CASE REPORT

A Rare Case of CPFE Syndrome: An Unacknowledged Entity

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Abstract

Introduction: Combined pulmonary fibrosis with emphysema (CPFE) is an under-recognized pulmonary syndrome characterized by the coexistence of the upper lobe-predominant emphysema and lower lobe-predominant fibrosis. Severe dyspnea and incommensurately impaired gas exchange with preserved lung volume are its features.

Case description: A 51-year-old male smoker presented with shortness of breath for 5 months, which increased since 10 days, cough with mucoid expectoration. On examination: SPO_2: 84% on room air, Grade-2 clubbing, bilateral pitting-type pedal edema, and bibasilar inspiratory fine crackles were heard. The chest radiograph showed increased translucency in the upper zone and irregular linear opacities in the lower zones of the lungs. He had uncompensated respiratory acidosis on arterial blood gas analysis with elevated total WBC counts. High-resolution computer tomography of the chest (HRCT Chest) showed dilated main pulmonary artery diameter, pan-acinar emphysematous changes in bilateral upper lobes, and subpleural basal reticular opacities with minimal honeycombing in the lower lobes. His two-dimensional echocardiography was suggestive of moderate pulmonary hypertension (PH). Pulmonary functional testing showed a low normal FEV1/FVC ratio and significantly reduced diffusing capacity of the lungs for carbon monoxide (DLCO).

Discussion: Combined pulmonary fibrosis with emphysema is an uncommon syndrome with progressive dyspnea, fractious cough, and recurring exacerbations. Risk factors being male gender, smoking, and genetic susceptibility to early-onset pulmonary hypertension with an increased risk of lung cancer and reiterative exacerbations are its complications. Mortality is significantly high in patients with CPFE, with a median survival of 2–8.5 years.

Conclusion: Combined pulmonary fibrosis with emphysema syndrome should be surmised in male smokers with sternly impaired DLCO and well-nigh preserved lung volumes, and the diagnosis to be confirmed using HRCT chest. Complications such as PH and increased lung cancer risk are more common in CPFE, leading to a dismal prognosis. Hence, early diagnosis and pertinent therapy are of utmost importance in ameliorating the median survival of the infirm.

Keywords: Case report, Combined pulmonary fibrosis with emphysema, Emphysema, Fibrosis, Pulmonary hypertension.

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Abbreviations Used in this Article

ABG = Arterial blood gas; BMI = Body mass index; CPFE = Combined pulmonary fibrosis with emphysema; DLCO = Diffusing capacity of the lungs for carbon monoxide; FEV1/FVC = Ratio forced expiratory volume in 1st second/forced vital capacity; HRCT = Chest High-resolution computer tomography of the chest; LTOT = Long-term oxygen therapy; MPA = Main pulmonary artery; NSCLC = Non-small cell lung cancer; OP = Organizing pneumonia; PFT = Pulmonary function testing; PH = Pulmonary hypertension; 2DECHO = Two-dimensional echocardiography.

Introduction

Combined Pulmonary Fibrosis with Emphysema (CPFE) is an under-recognized pulmonary syndrome characterized by the contemporaneousness of emphysema and fibrosis to varying extents within lung parenchyma. Severe dyspnea and incommensurately impaired gas exchange with embalmed lung volume are its features.[1]

Aim and Objective

To divulge a case of CPFE syndrome, an unacknowledged entity.

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Case Description

A 51-year-old male smoker presented with shortness of breath for 5 months, which was increased for 10 days, cough with mucoid expectoration that increased in amount for the last 10 days, no

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known comorbidities, no history of long-term drug intake, no pet exposure, occupation bookseller, and no significant family history.

On Examination

The patient is moderately built with a body mass index (BMI) of 22.87 kg/m^2, peripheral arterial saturation of 84% with room air, Grade-2 digital clubbing, bilateral pitting-type edema noted in lower extremities, bibasilar inspiratory fine crackles with decreased breath sound intensity in all areas were heard on auscultation. He had an uncompensated respiratory acidosis on arterial blood gas analysis (ABG) (Table 1) with elevated total WBC counts.

Chest radiograph showed increased translucency in the upper zone and irregular linear opacities in the lower zones of the lungs. High-resolution computed tomography (HRCT) of the chest showed dilated main pulmonary artery (MPA) trunk diameter, pan-acinar emphysematous changes in bilateral upper lobes, right middle lobe traction bronchiectasis, and subpleural basal reticular opacities with minimal honeycombing and subpleural cysts in lower lobes.

The CTD profile showed negative serology for autoantibodies. His two-dimensional echocardiography (2DECHO) showed dilated RA, RV, and flattened interventricular septum causing a D-shaped left ventricle, with moderate tricuspid regurgitation, suggestive of moderate PH. Pulmonary function testing (PFT) showed a low normal forced expiratory volume in 1st second/forced vital capacity (FEV1/FVC Ratio) that was 68% predicted in the prebronchodilator test, glaringly reduced DLCO by 45.9% predicted (Table 2).

The patient had tachypnea on presentation with low peripheral arterial saturation and respiratory acidosis evident in ABG. The patient was admitted to the ICU and given pressure support ventilation with NIPPV bilevel mode. Treated with IV antibiotics, systemic steroids, bronchodilators, and diuretics fluid management, and supportive care was given. The patient clinically improved and weaned off from pressure support to oxygen therapy on 4th day. Later, after stabilizing patient was discharged on long-term oxygen therapy (LTOT), antifibrotic drugs, and respiratory vaccinations were admonished.

Table 1: Arterial blood gas analysis of patient at the time of presentation

Parameters	*Values*
PH	7.22
$PaCO_2$ (mm Hg)	63.35
PO_2 (mm Hg)	58.12
HCO_3 (mmol/L)	26.50
SaO_2 %	92.12
Na (mmol/L)	141.7
Cl (mmol/L)	106.2
Se. Albumin	4.02
Hemoglobin (gm %)	15.29
Hematocrit	45.88

Discussion

In 2005, Cottin et al. defined a syndrome termed "combined pulmonary fibrosis and emphysema (CPFE)", which is characterized by a history of heavy smoking, exercise-induced hypoxemia, upper lobe emphysema, lower lobe fibrosis, unanticipated near normal spirometric volumes but disproportionately severe reduction of carbon monoxide transfer.[2–4]

Male gender, current or former heavy smoking, genetic susceptibility to SFTPC mutation, ABCA3 mutation, and MMP-1 Gene dysfunction are the risk factors for this syndrome.[5–7]

Diagnosis of CPFE Syndrome is based on HRCT chest imaging showing the coexistence of apparent interstitial pneumonia pattern with pulmonary emphysema mixed with large thick-wall cysts.[8]

In the upper lobe, emphysema is prevailing (Fig. 1). All three major subtypes, pan-acinar, centrilobular, and paraseptal

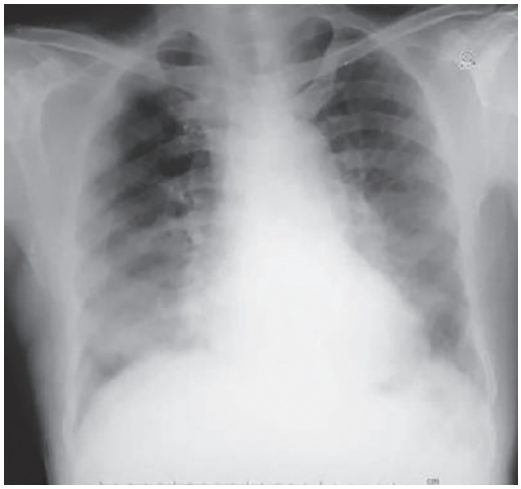
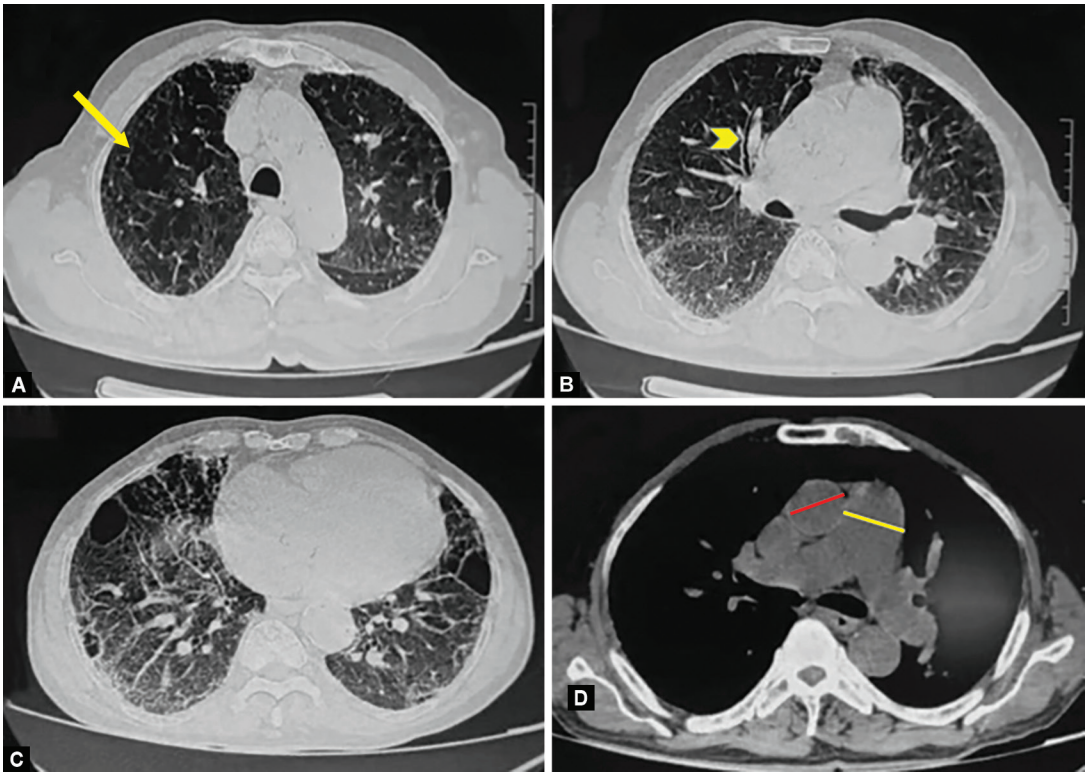


Fig. 1: Chest radiograph (posteroanterior view): Showing increased translucency in B/L upper zones, B/L Irregular radiodense linear opacities in lower zones of lung fields

Table 2: Pulmonary function test values of the patient

	Prebronchodilator			*Postbronchodilator*	
Test	*Predicted value*	*Actual value*	*% Predicted value*	*Actual value*	*Percent change*
FVC (L)	4.22	3.19	76	3.33	5%
FEV1 (L)	3.39	2.18	64	2.23	3.3%
FEV1/FVC	80	68		71	4%
RV (L)	2.32	2.72	117		
TLC (L)	6.09	6.19	101		
RV/TLC	38.0	43.9			
DLCO (mL/min/mm Hg)	28.05	12.9	45.9		



Figs 2A to D: (A) High-resolution computed tomography chest (axial view-lung window) at the level of the arch of aorta showing pan-acinar emphysema (Yellow arrow) with few reticulations and subpleural cysts with centrilobular nodules corresponding to airway cantered fibrosis in the right lung field; (B) At the level of the right pulmonary artery unveiling traction bronchiectasis in the right middle lobe (Yellow arrowhead), enlarged AP window node, with basal reticulations in B/L lower lobes of lung fields; (C) At the level of cardiac ventricular showing subpleural basal reticular opacities with minimal honeycombing in lower lobes–Usual interstitial pneumonia pattern (early fibrotic changes). Along with a thick wall (> 1 mm), cystic lesions of diameter >1 cm situated just beneath the pleura are noted; (D) High-resolution CT chest (axial view-mediastinal window) at the level of bifurcation of pulmonary trunk showing dilatation of pulmonary trunk with a diameter of 35 mm (Yellow line), with descending aorta diameter of 29 mm (Red line). An increase in the pulmonary trunk to descending aorta diameter ratio indicates PH

emphysema can occur in CPFE. The most common is the pan-acinar type of emphysema, as seen in our patient (Fig. 2A). The presence of paraseptal emphysema is associated with a worse prophecy.[1]

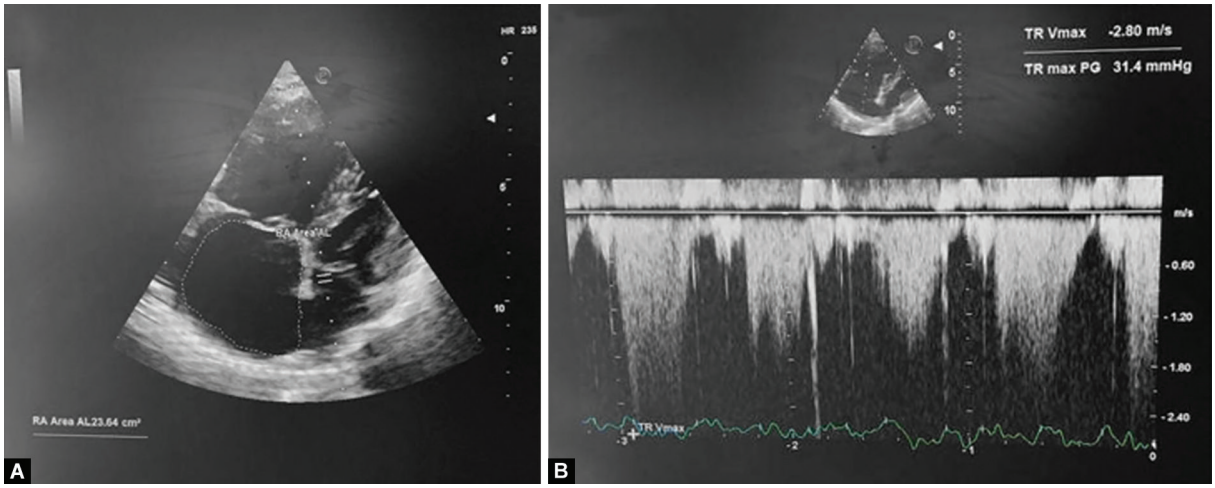
In the lower lobe fibrosis is predominant, and the most common interstitial pneumonia pattern is UIP as seen in our case with diffuse basal predominant posterior subpleural peripheral irregular reticular opacities with traction bronchiectasis (Fig. 2B), honeycombing (Fig. 2C), the other being NSIP pattern with bilateral lower zone predominant ground glass opacities with or without consolidations with reticular opacities, traction bronchiectasis with subpleural sparing. The organizing pneumonia (OP) pattern is basal predominant patchy ground glassing with or without the reverse halo sign with centrilobular nodules; RB-ILD patterns are also possible. Cysts of varying size usually more than 1 cm, with thick walls of 1mm appear mostly in subpleural locations (Figs 2A and C) and can also be centrilobular in location. Fibrotic changes along the respiratory bronchioles appear as centrilobular lesions corresponding with airway-centered fibrosis.

On lung function testing, the fibrotic component fosters a restrictive pattern, that is counterbalanced by emphysematous components causing obstructive disorder in CPFE leading to a delayed diagnosis. Markedly impaired DLCO is an important clue in the diagnosis of CPFE. This is due to (A) Progressive loss of functional alveoli because of emphysema. (B) Fibrotic component leading to a decline in pulmonary capillary volume causing ventilation-perfusion discrepancy.[9,10]

Respiratory tract infections, pneumothorax, heart failure, and pulmonary thromboembolism, are the causes of exacerbations in CPFE. Clinically, Acute exacerbation of CPFE is characterized by bronchospasm airflow obstruction, radiological atelectasis, mucus impaction, airway wall thickening, mediastinal lymphadenopathy, and consolidations. In case of clear signs of bacterial infection, such as if two of the three Anthonisen criteria are present antibiotics are to be added to management.[11,12]

Mortality is significantly high in the patients with CPFE with a median survival of 2.1–8.5 years.[13] Predictors of mortality in CPFE syndrome are Low BMI, clubbing, abridged FEV1, and early onset PH.[14] Our patient had clubbing and also instigated moderate PH.

Pulmonary hypertension occurs early after diagnosis of CPFE and is more common in patients with emphysema-predominant CPFE, as in our patients.[15,16] High-resolution computer tomography of the chest mediastinal window (Fig. 2D) showed increased pulmonary artery to descending aorta diameter ratio indicating PH (normal ratio 1:1). The normal MPA in males is 29 mm and in females is 27 mm. His 2DECHO showed dilated RA, RV, and flattened interventricular septum causing a D-shaped ventricle (Fig. 3A), with moderate tricuspid regurgitation (Fig. 3B). A study conducted by Sir Joseph Jacob et al. concluded that PH association is more common in CPFE than in IPF cases alone without emphysema.



Figs 3A and B: (A) Two-dimensional echocardiogram (apical four-chambered view) showing end-systolic right atrial area > 18 cm^2. Dilated RA, RV, and D-shaped left ventricle due to flattening of interventricular septum, are all the signs suggestive of pulmonary hypertension; (B) Two-dimensional echocardiogram continuous wave Doppler of tricuspid valve showing peak tricuspid regurgitation velocity (here TR V max is 2.80 m/s). This TR V max with the presence of other signs of PH signs, echocardiographic probability of pulmonary hypertension is intermediate in this patient

Combined pulmonary fibrosis with emphysema is associated with an increased risk of lung cancer. More common is non-small cell lung cancer (NSCLC) squamous cell type, compared to individual IPF or emphysema alone.[17] The prognosis worsens as the patient develops lung malignancy. Due to poor lung functional reserve, the patients cannot undergo surgery, and radiotherapy may further enhance lung fibrosis.

Conclusion

- Combined pulmonary fibrosis with emphysema syndrome should be surmised in male smokers with sternly impaired DLCO and well-nigh preserved lung volumes. The diagnosis should be confirmed using an HRCT chest.
- Complications such as PH, increased lung cancer risk, and reiterative exacerbations are more common in CPFE, leading to a dismal prognosis.
- Hence, early diagnosis and appropriate therapy are of utmost importance to ameliorate the median survival of the infirm.

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