

Combined Pulmonary Fibrosis and Emphysema in a welder

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ABSTRACT: *Combined Pulmonary Fibrosis and Emphysema in a welder. R. Roshan, M. Gupta, R. Kulshrestha, B. Menon, S.K. Chhabra.*

Combined pulmonary fibrosis and emphysema (CPFE) syndrome is an uncommon entity characterised by emphysema of the upper lobes and diffuse fibrosis of the lower lobes and carries a bad prognosis with the onset of pulmonary hypertension. Lung involvement due to exposures suffered by welders is generally considered benign though, rarely, a diffuse interstitial fibrotic disease has been reported. CPFE syndrome has however never been reported in welders. A 65-year-old man, welder by occupation and an ex-smoker, presented with progressive exertional dysp-

noea associated with dry cough noticed for the last four months. On examination, there was mild tachypnea, clubbing and bilateral basal velcro crepitations on chest auscultation. Lung function test revealed mild mixed ventilatory impairment with severe diffusion defect. HRCT chest showed bilateral upper lobe emphysema and diffuse interstitial fibrosis in the lower lobes. Transbronchial lung biopsy revealed interstitial fibrosis, chronic inflammation and iron deposits. A diagnosis of combined pulmonary fibrosis with emphysema (CPFE) with interstitial pulmonary siderofibrosis (IPS) was established. A review of literature did not show any other report of a similar nature.

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Introduction

Combined pulmonary fibrosis and emphysema (CPFE) syndrome, an uncommon entity characterised by upper lobe emphysema and pulmonary fibrosis of the lower lobes was first described by Wiggins *et al.* in 1990 [1]. It has since been increasingly recognised as a distinct syndrome occurring most often in association with Idiopathic Pulmonary Fibrosis (IPF) but also in pulmonary fibrosis due to other chronic interstitial pneumonias and connective tissue disorders [2, 3]. Its distinctive features include a male predominance, association with tobacco smoking, severe hypoxemia on exercise, nearly normal lung volumes and airflows, and severely impaired transfer capacity for carbon monoxide [2]. There is a high prevalence of severe pulmonary hypertension that worsens the prognosis [4]. Whether this unique combination of an obstructive and a restrictive lung disease represents simultaneous or sequential occurrence of the two diseases or these share a common pathway of pathogenesis is debatable.

Welding processes produce iron fumes and irritant gases. Lung involvement due to such exposure is generally considered benign although documented effects in welders include metal fume fever, airway irritation, lung function changes, susceptibility to pulmonary infections, and even lung

cancer. Causality and possible underlying mechanisms remain unclear [5-7]. A diffuse interstitial fibrotic disease, labeled as interstitial pulmonary siderofibrosis (IPS) has also been described on long-standing and heavy exposure to welding fumes but is rare [8, 9]. We recently managed the case of a welder who had clinical features of CPFE syndrome. The fibrotic condition of the lung was histologically found to be associated with iron deposition. As CPFE syndrome complicating IPS has never been reported earlier in a welder, we report this case.

Case Report

A 65-year-old male cigarette smoker (40 pack years) presented with progressive exertional dyspnoea and mostly dry cough of four months duration. He had been a welder in an iron industry for forty years. On examination, there was a mild tachypnea, normal pulse oximetry, clubbing and bilateral basal end-inspiratory crackles. Blood counts, glucose and renal biochemistry were in the normal range. The chest radiograph showed bilateral basal reticulations. Lung function tests revealed a mixed obstructive-cum-restrictive ventilatory defect with severe diffusion capacity impairment. The lung function parameters were: Forced vital capacity (FVC): 2.84L (86%pred);

Forced expiratory volume in 1s/ Forced vital capacity ratio (FEV_1/FVC): 67%, Residual volume (RV): 1.16L (55%pred); Total lung capacity (TLC): 3.99L (74%pred); single breath diffusion capacity of lung for carbon monoxide ($DLCO_{SB}$): 5.95 ml/min/mmHg (25%pred); and $DLCO_{SB}$ corrected for alveolar volume ($DLCO/VA$): 1.78 (53%pred). The electrocardiogram was within normal limits. Two-dimensional and colour Doppler echocardiography at rest revealed normal-sized right ventricle and right atrium and no significant tricuspid regurgitation. The estimated mean pulmonary artery pressure was in the normal range.

High resolution computed tomography (HRCT) showed bilateral upper lobe centrilobular and paraseptal emphysema, and diffuse interstitial fibrosis with interlobular and intralobular septal thickening and ground glass opacification mainly in the lower lobes (figs. 1 and 2). The electrocardiogram was within normal limits. Fiberoptic bronchoscopy was carried out. Cytological examination of the bronchial aspirate revealed numerous pigment laden alveolar macrophages. Bronchoalveolar lavage fluid differential was: macrophages: 51%, neutrophils: 28% and lymphocytes: 21%.

The transbronchial lung biopsy specimen revealed marked distortion of alveolar architecture, chronic interstitial inflammatory infiltrate and areas of interstitial fibrosis associated with deposition of coarse iron pigment that stained positive with Prussian blue stain (fig. 3 and 3a). These appearances were consistent with a diagnosis of IPS [9]. Combined with the HRCT picture and the lung function data, a final diagnosis of CPFE syndrome with IPS was established.

The patient was advised inhaled budesonide and formoterol with oral prednisolone. Follow-up data is not available as the patient did not return for a review.

Discussion

Pulmonary siderosis, arising from occupational exposure to iron dust and fumes has generally been considered to be a benign condition although structural and function changes in the lungs have



Fig. 1. - High resolution computed tomography of the chest (lung window) showing centrilobular and paraseptal emphysema in both upper lobes.

been described [5]. The features of obstructive airway disease observed in occupational surveys were explained by concomitant smoking and exposure to noxious fumes and gases in welders. Some of the earlier reports documented radiological changes in asymptomatic subjects that receded on cessation of exposure [6].

The occurrence of pulmonary fibrosis on long-term exposure to iron fumes was, until recently, a matter of debate. The fibrotic response was initially ascribed to a concomitant exposure to contaminating silicates. Morgan and Kerr [7] found little interstitial fibrosis on histological evaluation. Funahashi *et al.* [8] contradicted this view in their histological studies. Energy dispersive x-ray analysis of lung tissue revealed significant amounts of iron deposits in the welder's lung but there was no difference in the silicon content from age-matched control subjects. As most of the iron deposit was seen in the fibrosed alveolar septa, the observed interstitial fibrosis was proposed to be a reaction to the iron particles rather than to contaminating silicosis. Buerke *et al.* [9] subsequently provided definite evidence of diffuse pulmonary fibrosis in welders after long-term exposure, thus establishing a cause-effect relationship between iron deposition and interstitial fibrosis. The disease was labeled as Idiopathic Pulmonary Siderofibrosis (IPS).

The syndrome of CPFE initially described in association with idiopathic pulmonary fibrosis [1, 2] has also been reported in other chronic interstitial pneumonias as well as in diffuse fibrosis associated with connective tissue disorders [2, 3]. The combination of fibrosis and emphysema results in relatively maintained airflows and lung volumes but "out-of-proportion" impairment of diffusion capacity and desaturation on exercise. Pulmonary hemodynamic impairment is especially marked and these patients have a poorer prognosis [10]. In our case, there was no clinical or echocardiographic evidence of pulmonary hypertension or cor pulmonale, probably due to the short duration of history.

In our patient, a history of smoking, the lung function abnormalities of mild airflow limitation and reduction of total lung capacity with severely



Fig. 2. - High resolution computed tomography of the chest (lung window) showing interlobular and intralobular septal thickening, and ground glass opacification in both lower lobes.

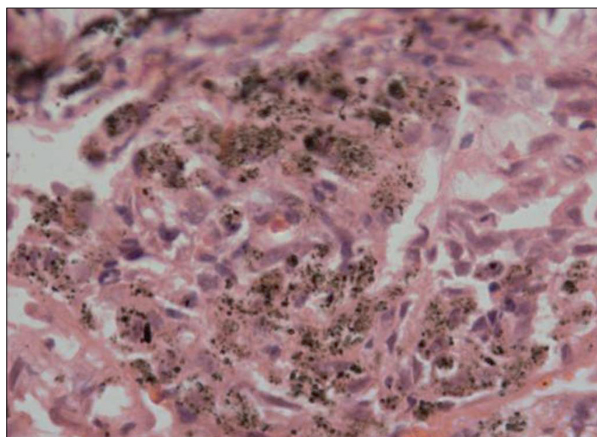


Fig. 3. - Histopathological section of transbronchial biopsy specimen showing interstitial fibrosis with chronic inflammatory cellular infiltration and coarse iron deposits (H & E x 400).

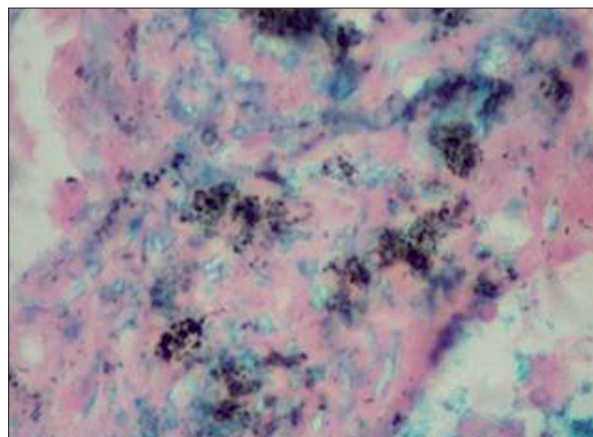


Fig. 3a. - Prussian blue stain of showing positivity for iron in a background of fibrosis (40 x).

impaired diffusion capacity, and the characteristic HRCT picture of upper lobe emphysema and lower lobe fibrosis established the diagnosis of CPFE. While the histopathologic data is compatible and consistent with the association between iron deposition and interstitial fibrosis established in previous studies [8, 9], a cause-effect relationship can only be presumed and not definitively established in a single case report. While smoking explains the occurrence of emphysema, it may also contribute to the occurrence of fibrosis. It has been associated with fibrotic diffuse parenchymal lung disease [11]. Thus, both occupation and smoking may have contributed to the genesis of CPFE syndrome in our patient. A review of literature did not reveal any other report of CPFE syndrome occurring in association with IPS.

The molecular mechanisms of pathogenesis of emphysema and fibrosis in CPFE syndrome are not clear at present. Though over-expression of tumour necrosis factor-alpha (TNF- α) and platelet-derived growth factor (PDGF) have been shown to cause pathologic changes consistent with both emphysema and pulmonary fibrosis in mouse lungs [12, 13], it remains to be established whether emphysema and fibrosis occur independently or have a common pathogenesis.

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