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CASE REPORT

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Lung parenchymal calcifications in a child with cystic fibrosis

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Abstract

We describe a 6-year-old girl with homozygous p.Phe508del cystic fibrosis with severe multi-lobar bronchiectasis and obstructive lung disease who was found to have prominent parenchymal calcifications in the right middle lobe on a computed tomography scan of the chest. Histopathology from the calcified area of lung biopsy showed fibrous tissue with chronic inflammation with CD3+ T-lymphocytes and macrophages with no granulomas. Dystrophic calcification was seen within this necrotic debris.

KEYWORDS
cystic fibrosis, lung calcifications

INTRODUCTION

Cystic fibrosis (CF) is a multi-system disease that results in chronic pulmonary suppuration and bronchiectasis.[1] Pulmonary calcifications are typically caused through two mechanisms, the dystrophic and metastatic forms. Although patients with CF are regularly exposed to pathogenic organisms and have ongoing pulmonary inflammatory process, macroscopic lung calcifications are uncommon and, to our knowledge, there has been no other such case report of pulmonary parenchymal calcifications in a child with CF. We present a case where a 6-year-old child had significant lung calcifications and review the literature.

CASE REPORT

A 6-year-old female diagnosed neonatally with homozygous p.Phe508del CF was admitted for further investigation and pulmonary optimization following consultation with the lung transplant team. Severe obstructive lung disease with forced expiratory volume of 1 s of 43% predicted and its rapid decline over the preceding 12 months was the reason for the referral to the lung transplant team. She was chronically colonized with mucoid strain of *Pseudomonas aeruginosa* and had also previously isolated *Mycobacterium intracellulare*, which had been treated with a 12-month course of azithromycin, rifampicin and ethambutol in addition to 3 months of clofazimine.

A routine chest computed tomography (CT) as part of her transplant workup showed widespread cylindrical bronchiectasis with associated bronchial wall thickening and mucus plugging. Incidentally, CT imaging also demonstrated a region of collapse/consolidation in the right middle lobe (RML), which also contained the area of prominent calcification (Figure 1). These calcifications were not visible on a chest radiograph taken at the same time. At the time of this CT, she was negative for atypical organisms but was colonized with mucoid *P. aeruginosa*. Biochemistry revealed CF-related diabetes and mild transaminitis. Serum calcium, magnesium and phosphate levels were within the normal limits. An interferon-gamma release assay (QuantiFERON-TB Gold) was negative. A CT-guided core needle biopsy obtained tissue from the partly calcified lesion in the medial RML. Microscopic appearance showed sheets of necrotic debris with focal calcification, which was considered to be dystrophic. There was also fibrous tissue with chronic inflammation seen with no evidence of granuloma

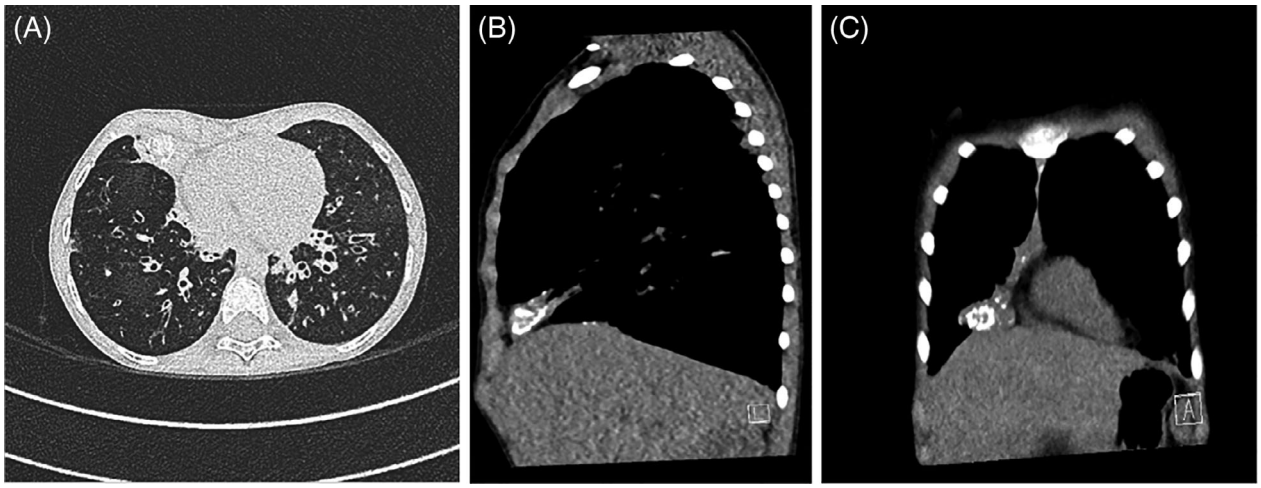

FIGURE 1 (A) Chest computed tomography (CT) axial cut showing calcification in the right middle zone containing air fluid level. (B) Chest CT coronal showing calcification in the right middle zone. (C) Chest CT sagittal showing calcification

formation, no amyloid deposit and no evidence of sarcoidosis with negative periodic acid-Schiff, mucicarmine and Grocott methenamine silver stain. No fungal elements or acid-fast bacilli were seen. CD3+ T-lymphocytes were seen on additional immunohistochemistry. Cultures were inoculated and incubated for 6 weeks producing no growth.

DISCUSSION

Lung parenchymal calcifications in the CF population are a rare occurrence with no other reported paediatric cases in the literature to our knowledge. Here, we describe a 6-year-old girl with CF who presented with prominent lung calcification on CT chest in the RML, which underwent biopsy and was negative for tuberculosis and other atypical microorganisms.

While literature on pulmonary calcification is sparse, CF has not been reported to be one of the possible underlying aetiologies.[2,3] The prevailing aetiology for lung calcifications includes a dystrophic and metastatic type. The dystrophic type occurs following insult as an inflammatory process triggered by an injury such as *Mycobacterium tuberculosis*, bleeding, occupational dust exposure or pulmonary infarction.[2,3] Chronic inflammation is the key hallmark of the dystrophic calcification. It is an organized process with local deposition of hydroxyapatite calcium salt and normal serum phosphate and calcium levels.[3] Macroscopically, multiple large calcified nodules usually distinguish the dystrophic form from metastatic, which is by comparison small and diffuse.[4] Evidence of the surrounding tissue damage such as granulomas or metastasis and lymph node enlargement or calcification are also often present.[4] Frequent causes include a Ghon focus, an often calcified tuberculous granuloma in the lung.[3] Conversely, metastatic calcifications are caused by high serum calcium and phosphate levels that result in deposition of these in the lung tissue.[3] Conditions such as hyperparathyroidism, chronic renal failure or neoplastic lesions of the bone can result in such high serum calcium and phosphate levels and have been associated with metastatic lung calcifications.[3] While children and adults with CF may also have chronic kidney disease and increased parathormone related to CF bone disease,[5] a normal serum biochemistry as well as the localized nature of the calcification in our patient preclude this type of calcification.

Amyloidosis is a chronic inflammatory condition characterized by extracellular deposition of protein fibrils in multiple organ systems resulting in cardiomyopathy and congestive heart failure, nephrotic syndrome and peripheral neuropathy.[6] Pulmonary nodular amyloidosis, although rare, has also been reported to result in lung calcification[6]; however, the histology of the lung calcified tissue in our patient did not support this diagnosis.

Extensive parenchymal calcification as in our child has never been previously reported. Cantet and colleagues[7] reported seeing crystalline structures on cytological analysis of lung tissue from a patient with CF following lobectomy which were likely to be calcium phosphate deposits.[7] It is unclear if the calcification was seen macroscopically in that case. The authors hypothesized that the calcium was possibly sequestered by mitochondria and Golgi apparatus partly due to an increase in electron transport chain activity.[7] We believe the parenchymal calcifications found in this case signify ongoing chronic inflammation consistent with the dystrophic type of lung calcifications. The lack of causative organism or hamartoma raises the question if this is an inherent property of CF. It is possible, but conjectural, that the non-tubercular mycobacterial infection exacerbated this process.

In conclusion, we report a case of prominent macroscopic lung calcifications in a child with CF. Despite thorough microbiological, biochemical and histopathological investigations, no clear cause of this calcification was found, and this was hence attributed to chronic inflammation.

Pulmonary calcifications have a complicated and highly variable aetiology. CF is also highly variable in presentation and historically not associated with pulmonary calcifications. The relationship between CF and pulmonary calcifications remains unclear and needs further investigation.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Heidi Lynch: Writing – review and editing. Frank Qian: Writing – original draft. Matthew D. Wong: Writing – review and editing. Rahul J. Thomas: Writing – review and editing. Nitin Kapur: Supervision, project administration, resources, writing – review and editing.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no data sets were generated or analysed during the current study.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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