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Epidemiological, Clinical and Outcome Aspects of Combined Pulmonary Fibrosis and Emphysema Syndrome: About 8 Cases

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Abstract **Original Research Article**

The combination of pulmonary fibrosis and emphysema (CPFE) has been suggested to be a syndrome in 2005, based on distinctive clinical, radiological, functional and outcome features. It is often hard to make the difference with IPF given the similarities between these two entities, including tobacco exposition and fibrosis of the lower zones. We present a series of 8 male patients with CPFE who were referred to the pulmonology department with a history of acute exacerbation. The prognostic is often linked to evolutive complications representing acute exacerbation of pulmonary fibrosis and pulmonary hypertension. This paper supports early diagnosis in patients with this "orphan disease", so that a decline in respiratory function or right heart failure resulting from possible complications of CPFE may be prevented.

Keywords: Emphysema, pulmonary fibrosis, exacerbation, pulmonary hypertension.

INTRODUCTION

The combination of pulmonary fibrosis and emphysema (CPFE) has been suggested to be a syndrome in 2005 [1,2], based on distinctive clinical, radiological, functional and outcome features [3]. We conducted a retrospective study of 8 patients with both emphysema of the upper zones and diffuse parenchymal lung disease with fibrosis of the lower zones of the lungs on chest computed tomography.

PATIENTS AND METHODS

This retrospective study was conducted at the Pulmonology Unit of Moulay Youssef Hospital during a period of 16 months (January 2018 to April 2019). Cases were acceptable for inclusion if the following criteria were:

- Presence of emphysema on CT scan with upper zone predominance.
- Presence of a diffuse parenchymal lung disease with significant pulmonary fibrosis on CT scan with peripheral and basal predominance.

Only cases for which a CT scan was available for review were included. The patients who were excluded from the study had connective tissue disease at the time of the diagnosis of CFPE, as well as patients with a diagnosis of other interstitial lung diseases, such as drug-induced interstitial lung disease, pneumoconiosis, hypersensitivity pneumonitis, sarcoidosis and eosinophilic pneumonia.

RESULTS

Clinical presentation

All patients were male, with an average age of 66 years, either current or ex-smokers. Ex-smokers had quit smoking for an average period of 14 months. Three patients had a history of atherosclerotic coronary artery disease. The mean time between the first symptoms and diagnosis of CPFE was 4 years. An acute increase of dyspnoea was found to be a major clinical symptom in all patients, out of wich 6 had cough. Finger clubbing was reported in 87,5% of the cases, and fever in 25% of them. Auscultation of the lungs found bilateral crackles of the lower zones of the lungs in 62,5% and rarely wheezes in 37,5%. The body mass index was normal in 4 cases, >25 in 2 cases and <18 in 2 cases. The imaging diagnosis of emphysema preceded the identification of fibrotic changes in 2 cases, and emphysema and fibrosis were discovered concomitantly in 6 patients.

Biology

Polycythemia was found in 2 cases. Inflammation was reported in 4 cases. The average CRP level was 102 mg/L and blood leucocyte count was 13200 elements/mm3. Searching for Mycobacterium tuberculosis in sputum was negative in

all cases.The bacteriological examination of sputum isolated Pseudomonas aeruginosa in one case and Klebsiella pneumoniae in an another one (non-resistant in both cases). Arterial gas blood pressure showed hypoxemia (PaO2<70mmHg) in 6 cases with an average of PaO2=47mmHg, and elevated PaCO2 in one case (PaCO2=56mmHg).

Pulmonary function tests

3 of the patients presented with an obstructive ventilatory defect (defined by FEV1/FVC<70%). The FEV1 was <80% in 3 patients and the FVC was <80% in 7 patients. None improved FEV1 after use of bronchodilatators. A restrictive ventilatory defect was shown in one case. Transfer factor for carbon monoxide (TLCO) was measured only in 4 cases due to a bad execution. All 4 cases showed a transfer coefficient of the lung (KCO) <80%.

Pulmonary arterial hypertension

All patients had echocardiography at diagnosis. The prevalence of PAH was 37,5%. The mean sytolic arterial pulmonary pressure was 52 mmHg. No right heart catheterization was performed.

Computed tomography of the chest and pathology

The CT scan of all of the patients' chests showed coexistence of emphysema with upper zone predominance and parenchymal lung disease suggestive of pulmonary fibrosis of the lower lobes. (Figure 1) Paraseptal emphysema was particularly frequent in this population (75%). Honeycombing, traction bronchiectasis and reticular intralobular opacities were the most frequent findings, present in 100%, 62,5%, and 50% of the cases, respectively. Focal ground-glass opacities and areas of alveolar condensation were associated in 3 and 2 cases respectively. No case of pulmonary embolism or pneumothorax was found.

Treatment and outcome

During their stay at the hospital, all patients received an oral short course corticoseroid therapy, with preventive heparin. Oxygenotherapy was administered in all cases, associated with non invasive positive pressure ventilation in one case with elevated PaCO2. Three patients received long-term inhaled corticosteroids and bronchodilators. Antibiotics were administered in 4 cases (Amoxicillin-claculanic acid in 3 cases, Ceftriaxone in one case), with a clinical, biological and radiological improvement at follow-up. During the follow-up period, 6 of the patients were at a chronic respiratory stage, out of which 3 needed long term nasal oxygen therapy at home. 2 patients developed right cardiac failure during follow-up and were referred for cardiological care. Three patients were hospitalised for a second acute increase of dyspnoea, and one died during follow-up (due to heart failure on severe pulmonary hypertension).

Chest computed tomography images from a patient with combined pulmonary fibrosis and emphysema.

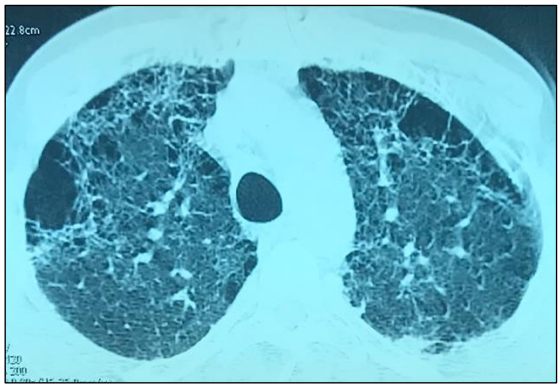

Fig-1 : (A) Paraseptal and centrilobular emphysema of the upper zones of the lungs.

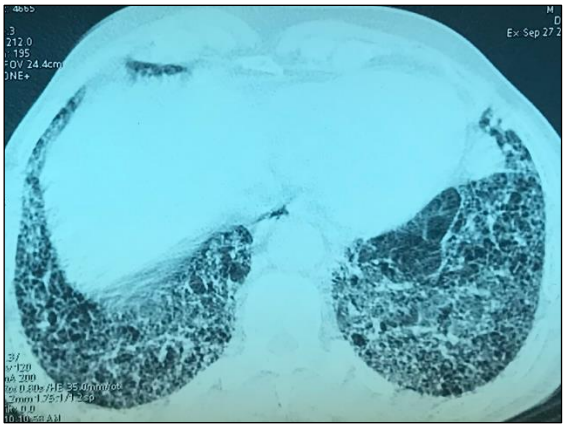

Fig-1 : (B) Reticular opacities, honeycombing, and traction bronchiectasis of the lower zones of the lungs.

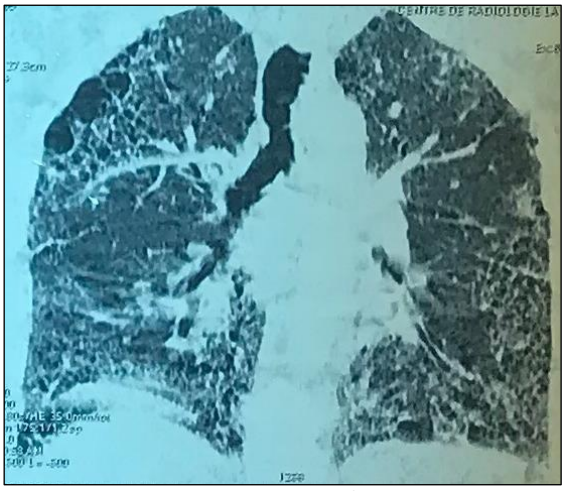

Fig-1: (C) Reconstruction in frontal section

DISCUSSION

The CPFE syndrome was coincidentally reported for the first time in 1990 in a series of 8 patients by Wiggins et al in London. It is until 2005 that the Groupe d'Etudes et de Recherche sur les Maladies "Orphelines" Pulmonaires (GERM"O"P), a collaboration dedicated to the study of rare (so-called "orphan") pulmonary diseases, characterized it as a

distinct entity in a series of 61 patients. Nowadays, this syndrome is a matter of growing interest by respiratory clinicians [1-4]. Its occurrence remains not very well known, but an emphysema is present in 8 to 36% of the patients having IPF.

This syndrome is clinically characterized with a male predominance, an exposition to tobacco and an often-severe dyspnea. The median age during the diagnostic is between 65 to 70. Auscultation of the lungs often finds bilateral crackles of the lower zones of the lungs. All of our patients fit these characteristics. On the respiratory functional level, an effort hypoxemia is found as well as a low transfer capacity for carbon monoxide often contrasting volumes frequently conserved at the spirometry because it is associated with the fibrose and emphysema [1]. Despite moderate or severe emphysema, a large proportion of patients with CPFE have FEV1/FVC > 70% indicating that GOLD criteria for chronic obstructive lung disease may not be applicable. In fact, only 3/8 of our cases had FEV1/FVC < 70%.

The diagnostic stands on the high definition scanning of emphysema with upper zone predominance, and significant pulmonary fibrosis with peripheral and basal predominance, that corresponded to the inclusion criteria of our study.

A complication reported within all cases of our series is the episodes of exacerbation of pulmonary fibrosis (estimated at 10-24%) happening during the CPFE evolution. The main cause of exacerbation was respiratory infection in 50% of cases and heart failure in 25% of them. Within the remaining 25%, the exacerbation was due to the natural course of the disease. No case of pulmonary embolism or pneumothorax was found.

However, the main predictor of subsequent mortality remains precapillary pulmonary hypertension [5], as in the case who died in our study. Severe pulmonary hypertension is often associated with CPFE, (30-50%) and according to studies [1-5], its presence lowers the survival median to 5 years (from 75% to 25%), which explains the interest in a systematic echocardiography in the medical care of these patients. The CPFE patients have an estimated survival median of 6 years [1], that is apparently better than the IPF of 3 years, even though studies suggest an identical prognostic between these two entities [6].

On the therapeutic level, there is no consensus to this day in treating pulmonary fibrosis, emphysema or pulmonary hypertension linked to CPFE. Smoking cessation is obviously necessary, and bronchodilatators can be suggested. Some isolated observations indicate that therapy specific for pulmonary hypertension may improve hemodynamics, but the potential clinical and survival benefit is unknown. Similarly, corticosteroids are often prescribed to patients with pathologic pattern of nonspecific interstitial pneumonia. The potential benefit of anti-fibrotic drugs (pirfenidone, nintedanib) in patients with CPFE has not been specifically evaluated [7-8]. Practically, the care relies often on symptomatic treatments, including long-term oxygen therapy.

It is clear than many aspects of the CPFE syndrome remain to be explored. The pathophysiology of the syndrome is unclear [9], although tobacco smoking is definitely a major cause. Obviously, much progress is required regarding the management and treatment of patients with CPFE, with and without severe pulmonary hypertension, as no treatment is currently available to save them from a dire prognosis.

ABBREVIATIONS

CPFE : combination of pulmonary fibrosis and emphysema – CT: computed tomography – COPD : Chronic Obstructive Pulmonary Disease – PAH : Pulmonary arterial hypertension – IPF : Idiopathic Pulmonary Fibrosis

CONSENT

Written informed consent was obtained from the patients for publication of this report and any accompanying images.

CONFLICTS OF INTEREST

There are no conflicts of interest between the authors and between the authors and the patient.

DISCLOSURE:

These case series were written based on clinical observation without any funding.

AUTHORS' CONTRIBUTIONS

Salim Naciri drafted this manuscript under Mouna Soualhi's supervision. Rachida Zahraoui and Jamal-Eddine Bourkadi have been involved in drafting the manuscript. All authors read and approved the final manuscript.

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