Case Report

CPFE : The widening spectrum of Smoking related diseases

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Abstract:

Several recent studies have described a syndrome in which idiopathic pulmonary fibrosis (IPF) coexists with pulmonary emphysema. This comes as no surprise since both diseases are associated with a history of exposure to cigarette smoke. We report a case of combined pulmonary fibrosis and emphysema (CPFE) with severe pulmonary hypertension and corpulmonale in a 53-year-old farmer associated with tobacco smoking. Environmental exposure in the form of agrochemical compounds may be an additional risk factor in this case and confirms the clinical features of CPFE described elsewhere.

Key words Combined pulmonary fibrosis and emphysema (CPFE), idiopathic pulmonary fibrosis (IPF), pulmonary hypertension (PH).

Introduction

The findings of co-existing IPF and emphysema were first described in 1990 by Wiggins et al and the term combined pulmonary fibrosis and emphysema (CPFE) was coined by Cottin et al.[1] CPFE has been proposed as a new clinical entity in smokers or a different clinical phenotype in smokers developing idiopathic pulmonary fibrosis (IPF). These patients have severe dyspnoea, nearly stable lung functions, exercise desaturation, reduced diffusion capacity, severe pulmonary hypertension (PH) and associated shortened survival. High-resolution computed tomography (HRCT) usually shows upper lobe centrilobular emphysema and lower lobe fibrosis. The prevalence of CPFE may be close to 30% among cases of IPF and they have a significantly lower survival than those with only IPF.[2]

Case Report

A 53 year old farmer from Wayanad district of Kerala presented with progressive dyspnoea on exertion from grade 1 to grade 3, cough with scanty mucoid expectoration of 4 years and tiredness/fatigue on exertion of 1year duration which worsened since last one month with symptoms at rest. He, along with his father, were involved in agricultural activities from the age of fifteen, cultivating coffee, pepper and rice; not associated with rearing of cattle or birds. On examination, he was tachypnoeic, with a respiratory rate of 36/min, showed clubbing, had pedal oedema with elevated jugular venous pressure and bilateral fine crackles and minimal wheeze. His blood and sputum tests were within normal limits. Though he had a raised RA factor of 153, there were no joint symptoms or stigmata suggestive of a connective tissue disease. Arterial blood gas analysis showed pH 7.39/ PaO2 36.7/ PaCO2 49.3/ HCO3 29.8, with an alveolar arterial gradient of 67.13. X-ray chest [Figure 1] showed reticulonodular pattern mainly on left. HRCT [Figure 2] showed extensive fibrosis and ground glass pattern with mid-zone predominance with areas of honeycombing and upper lobe bullae. Spirometry showed mild restrictive abnormality with forced vital capacity (FVC) 1.86 L (65%predicted), forced expiratory volume in one second (FEV1) 1.48 L (65% predicted) and FEV1/FVC 80%. Diffusion capacity for carbon monoxide (DLCO) was 36% of the predicted value. On performing a six minute walk test, he could cover 56 metres only in two minutes with 11% Spo2 fall and increase in dyspnoea to 9 in BORG scale along with a pulse rate of 140/min and BP of 140/88 following which the test was terminated. Two-dimensional echocardiography (2D-ECHO) showed PH with tricuspid

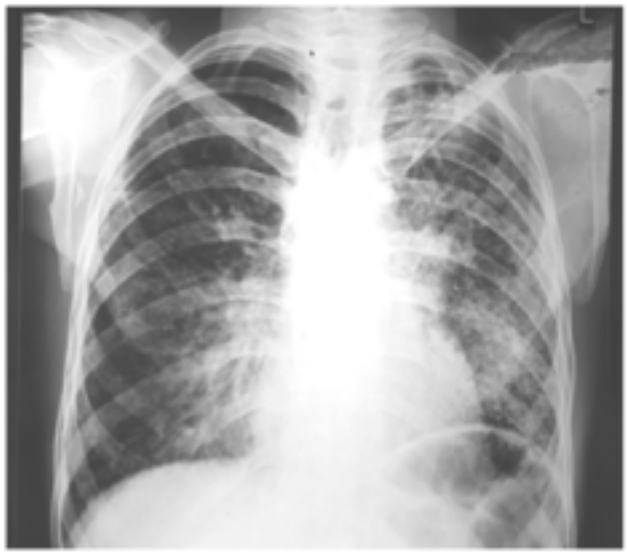

Fig. 1: Chest X-ray P/A view

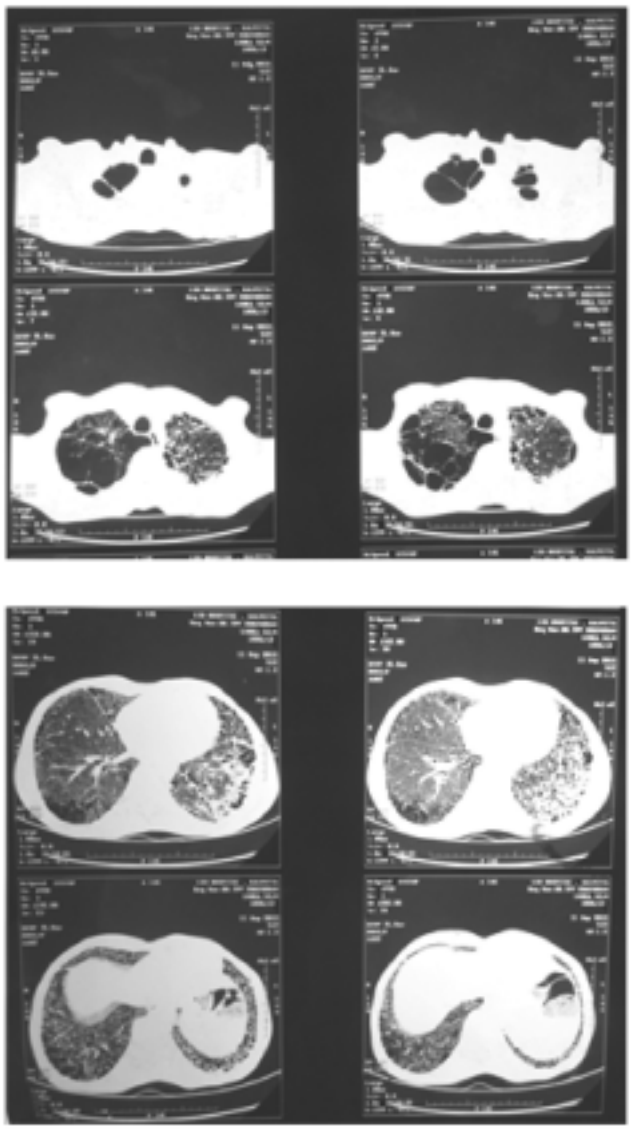

Figure2: HRCT Thorax

regurgitation (TR) jet- estimated pulmonary artery systolic pressure (PASP) of 68 mmHg with dilatation of right atrium and right ventricle. The clinical features, Pulmonary function tests and radiological picture was suggestive of CPFE. Thus a diagnosis of CPFE with corpulmonale was made and patient was treated with bronchodilators, LTOT, N Acetyl Cysteine, anticoagulants and other supportive measures. His condition gradually worsened over next two months period and finally succumbed to his illness.

Discussion

CPFE is most often observed in males (mean age of 65 years) who are tobacco smokers or ex-smokers of >40 pack-years [3]. CPFE has a poor prognosis, with a 5-year survival of 55%. CPFE may be found in patients presenting with lung cancer and cancer may develop in patients followed for CPFE, probably reflecting similarities in the susceptibility to chronic smoking-induced inflammation and carcinogenesis [4].Its association with connective tissue diseases like rheumatoid arthritis and systemic sclerosis and exposure to agrochemical compounds has also been described [5]. The risk of development of PH is higher (about 50%) in patients with CPFE than either IPF or emphysema alone, and its onset heralds a poor prognosis and increased mortality.

In most cases, CPFE occurs as a result of development of fibrosis in a known case of emphysema that may modify its progression. Conversely, the presence of pulmonary emphysema modifies the outcome of patients with IPF. A variety of pathologic patterns of pulmonary fibrosis have been reported in conjunction with emphysema in the CPFE syndrome including usual interstitial pneumonia, airspace enlargement with fibrosis, nonspecifc interstitial pneumonia, respiratory bronchiolitis associated interstitial lung disease with alveolar septal fbrosis, desquamative interstitial pneumonia with extensive fbrosis and unclassifiable smoking-related interstitial fbrosis.

Smoking results in the over expression of tumor necrosis factor-alfa (TNF-α), IL-1ß and neutrophil elastase which may be important in producing emphysema and pulmonary fibrosis. In a study by Wei et al, [6] pulmonary fibrosis in CPFE showed intrinsic characteristics, with smoking not being the major or direct pulmonary fibrosis-

driven factor. He suggested the role of serum pro-collagen III N-terminal peptide (PIIINP) as a marker of early detection and efficacy assessment parameter of treatment and the possible utility of anti-lymphocytes and immune regulation strategy for disease intervention. A heterozygous mutation in SFTPC (the gene encoding surfactant protein C) has been reported in a non-smoking young female with CPFE. In addition, both fibrosis and emphysema are associated with shorter telomeres and smokers also have shorter telomeres as compared with non-smokers.

The physiologic consequences of the CPFE syndrome include preservation of spirometric values and lung volumes despite extensive radiographic evidence of lung disease as well as marked impairment of gas exchange manifested as a reduction in DLco. Resting and exertional hypoxemia is common in CPFE syndrome. In the series by Cottin et al, mean PaO2 at rest on room air was 63± 14 mm Hg, with an elevated average A-a gradient of 41± 16 mm Hg and average exertional desaturation of 8.9% during 6-min walk testing.

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. The composite physiologic index (CPI) was developed to improve on previous prognostic measures in IPF by adjusting for emphysema and incorporating multiple measures of pulmonary function, namely forced expiratory volume in 1 s (FEV1), FVC and DLCo . The CPI score at diagnosis more accurately predicted mortality than the individual pulmonary function tests (PFTs) alone in patients with concomitant emphysema.

Therapeutic options for patients with CPFE are limited and may require treatment for both IPF and emphysema. 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. Lung transplantation should be considered for patients with CPFE, given the signifcant mortality associated with this disorder. The relatively preserved spirometry associated with CPFE may disfavour such patients for lung allocation.

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