Case report

Combined pulmonary fibrosis and emphysema in a smoker

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Abstract

There is increasing clinical, radiologic and pathologic recognition of the coexistence of emphysema and pulmonary fibrosis, resulting in a clinical syndrome known as combined pulmonary fibrosis and emphysema (CPFE). It is characterized by dyspnoea, upper-lobe emphysema, lower-lobe fibrosis and abnormalities of gas exchange. This syndrome is frequently complicated by pulmonary hypertension, acute lung injury and lung cancer. The CPFE syndrome typically occurs in male smokers, and the mortality associated with this condition, especially if pulmonary hypertension is present, is significant. Although most cases of CPFE are likely to represent the common fibrotic pattern of upper lobe fibrosis (UIP), a few cases have been reported as showing desquamative interstitial pneumonia (DIP) or unclassified interstitial pneumonia.

We present a case of CPFE which has HRCT evidence of emphysema of upper lobes and NSIP type of fibrosis in lower lobes in a smoker with normal pulmonary function.

Introduction

Combined pulmonary fibrosis and emphysema (CPFE) is one of smoking-related lung diseases. Emphysema is characterized by the permanent abnormal enlargement of airspaces distal to the terminal bronchioles, accompanied by destruction of their walls. The characteristics of emphysema do not, by definition, include thickening of the alveolar septa and fibrosis. However, coincidental idiopathic pulmonary fibrosis (IPF) and emphysema was firstly reported in 1990 by Wiggins et al[1] in London. The term, CPFE, first described by Cottin et al. was defined radiographically by the presence of classic features of centrilobular and/or paraseptal emphysemas in the upper lobes and pulmonary fibrosis (mainly IPF/UIP) in the lower lobes[2]. Smoking-related interstitial lung disease (SRILD) include desquamative interstitial pneumonia (DIP), respiratory bronchiolitis-related interstitial lung disease (RB-ILD), pulmonary Langerhan cell histiocytosis (LCH) and idiopathic pulmonary fibrosis (IPF).[3] Smoking is a common risk factor for both emphysema and pulmonary fibrosis. Most CPFE patients have mixed pattern on pulmonary function and marked reduction in diffusing capacity for carbon monoxide (DLCO) which is associated with a high prevalence of pulmonary hypertension.

Case report

A 60-year-old man was referred by a cardiologist for evaluation of dyspnoea. He had a dyspnoea of MRC grade 3 which was of insidious onset and progressively worsening over the last 6 years. It was associated with a mild non productive cough but without pleurisy, angina, orthopnoea, paroxysmal nocturnal dyspnoea or constitutional symptoms. He had a history of essential hypertension and diabetes for 10 years and an inferior ST elevation myocardial infarction complicated with acute left ventricular failure which was treated with thrombolysis in 2011. He was followed up at a cardiology clinic and he was taking aspirin, carvedilol, captopril, atorvastatin and metformin. He had no past history of pulmonary or autoimmune disorders. Currently he smokes 20 cigarettes a day and he has a 40 pack year smoking history. He is a spray painter since 20 years of age.

Physical examination revealed oxygen saturation of 95%, digital clubbing and hyperinflation of upper chest and end inspiratory crackles in both lung bases with scattered rhonchi. Laboratory values were as follows: White cell count 9000/mm3 with normal differentiation, haemoglobin 16.4g/dl, pack cell volume 57, platelet count 344000/mm3, ESR 11mm/1st hour, C-reactive protein 2.5mg/dl, fasting blood sugar 100mg/dl and ANA negative. Chest radiograph showed fine reticulation in the lower zones with relative hyper lucent lung fields in the upper zones (Figure 1). High resolution computed tomograghy (HRCT) demonstrated paraseptal emphysema (more than 10% of the lung) in the upper lung field (Figure 2) and intra and inter-lobular septal thickening and traction bronchiectasis sparing subpleural areas in the lower lung field (Figure 3). There was no honey combing.

Pulmonary function testing showed a FVC of 1.91 L (79.5% of predicted), FEV1 of 1.71 L (87.1% of

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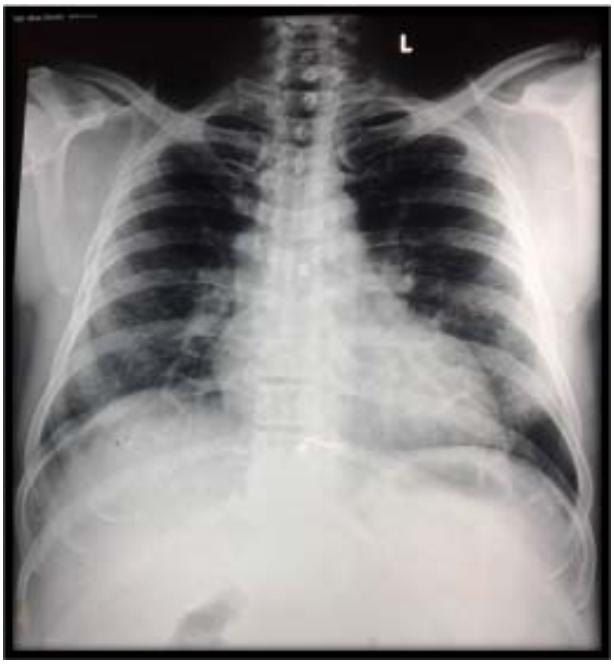

Figure 1. Chest radiograph showing fine reticulation in the lower zones with relative hyper lucent lung fields in the upper zones.

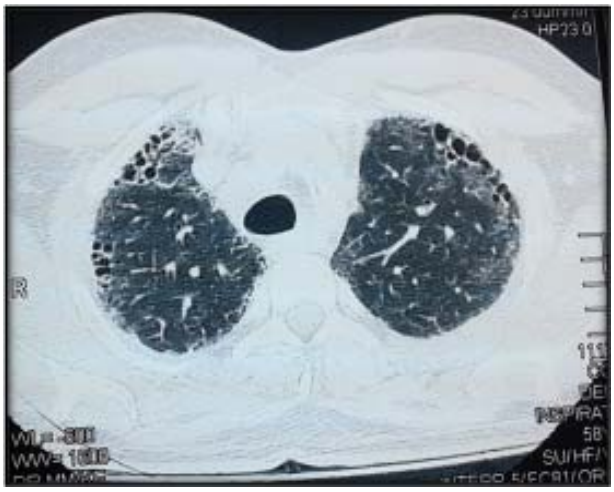

Figure 2. HRCT demonstrating paraseptal emphysema (more than 10% of the lung) in the upper lung field.

predicted) and FEV1/FVC was 89.1%. Reversibility was not achieved with bronchodilators. Six minute walk test showed a desaturation of 6% from the base line value of 95%. Diffusion capacity was not done due to unavailability. Bronchoalveolar lavage (BAL) revealed total cellularity of 30 cells/ml consisting of 70% lymphocytes and 30% neutrophils. Bronchial wash for cytology showed pigment laden macrophages. 2D echocardiogram revealed mild impairment of left ventricular function with ejection fraction of 45% and

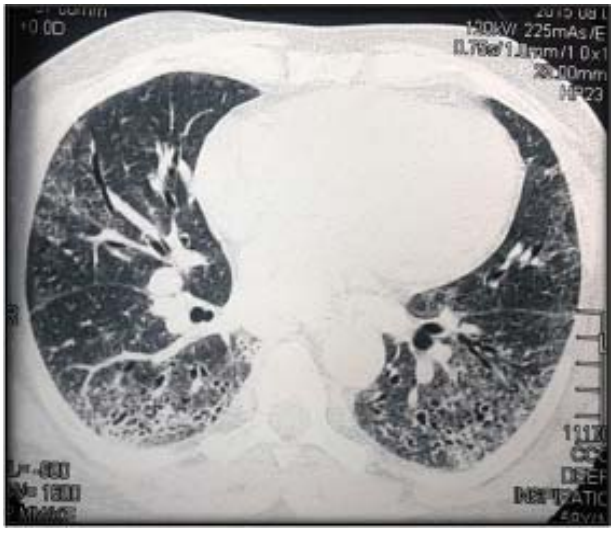

Figure 3. HRCT demonstrating intra and interlobular septal thickening and traction bronchiectasis. No ground glass changes.

inferoposterior hypokinesia, without pulmonary hypertension. Clinical, radiological and cytological information established the diagnosis of combined pulmonary fibrosis and emphysema. We advised the patient regarding complete cessation of smoking and treated him with tiotropium bromide 18mcg inhaler and sustained release theophylline 300mg bid.

Discussion

CPFE is a newly defined syndrome, in which upper lobe emphysema (>10% of the lung volume) coexists with significant pulmonary fibrosis in the lower lobe defined by honeycombing, reticular opacities, and/or traction bronchiectasis on HRCT. CPFE has been receiving considerable attention because pulmonary hypertension and severe reductions in diffusion capacity are highly prevalent in CPFE.[4] However, the prevalence of CPFE is still not specifically known. CPFE is most often observed in males (mean age of 65 years) who are tobacco smokers or ex-smokers of 40 pack-years.[5]

The pathogenesis of CPFE has not been fully elucidated to date. It is still unclear whether emphysematous and fibrotic lesions progress independently or if one results from the other. Perhaps there are some undiscovered mechanisms, which may involve a variety of cytokines and shared signaling pathways, resulting in both emphysema and pulmonary fibrosis in genetically susceptible individuals after the exposure to environmental triggers (such as smoking).[6] In addition to tobacco exposure, other environmental exposure as a potential trigger of lung injury in the CPFE syndrome is also possible i.e. agrochemical compounds.[7]

Cough and dyspnea are common symptoms in patients with CPFE, COPD and IPF. Other common signs and symptoms of respiratory tract, such as cough, wheezing, cyanosis, asthenia and so on, may also appear in some patients. On physical examination, patients with CPFE usually have inspiratory dry crackles named 'velcro sounds' from the underlying pulmonary fibrosis on chest auscultation, as reported in 87-100% of cases, and a number of them (43-45%) have finger clubbing.[2]

However, although pulmonary function tests usually show respiratory volumes and flows that are normal or subnormal, diffusing capacity of the lung for carbon monoxide (DLCO) is substantially reduced and exercise hypoxaemia is common. Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), arterial oxygen tension (PaO2) and arterial oxygen saturation (SaO2) at rest, and SaO2 and PaO2 at exercise are significantly decreased in patients with CPFE.[2]

The diagnosis of the CPFE syndrome is based on findings on high-resolution computed tomography (HRCT) of the chest.[8] Although emphysema may modify the HRCT appearance of fibrosis, the characteristic imaging features of CPFE include radiological evidence of emphysema in the upper zones (i.e. centrilobular and/or paraseptal emphysema in 90% of cases), and diffuse infiltrating fibrosing lung disease at the bases (subpleural reticular opacities, honeycomb images and traction bronchiectasis), with more frequent ground-glass opacities than in IPF. However, patients with CPFE show a high HRCT fibrotic score.

Although the pathology of CPFE is heterogenous and includes DIP, organizing pneumonia, and unclassifiable interstitial pneumonia, UIP is the most common pattern and biopsy-proven NSIP has not yet been reported. Drug-induced NSIP is rare and NSIP may also be caused by the inhalation of high levels of mould and/bacteria. However, in our case, no changes in drug ingestion, living environment, or other exposures associated with NSIP were noted. He is a spray painter and this is known to cause occupational asthma than lung fibrosis. Broncho-alveolar lavage (BAL) showed pigment laden macrophages which confirms the association with smoking related interstial lung disease.

Therapeutic options for patients with CPFE are limited and may require treatment for both IPF and emphysema. According to the most recent international guidelines, there are no data on which to make recommendations for treatment of emphysema in the setting of IPF.[9] Smoking cessation is an obvious objective. Oxygen therapy is appropriate for the management of hypoxaemia. Inhaled bronchodilators are often prescribed. Treatment with immunomodulator therapy, similar to that used for treating IPF, e.g. N-acetylcysteine or novel agents such as pirfenidone, has been considered, although no studies have been published to date on this issue.

Conclusion

In summary, our case describes CPFE in a smoker, which is a distinct but under-recognized and common syndrome with a characteristic presentation. It is more frequent than previously believed and may have a worse prognosis than IPF alone, with PH being the major determinant of morbidity and mortality. It is clear that many aspects of the CPFE syndrome remain to be explored.

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