Combined pulmonary fibrosis and emphysema with pulmonary arterial hypertension: A Rare Case Report

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Combined pulmonary fibrosis and emphysema (CPFE) is a recently recognized radiologically defined syndrome characterized by simultaneous coexistence of both upper lobe emphysema and lower lobe pulmonary fibrosis. We present a case of CPFE in a 57-year-old male smoker who presented with dry cough, progressive breathlessness, and swelling of feet. His chest X-ray revealed bilateral lower Zone reticulonodular opacities with hyperlucent upper Zones. Pulmonary function tests showed well-preserved lung volumes and reduced diffusing capacity of the lung for carbon monoxide. High-resolution computed tomogram showed bilateral lower lobe subpleural honeycombing along with fibrosis and traction bronchiectasis with bilateral upper lobe emphysema predominantly paraseptal type. His 2D echo was suggestive of moderate pulmonary arterial hypertension.

Keywords: Combined pulmonary fibrosis and emphysema, Diffusing capacity of the lung for carbon monoxide, High-resolution computed tomogram, Pulmonary arterial hypertension

INTRODUCTION

Combined pulmonary fibrosis and emphysema (CPFE) is a recently recognized radiologically defined syndrome characterized by simultaneous coexistence of both upper lobe emphysema and lower lobe pulmonary fibrosis. These patients present with a unique lung function profile of apparently normal or minimally altered lung volumes along with a significant reduction of diffusing capacity of the lung for carbon monoxide (DLCO) and hypoxemia which worsens with exercise. Morbidity in patients with CPFE is largely attributable to the development of pulmonary hypertension, which is the principal prognostic factor for this condition.

CASE REPORT

A 57-year-old man, smoker of 30 pack-years, presented with dry cough, progressive breathlessness since 5 months, facial puffiness and swelling of feet since 1 month. Initially, patient was breathless only with severe exertion, but it progressively got worse to the point where the patient has to stop for breath after walking 100 yards. He is a farmer and there was an exposure to agrochemical compounds for the last 30 years. There were no similar complaints in the past. There was no history suggestive of connective tissue disorders. On general examination, clubbing of grade 3 present and he had pedal edema of pitting type with raised jugular venous pressure. On auscultation, bilateral basal end-inspiratory fine crackles were heard.

Investigations

Routine hematological and biochemical investigations were within normal limits. Sputum smear microscopy for acid-fast bacilli negative for 2 consecutive days.

Chest X-ray posteroanterior view showed bilateral lower Zone reticulonodular opacities with hyperlucent upper Zones (Figure 1).

HRCT chest showed bilateral lower lobe subpleural honeycombing along with fibrosis and traction bronchiectasis with bilateral upper lobe emphysema predominantly paraseptal type (Figures 2-4).
Spirometry showed relatively preserved lung volumes with (FEV1) of 86% predicted, forced vital capacity (FVC) of 87% predicted and FEV1/FVC ratio of 98% of predicted, forced expiratory flow 25-75% was 49% of predicted, indicating early smaller airway obstruction. Despite well-preserved lung volumes DLCO reduced to 30% of predicted.

6 min walk test: Patient walked 335 m with 5% desaturation from baseline 97% SpO2 with room air.

Polysomnogram report: Apnea-hypopnea index was 9.7, but the patient had no symptoms suggestive of obstructive sleep apnea. Therefore, this report can be regarded as normal according to INOSA guidelines 2014.

2D Echo showed moderate pulmonary hypertension with TR Jet 3.7 m/s and RVSP 50 mmHg.

**DISCUSSION**

The histopathological coexistence of pulmonary fibrosis and emphysema first appeared in literature in 1970s described by Auerbach et al.\(^3\) CPFE, a distinct clinical entity characterized by the simultaneous coexistence of upper lobe emphysema and lower lobe pulmonary fibrosis was first described radiologically by Wiggins et al. in 1990.\(^4\) Initially, it was thought to be coincidental, but later Cottin et al. proposed as a distinct syndrome.\(^5\) Studies estimated the prevalence of CPFE to be between 5 and 10% of cases of diffuse interstitial lung disease, although the exact prevalence remains unknown.\(^5\)

Smoking is an important risk factor that is consistently associated with CPFE. Tobacco smoke-induced oxidative and nitrative stress in the lungs may amplify inflammation due to reduced histone deacetylase activity that may contribute pathogenetically to both emphysema and fibrosis.\(^6\) Smoking may also contribute to both emphysema
and fibrosis by overexpression of tumor necrosis factor - α and platelet-derived growth factor - β (PDGF-β). Exposure to agrochemical substances has also been described as risk factor for CPFE. Diaz Cle Leon et al. demonstrated evidence of emphysema in 20% of telomerase mutation carriers with idiopathic pulmonary fibrosis (IPF). Cottin et al. reported a dominant mutation 173T in the surfactant protein C gene in a patient with CPFE. These findings merit further studies.

In contrast to classical CPFE, which is more common in male smokers, an associated form of CPFE with CTD is more common in young female smokers which has less adverse prognosis. Predominant CTDs associated with CPFE are rheumatoid arthritis, systemic sclerosis, and mixed CTDs.

Kitaguchi et al. reported that 47% of patients with CPFE had lung cancer and squamous cell carcinoma was the most common subtype. Lung cancer may be more prevalent in CPFE patients than patients with COPD or IPF alone.

Exertional dyspnea is the most common presenting symptom in patients with CPFE. Cough with or without sputum production, chest pain and wheeze may also be seen. On examination, end-inspiratory fine (velcro) crackles mainly in basal regions are the predominant findings and digital clubbing may also be seen in many of these patients.

Chest X-ray may reveal reticulonodular infiltrates in both lung bases or an interstitial pattern and hyperlucency in the apices. HRCT is the imaging of choice to establish the diagnosis of CPFE. Upper lobe emphysema and lower lobe interstitial pulmonary fibrosis are the characteristic HRCT features suggestive of CPFE. Kitaguchi et al. found paraseptal emphysema as most common emphysematous lesion among bullous, paraseptal and centrilobular changes. Mejia et al. were quantified and graded the emphysematous lesions as percentage and more than 10% of the affected lung was required for the diagnosis of CPFE. Cottin et al. found that the HRCT pattern in the lower lobes was typical of IPF in 51% of cases, strongly suggestive of IPF or fibrosing nonspecific interstitial pneumonia in 34% of cases and showed complex pattern with predominant reticular opacities in the remaining cases. Honeycombing, reticular intra-lobular opacities and traction bronchiectasis were the most frequent findings. Brillet et al. described three HRCT patterns as (1) progressive transition with diffuse emphysema (centrilobular and/or bullous) and zone of transition between bullae and honeycombing; (2) paraseptal emphysema with predominant subpleural bullae of enlarging size at the bases; (3) separate processes with independent areas of fibrosis and emphysema, and correlated with clinical and functional variables and found that progressive transition group patients had higher therapeutic lifestyle changes, and lower FEV₁/FVC when compared with other 2 groups.

These patients present with unique lung function profile often with preserved lung volumes in contrast with DLCO, which is markedly reduced. Forced expiratory volume in the first second, FVC, and total lung capacity are either normal or within subnormal range. Preserved lung volumes may be due to increased compliance by emphysema compensates the loss of volume by pulmonary fibrosis. The presence of both pulmonary fibrosis and emphysema accounts for the marked reduction in DLCO.

The prevalence of pulmonary arterial hypertension (PAH) is higher in CPFE (47-90%) when compared to emphysema and pulmonary fibrosis alone. Severity of PAH appears to be higher in CPFE patients.

At present, there are no effective treatment options for CPFE. Lung transplantation may also be considered as an option for CPFE like IPF patients.

Change in FEV₁ appears to be the best predictor of mortality in CPFE patients. Presence of PAH, finger clubbing, %FEV₁/%FVC >1.2, lower diffusing capacity are the independent predictors of survival. In study conducted by Cottin et al. (2005), survival rate was 91.7% at 1 year, 87.5% at 2 years, and 54.6% at 5 years, with a median survival of 6.1 years.

CONCLUSION

We report a case that highlights a number of characteristics of combined pulmonary fibrosis and emphysema. CPFE is a recently recognized radiologically defined syndrome that pulmonologists should be aware of and should consider in the differential diagnosis when evaluating patients with markedly reduced diffusing capacity and relatively well-preserved lung volumes. Further research is essential regarding etiology, pathophysiology, and management of this distinct clinical entity.

REFERENCES


