxylin and eosin for light microscopy. A lesion was found in only one of the fragments. No special technique was used to treat any artifact effect. At 48 months of follow-up, the patient had no dyspnea but continued with mild, sporadic, nonproductive cough, and his most recent chest CT showed no evidence of disease progression.

Discussion

Pulmonary ossification is an unusual condition of unknown etiology and has been recognized in the following 2 forms: granular (nodular) and dendriform. The nodular type of ossification has been linked to passive congestion due to chronic heart failure, mitral stenosis, and hypertrophic subaortic stenosis. Dendriform ossification is idiopathic or occurs in association with primary lung diseases. Dendriform pulmonary ossification is less common than the nodular type.[1-3]

Some patients are asymptomatic; therefore, lung ossification is an incidental finding. Others are misdiagnosed with interstitial lung disease. The differential diagnosis includes inflammatory disease (granulomatosis with polyangiitis, sarcoidosis), infection (tuberculosis, histoplasmosis), vascular disease (prior infarction, hemorrhage), malignancy (primary or secondary cancer), and other diseases such as amyloidosis and pneumoconiosis.[2]

Table 1. Summary of Published Cases of Dendriform Pulmonary Ossification

Parameter	Values
Age (mean ± SD), y	64 ± 17
Gender, *n* (%)	
Male	36 (85.71)
Female	6 (14.28)
Symptoms, *n* (%)	
Respiratory	27 (64.28)
Pneumothorax	4 (9.52)
Radiological finding	11 (26.19)
Location, *n* (%)	
Right lower lobe	4 (9.52)
Left lower lobe	5 (11.90)
Bilateral lower lobes	27 (64.28)
Others	6 (14.28)
Diagnosis, *n* (%)	
Autopsy	20 (47.61)
Surgery	19 (45.23)
Radiology	3 (7.14)
Treatment, *n* (%)	
Surgery	19 (45.23)
No treatment	3 (7.14)
Outcome, *n* (%)	
Radiological stability	22 (52.38)

We identified 42 reported cases of dendriform pulmonary ossification. The male-to-female ratio was ~6:1, with an average age of 64 ± 17 y (mean ± SD) at the time of diagnosis. A total of 20 diagnoses were made by autopsy, 19 were made by surgery, and 3 were made by radiology studies.

Only 11 cases were asymptomatic. Twenty-seven patients reported respiratory symptoms such as bronchial hyperactivity, cough, and dyspnea. Pneumothorax was the clinical presentation in 4 patients. Published comorbidities with dendriform pulmonary ossification included 28 patients with a history of lung disease as follows: 10 patients with pulmonary fibrosis, 12 patients with COPD, and 6 patients with pneumoconiosis. Previous malignancy was found in 6 patients. A summary of the published cases containing demographics, clinical presentation, diagnosis, treatment, and outcomes is presented in Table 1.[1-21]

Chest CT has a high diagnostic yield for pulmonary ossification. Kim et al[16] evaluated the incidence of dendriform pulmonary ossification in usual interstitial pneumonia. In this study, 75 subjects were diagnosed with usual interstitial pneumonia by chest CT and open lung biopsy: 5 subjects presented with dendriform pulmonary ossification. The chest CT diagnostic yield for dendriform pulmonary ossification was 100%. The most common finding was diffuse ossification in the lower lobes bilaterally, sometimes associated with subpleural nodules.

Five cases from our literature review occurred in the left lower lobe, and 4 cases occurred in the right lower lobe. Histologic examination confirmed the diagnosis of dendriform pulmonary ossification. A histologic pattern of dendriform mature bone formation with marrow was seen in the alveolar spaces. Microscopic findings included identifiable marrow elements and fat, without cellular atypia. Electron microscopy revealed calcium deposits, predominantly in collagen fibers in areas within fibrotic interstitium but away from areas of bone formation.[1]

In our patient, the diagnosis was made by flexible bronchoscopy with transbronchial biopsies. This minimally invasive procedure is safe and may be performed on an out-patient basis.[22] Most cases reported previously were diagnosed during either surgery or autopsy. In the last 5 y, a total of 17 cases were reported in living patients, and most of these patients were diagnosed by surgery.

No specific treatment or management guidelines are published for dendriform pulmonary ossification. Symptomatic treatment for cough, bronchial obstruction, and other symptoms has been reported. Imaging follow-up is also suggested, although follow-up data are scarce. Only one patient in a previously published study had a 10-y follow-up, which showed no recurrence of the disease after surgical resection of the lesions.[4]

In conclusion, dendriform pulmonary ossification is a rare disorder diagnosed more commonly by either surgery or autopsy. It is frequently associated with other lung diseases such as interstitial pneumonia or pneumoconiosis. Bronchoscopy with transbronchial biopsies is a useful tool for diagnosing dendriform pulmonary ossification. Malignant disease must be excluded. Further studies including information about both treatment options and long-term outcomes are needed to guide management recommendations.

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