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Massive pulmonary ossification due to recurrent aspiration pneumonia

Bilal Battal, Murat Kocaoğlu, Fatih Örs, Sabahattin Vurucu

ABSTRACT
Pulmonary ossification is an idiopathic disorder that presents with the formation of mature bone in the pulmonary parenchyma. This is a very rare entity that occurs in conjuction with busulfan therapy as well as with a number of diseases including chronic bronchitis, cystic fibrosis, congestive heart failure, myositis ossificans, and idiopathic interstitial fibrosis. It is usually seen in older age groups. We present a 4-year-old boy with massive ossification secondary to recurrent aspiration pneumonia. This is the first reported case of pulmonary ossification secondary to recurrrent aspiration, and the first case in a child.

Key words: • *pathologic ossification* • *lung* • *tomography, x-ray computed* • *child, preschool*

Pulmonary ossification is described as mature bone in alveolar or intersitial spaces (1). It is a very rare condition that may occur in association with a variety of disorders including congestive heart failure, myositis ossificans, cystic fibrosis, hemodialysis, shock following cardiac valve replacement, acromegaly, busulfan therapy, idiopathic interstitial fibrosis, and chronic bronchitis (1–6). Pulmonary ossification is most commonly found in men between 70 and 80 years of age, but cases have been reported in younger men and women (1). To our knowledge, pulmonary ossification has not been reported due to recurrrent aspiration pneumonia in children.

Case report

A 4-year-old boy who had mental and motor retardation, epilepsy, epiglottic dysfunction, and recurrent aspiration pneumonia was admitted to our hospital. He had been evaluted for spinomuscular atrophy, hypotonia, and congenital muscular dystrophy. The diagnosis of epiglottic dysfunction (incomplete closure) had been established by fiberoptic endoscopy. His upper gastrointestinal series, performed at another institution, also showed aspiration without mechanical intestinal obstruction. Chest radiograph five months prior to admission also had some degree of pulmonary ossification according to the medical record; however, we could not evaluate the possible progressive nature of disease without reviewing the radiograph.

Because of recurrent aspiration, the patient had a percutaneous gastrostomy tube. On physical examination, bilateral rales were detected. Hematologic and blood chemistry values including C-reactive protein, erythrocyte sedimentation rate, serum Ca, P, and parathormone were unremarkable. Sputum culture revealed normal flora, and cytology revealed no abnormal findings. Hypercapnia and hypoxemia were noted.

Cranial magnetic resonance imaging, obtained to assess epilepsy, showed cerebral atrophy. Chest radiograph revealed bilateral reticulonodular pulmonary infiltrates, patchy consolidation, and pneumonic infiltrates resembling organizing pneumonia. Bilateral patchy radiopacities consistent with calcifications were also noted (Fig. 1). High resolution computed tomography (HRCT) showed bilateral subpleural or peribronchial areas of consolidation associated with massive ossification. HRCT also demonstrated areas of ground-glass attenuation, small ill-defined nodules, and irregular linear areas of increased attenuation (Fig. 2). The parents did not consent to biopsy. Clinical examination and imaging suggested massive pulmonary ossification with organizing pneumonia. No calcification or bone formation was found in other tissues.

From the Department of Radiology (B.B. ✉ *bilbat_23@yahoo.com*, M.K., F.Ö.), and the Division of Pediatric Neurology (S.V.), Gülhane Military Medical Academy, Ankara, Turkey.

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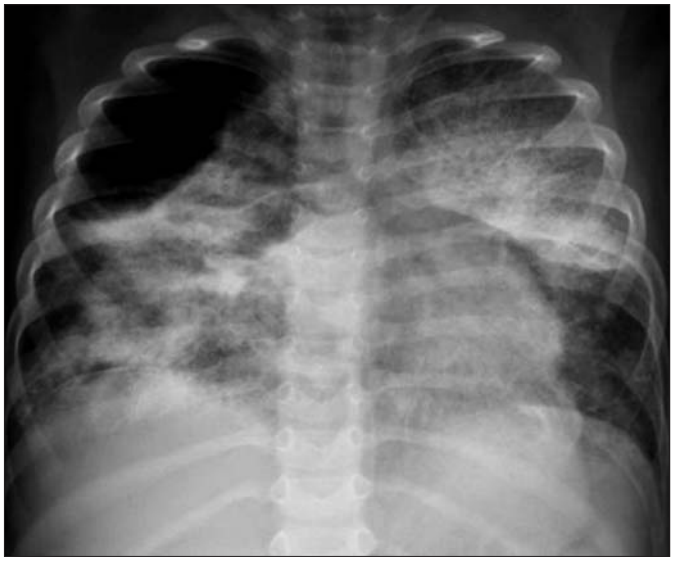

Figure 1. Frontal chest radiograph shows confluent and interstitial opacities throughout the left lung, and mid and lower zones of the right lung.

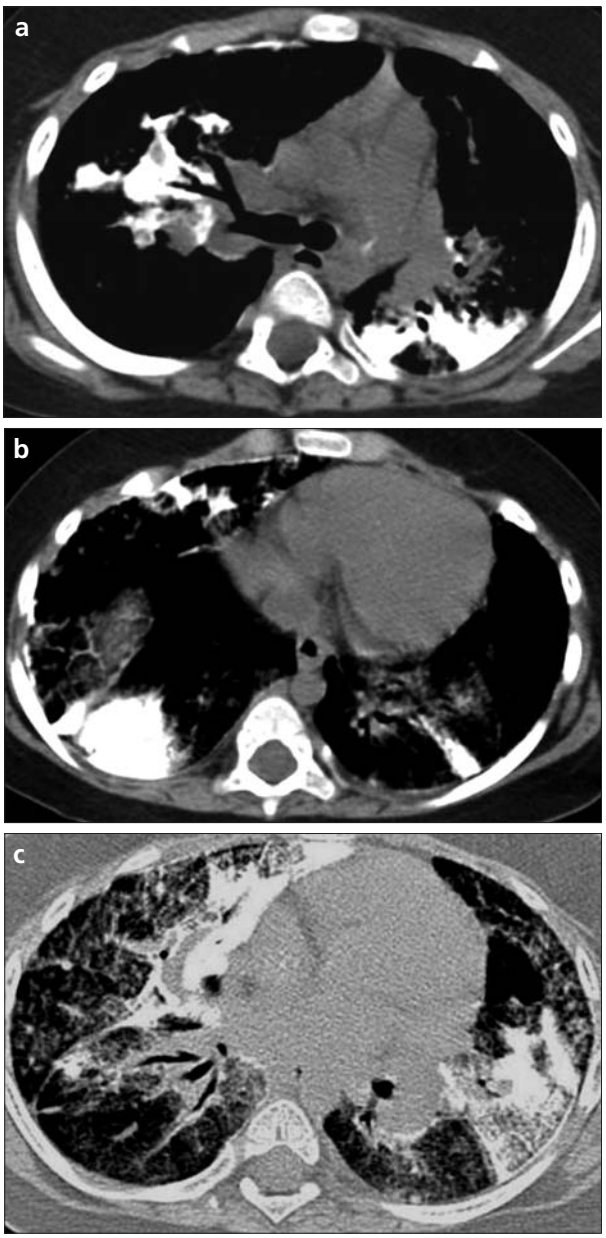

Figure 2. a–c. Axial CT images **(a–c)** show bilateral areas of consolidation in a patchy distribution and ossified areas. Right hilar lymphadenomegalies are present **(a)**. The consolidation and ossification have a predominantly peribronchial distribution. Pleural thickening, areas of ground-glass attenuation, and irregular linear areas of increased attenuation are also noted **(a–c)**.

Discussion

A variety of pulmonary, cardiac, and other diseases are associated with secondary pulmonary ossification (1–6); however, another type of benign ossification, idiopathic pulmonary ossification of the lung, also has been reported (7). Bony structure in pulmonary ossification is usually located in a limited region; however, it may also be widely distributed throughout the lung.

There are two histologic types of pulmonary ossification, dendriform and nodular, both of which have mature lamellar bone. The dendriform type consists of linear and branching bony deposits within the interstitium, and the ossification includes a marrow component composed of fat and hematopoietic cells. The dendriform type is frequently associated with chronic changes such as lung scarring and interstitial fibrosis. Radiographically, the dendriform type manifests as linear shadows in the lower fields (3, 8). The dendriform type is usually localized, and most cases are found incidentally at autopsy, because of the absence of symptoms during life. In contrast, the nodular type consists of ossific bodies in the alveolar space without a marrow component. The nodular type is particularly associated with chronic passive congestion, frequently secondary to mitral stenosis and pulmonary congestion (4). Radiographically, the nodular type manifests as scattered nodular calcific densities in the lower fields (3, 8).

The pathogenesis of pulmonary ossification is not completely understood. Various theories have been hypothesized to explain the development of pulmonary ossification. Most studies suggest that any fibrosis, regardless of the cause, may be a precursor of pulmonary ossification (1, 2, 4). In these cases, investigators have postulated repair of pulmonary tissue with fibroblasts and osteoblasts following interstitial exudate and hemorrhage. Others have suggested metaplasia of fibroblasts to osteoblasts in conditions such as tissue acidosis following hypoxia and capillary congestion. Metaplasia of this type may occur in patients with multiple episodes of pneumonia or other lung disease that leads to scarring (5, 6).

Radiographic and CT findings of our patient are consistent with neither a diffuse nor a nodular form of pulmonary ossification. Pulmonary ossification in our patient is best described as massive

ossification. To our knowledge, it is the first case described in conjunction with recurrent aspiration pneumonia, and in a pediatric patient. In general, lung biopsy is not used to diagnose aspiration pneumonia. Mukhopadhyay and Katzenstein (9) showed that organizing pneumonia is the most common histologic finding in aspiration pneumonia, characterized by a variable degree of intraluminal fibroblast plugs with lymphocytes and plasma cells, multinucleated giant cells, granulomas and acute/chronic inflammation. In some cases, fibrosis was more prominent than inflammation. In the present case, tissue hypoxia, fibrosis, and/or tissue acidosis due to aspiration of acidic content might have played some role in the formation of osseous tissue, since extramedullary hemopoiesis is not uncommon in patients with marked hypoxemia. Of course, lack of pathologic confirmation in this case is a limitation; however, imaging and clinical findings allowed us to reach diagnosis.

In conclusion, recurrent aspiration pneumonia may result in extensive pulmonary ossification in children. It would be useful to evaluate more cases in order to determine whether this finding has prognostic or therapeutic implications.

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