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Case Report

HRCT Diagnosis of Pleuroparenchymal fibroelastosis: Report of two cases

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ABSTRACT

Pleuroparenchymal fibroelastosis (PPFE) is a rare idiopathic interstitial pneumonia that is often underdiagnosed on computed tomography scans. The disease process involves a combination of fibrosis involving the visceral pleura and fibroelastic changes within the subpleural lung parenchyma. Although definitive diagnosis is based on pathological evaluation, this is often not feasible and pattern recognition on CT as "definite PPFE" or "consistent with PPFE" is important given that sub group of patients will undergo rapid progression with clinical deterioration.

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Introduction

Pleuroparenchymal fibroelastosis (PPFE) is one of the rare idiopathic interstitial pneumonias (IIPs) that is often underdiagnosed on computed tomography (CT) scans. The disease process involves a combination of fibrosis involving the visceral pleura and fibroelastic changes within the subpleural lung parenchyma. Although definitive diagnosis is based on pathological evaluation, this is often not feasible and pattern recognition on CT is important given that some patients will undergo rapid progression that ultimately may require lung transplantation. In this article, we will present two cases of PPFE and focus on the radiologic pattern recognition on CT.

Case 1

A 72-year-old female presented to the urgent care clinic complaining of productive cough and congestion. She denied any fever, shortness of breath, or chest pain. Initial chest x-ray showed interstitial thickening in the left lung base and mild biapical pleural scarring. The patient was started on Amoxicillin-clavulanate and Benzonatate for 5 days for treatment of possible bronchitis. On follow up, the patient mentioned that she had dry cough for several months before this recent exacerbation. She continued to have dry cough after completing her treatment course and high-resolution CT chest was ordered for further evaluation.

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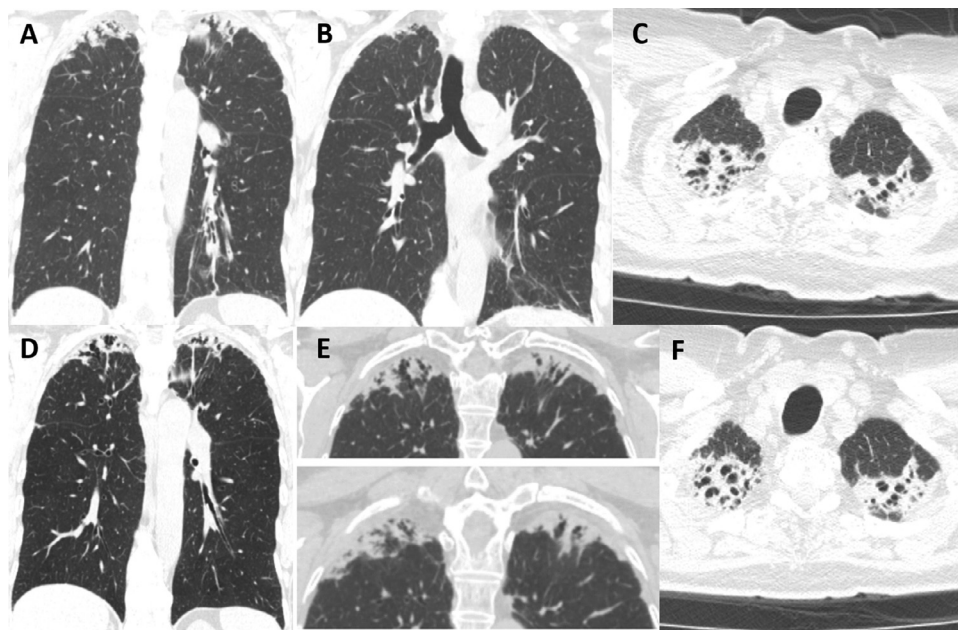


Fig. 1 – Coronal (A and B) and axial (C) unenhanced CT of the chest demonstrating biapical pleural thickening and subpleural fibrosis with elevation of the right hilum (B). Follow up unenhanced CT in coronal (D and E) and axial (F) planes demonstrate grossly stable findings of PPFE.

CT showed bilateral apical pleural thickening, subpleural parenchymal fibrosis with upper lobe volume loss and elevation of the hila (Fig. 1). No additional significant changes in the rest of the lungs identified. Repeat high resolution CT chest was obtained after four months to further evaluate the patient's persistent cough and showed stability of biapical pleuro parenchymal changes (Fig. 1). Imaging of this patient was done prior to the Covid-19 pandemic and she is due for follow up.

Case 2

A 53-year-old female with a reported history of non-defined connective tissue disorder for more than 10 years presented for follow up of dry cough and dyspnea associated with moderate physical activity. Initial chest x-ray showed bilateral apical linear opacities. Review of external records revealed biapical pleuro-parenchymal scarring on CT chest and normal pulmonary function tests (PFTs). Images one year prior and during the course of the admission while in the Covid-19 pandemic shown in Fig 2 demonstrate persistent and stable bilateral apical thickening, parenchymal fibrosis, upper lobe volume loss and traction bronchiectasis (Fig. 2). The CT images from 1-year prior were obtained for the purpose of comparison and showed stable bilateral upper lobe findings consistent with PPFE like current exam (Fig. 2). New PFTs were obtained and again showed normal spirometry. The patient was instructed to follow up in one year for repeat PFTs and CT chest.

Discussion

Idiopathic interstitial pneumonia classification was revised in 2013 and two rare interstitial pneumonias were recognized; idiopathic lymphoid interstitial pneumonia and PPFE (Table 1) [1]. PPFE is often idiopathic and familial in up to 57% of patients [2,3]. Several associations were described in the literature including bone marrow and lung transplant, chemotherapy, chronic hypersensitivity pneumonitis, prior infection and autoimmune diseases [4–9].

Clinical course is often benign with a median survival of approximately 11 years. However, some patients demonstrate rapid progression with clinical deterioration and poor lung function. This progressive phenotype has a median survival of 3–5 years and no definitive treatment is known other than lung transplantation [10].

The role of antifibrotic medications is unknown in PPFE but may stabilize and slow progression although no evidence exists due to rarity of condition. Two antifibrotic agents (pirfenidone and nintedanib) are approved by the FDA and recommended by clinical practice guidelines for the treatment of IPF [11]. Pirfenidone was reported to be used in isolated cases of PPFE with varying results [3,12]. The monitoring strategy is clinical observation with short- and long-term clinical assessment of PFTs.

Rosenbaum et al. suggested that PPFE is an underreported or underrecognized entity rather than being rare as they encountered five cases in the span of two years at their institution [13]. In our institution, we did a retrospective 5-year query of all chest CT scans with the term apical fibrosis in

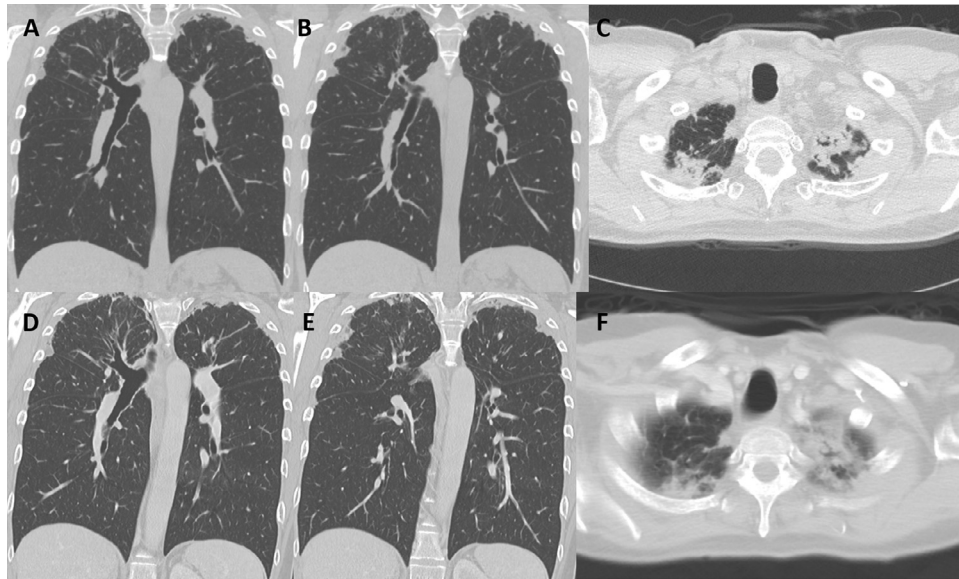


Fig. 2 – Coronal (A and B) and axial (C) unenhanced CT of the chest demonstrating biapical pleural thickening and subpleural fibrosis with elevation of the right hilum (A). Comparison of 1-year prior unenhanced CT in coronal (D and E) and axial (F) planes demonstrate grossly stable findings of PPFE.

Table 1 – Idiopathic interstitial pneumonia classification and CT features.

IIPs			CT features	
<i>Major</i>	<i>Chronic fibrosing IIPs</i>	<i>UIP</i>	Reticular pattern, with or without traction bronchiectasis Honeycombing Lower lobe and subpleural predominance UIP pattern absence is inconsistent with UIP	
		<i>NSIP</i>	Bilateral ground-glass areas Reticular opacities sparing sub pleural lung	
		<i>RB-ILD</i>	Poorly defined centrilobular nodules Centrilobular emphysema and/or bronchial wall thickening	
	<i>Smoking-related IIPs</i>	<i>DIP</i>	Diffuse ground-glass opacities Irregular linear opacities and microcysts	
		<i>Acute/subacute IIPs</i>	<i>COP</i>	Peripheral or peri bronchial patchy consolidations Ground-glass opacities with tendency to migration Rarely mass or nodules that may cavitate (“atoll sign”)
			<i>AIP</i>	Ground-glass attenuation areas with a mosaic pattern Air space consolidation in dependent area
<i>Rare</i>	<i>LIP</i>	Perivascular cysts and ground-glass opacities Centrilobular and subpleural nodules		
	<i>PPFE</i>	Apical, pleural and subpleural thickening and scarring Lower lobes are normal Pneumothorax and pneumomediastinum		

Table 1. Classification of Idiopathic Interstitial Pneumonias (IIP) by the ATS / ERS revision 2013. Major IIPs are chronic fibrosing (IPF and NSIP), smoking related (RB-ILD and DIP) and acute/subacute (COP and AIP). Rare IIPs are LIP and PPFE [1].

IIP idiopathic interstitial pneumonia, NSIP nonspecific interstitial pneumonia, RB-ILD respiratory bronchiolitis interstitial lung disease, DIP desquamative interstitial pneumonia, COP cryptogenic organizing pneumonia, AIP acute interstitial pneumonia, LIP lymphocytic interstitial pneumonia, PPFE pleuro parenchymal fibro elastosis.

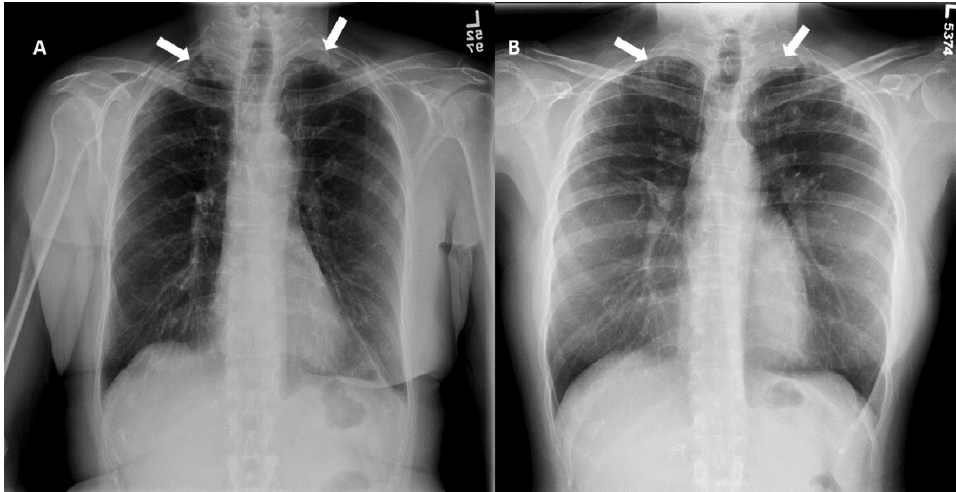


Fig. 3 – Posteroanterior (PA) chest radiograph for case number 1 (A) 2 years ago demonstrates subtle biapical pleural thickening (arrows) and left basilar atelectatic bands that is stable compared to prior radiograph 5 years ago. (B) corresponds to case number 2 with biapical findings seen in the PA chest radiograph. Note the absence of concomitant fibrotic changes in other lung fields.

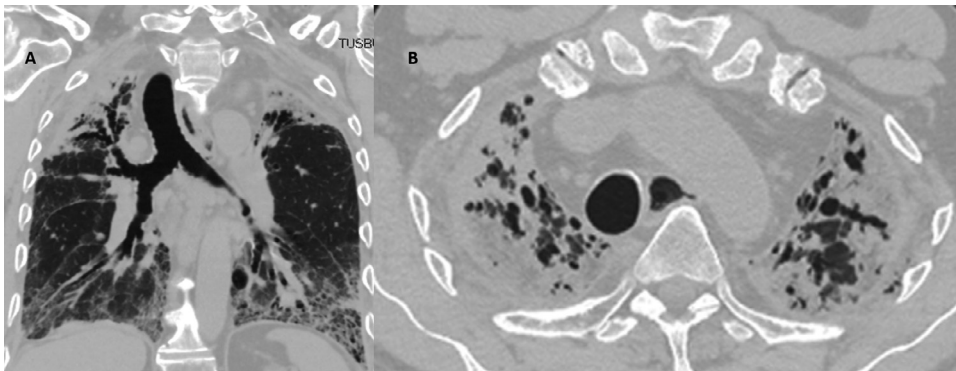


Fig. 4 – Coronal (A) and axial (B) unenhanced CT of the chest demonstrating biapical pleural thickening and subpleural fibrosis traction bronchiectasis and concomitant bilateral lower lobe fibrotic changes and honeycombing. Based on Reddy et al. classification, these findings are consistent with PPF.

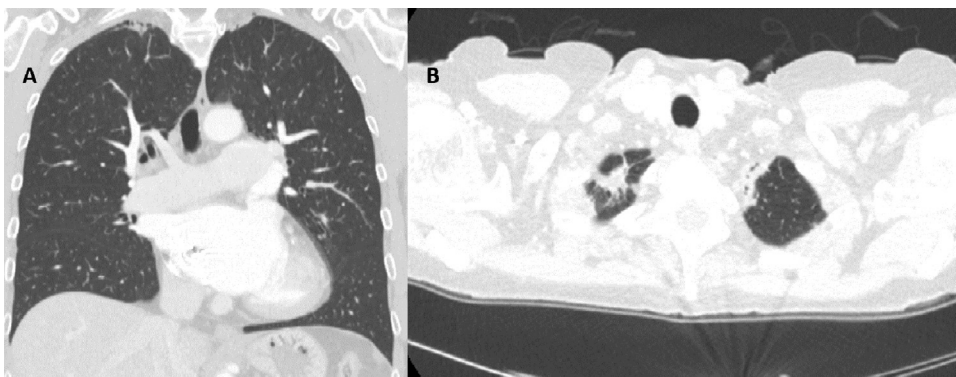


Fig. 5 – Coronal (A) and axial (B) unenhanced CT of the chest demonstrate biapical pleural caps measuring less than 5 mm in both hemithoraces.

the final impression. We identified 13 cases that were further reviewed by a radiology faculty, and of these cases, two met the radiographic characteristics for PPFE as discussed earlier.

Radiologic pattern recognition

In the early phases of the disease, chest radiograph may show subtle biapical pleural thickening, in an otherwise unremarkable exam (Fig. 3). As the disease progresses, additional findings can be appreciated, such as pleuro-parenchymal thickening, upper lobe volume loss and superior retraction of the hila.

The routine use of both axial and coronal reconstruction is recommended for evaluation of PPFE cases. Characteristic CT pattern of PPFE was described by Frankel et al. as bilateral apical pleuro-parenchymal fibrosis with subpleural lung involvement and reduction of upper lobe volumes [2]. Parenchymal retraction, traction bronchiectasis and upward displacement of hila are also commonly seen with PPFE [14]. Recurrent pneumothoraces were also reported in patients with PPFE following allograft bone marrow transplantation [15].

In the early stages of PPFE, CT findings are subpleural nodular and reticular opacities confined to the lung apices. Peribronchial consolidation with minimal basilar honeycombing can also be seen. As the disease progresses, progressive pleuro-parenchymal thickening, reticulation, septal thickening, and traction bronchiectasis develop. Eventually, lower lobe involvement occurs with volume loss and diaphragmatic elevation. In the end stage disease, large cysts and bullae can be seen in the upper lobes [2,16,17].

Reddy et al. proposed CT criteria for “definite PPFE” as pleural thickening with subpleural fibrosis in the upper lobes and minimal lower lobe involvement. They also proposed CT criteria for “consistent with PPFE” as pleural thickening with subpleural fibrosis not necessarily concentrated in the upper lobes or with concomitant features of other fibrotic lung diseases (Fig. 4) [17]. In the absence of these criteria, “inconsistent with PPFE” can be used.

Different patterns of coexisting lung fibrosis can be seen with PPFE. Most frequent of these are the usual interstitial pneumonia (UIP), followed by non-specific interstitial pneumonia (NSIP) and less frequently, hypersensitivity pneumonitis (HP) [17–20]. These changes tend to develop separate from the PPFE findings, towards the lower lobes.

The principal differential diagnosis is apical pleural cap which is a more frequently seen entity in elderly individuals [21]. Pleural caps typically do not exceed the apical 5 mm of both hemithoraces, unlike PPFE which can extend caudally (Fig. 5).

The most reported complication of PPFE is pneumothorax with a rate of occurrence ranging from 30% to 75%. The proportion of patients who experience pneumothorax is significantly higher in PPFE patients compared to idiopathic pulmonary fibrosis patients. Pneumothorax in PPFE patients tends to be recurrent in nature.

Biopsy when obtained shows benign findings dense pleural fibrosis, intra alveolar fibrosis and septal elastosis.

Conclusion

Recognition of PPFE on routine CT chest is important as this condition may not be as rare as initially thought. Identifying PPFE early on is clinically relevant as a subgroup of patients have rapid deterioration and poor prognosis. These patients need inter disciplinary follow up and may benefit from the use of antifibrotic medications or be candidates for lung transplant.

Patient consent statement

Formal consents are not required for the use of entirely anonymised images from which the individual cannot be identified- for example, xrays, ultrasound images, pathology slides or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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