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Scientific letter

Pleuroparenchymal Fibroelastosis. Is it Really Uncommon? Report of Eight Cases

Fibroelastosis pleuroparenquimatosa. ¿Es realmente infrecuente? Informe de ocho casos

Dear Editor,

We present 8 cases of pleuroparenchymal fibroelastosis (PPFE), exposing the main characteristics that led to establish such diagnosis (Table 1). Most of them were female, older than 50 years, with a history of autoimmune disease and dyspnea as the most frequent symptom. Microbiological studies ruled out active tuberculous infection in all of them, 3 patients had PPFE associated with idiopathic pulmonary fibrosis (IPF), 3 patients had elevated rheumatoid factor (RF) titers and 2 patients had an increased residual volume (RV)/total lung capacity (TLC) ratio. Regarding imaging techniques, 5 patients showed a definitive pattern of PPFE on chest computed tomography (CT), establishing the diagnosis based on the clinical and imaging test, and the remaining cases presented a consistent pattern of PPFE, but no biopsy was performed in them because they had a rapid progression of their disease, dying in less than 6 months. Regarding treatment, some of them sporadically received corticosteroids to try to maintain clinical–radiological stability and pulmonary function tests (PFTs). In addition, 3 cases required home oxygen therapy and 1 required lung transplantation due to rapid symptomatic and PFTs deterioration.

PPFE is little known, manifesting most frequently between 30 and 40 years of age, with no gender preponderance. There are 2 forms of presentation: idiopathic and secondary. The latter is related to lung transplantation, hematopoietic progenitor transplantation, chemotherapy, radiotherapy, autoimmunity, connective tissue diseases, hypersensitivity pneumonitis and even a familial form has been described.[1] There seems to be no correlation with smoking, but an association with exposure to asbestos, avian antigens or aluminum has been documented.[2] Many of the published cases refer to patients who have undergone lung transplantation, leading to theorize that PPFE is a chronic lesion secondary to an autoimmune response. This hypothesis is supported by the elevated levels of antinuclear antibodies or RF in some of these patients. It has also been proposed that chronic inflammation secondary to recurrent bronchopulmonary infections would account for the presence of fibrosis.[3,4]

The most typical clinical manifestations are cough, dyspnea, pneumothorax, and a low body mass index.[4] Radiological lesions may precede symptomatology by months/years.[5] In early stages, CT usually shows increased biapical subpleural density, which later develops into pleural thickening, with subpleural fibrosis and bronchiectasis/bullae.[4] Other possible findings are: decreased anteroposterior and transverse diameter of the thorax, hilar adenopathy or a reticulonodular pattern. In up to 75% of cases, radiological lesions of PPFE coexist with those of other entities (e.g., IPF, tuberculosis, systemic sclerosis).[2] Furthermore, due to the apical location, confusion with tuberculosis may arise, although unilateral involvement would be more indicative of the latter.[3–5] An increase in the RV/TLC ratio is characteristic, which is explained because apical fibrosis causes collapse, with compensatory bibasal hyperinflation.[2] The most notable histopathological findings are visceral pleural fibrosis and subpleural fibroelastosis.[3] Antifibrotic and immunosuppressive drugs have not proven to be useful. The only curative treatment is lung transplantation, otherwise the prognosis is poor, with median survival ranging from 4 months to 7 years.[1,2]

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Table 1
mMRC: modified Medical Research Council dyspnea scale #. RV/TLC: residual volume/total lung capacity ratio #. FCV: forced vital capacity #. KCO: Krogh coefficient #. DLCO: diffusing capacity for carbon monoxide #. PPFE: pleuroparenchymal fibroelastosis #.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Sex	Female	Female	Female	Female	Male	Male	Female	Male
Age years	71	53	48	56	79	72	48	79
Smoking	No	No	No	Yes	No	Yes	No	Yes
Risk factors/associated entities	Radiotherapy	Rheumatoid arthritis	Psoriasis	No	- Exposure to asbestos - Liver transplant. In treatment with Tacrolimus	No	Systemic lupus erythematosus	- Aluminum exposure - *M. avium* infection
Symptomatology	- Grade II dyspnea on the mMRC# - Hemoptysis	Grade II dyspnea on the mMRC	Grade II dyspnea on the mMRC	Asymptomatic	Grade III dyspnea on the mMRC	Grade III dyspnea on the mMRC	Asymptomatic	- Grade II dyspnea on the mMRC - Cough
Physical examination	Normal	Normal	Normal	Normal	Velcro-type bibasal crackles *A*	- Velcro-type bibasal crackles *A* - Acropachies *A*	Normal	Velcro-type bibasal crackles
Radiological findings *B*	Definite pattern of PPFE#	Definite pattern of PPFE	Definite pattern of PPFE	Definite pattern of PPFE	Consistent pattern of PPFE	Consistent pattern of PPFE	Definite pattern of PPFE	Consistent pattern of PPFE
Rheumatoid factor levels	Normal	High	Normal	Normal	High	High	Normal	Normal
FCV#	2080 ml (87%)	3260 ml (104%)	3650 ml (107%)	2840 ml (94%)	2050 ml (82%)	2100 ml (89%)	1100 ml (33%)	2030 ml (62%)
KCO#	92%	77%	98%	82%	90%	91%	66%	50%
DLCO#	80%	83%	90%	90%	82%	81%	66%	78%
RV/TLC ratio#	Normal	Normal	Normal	Increased	Normal	Increased	Decreased	Normal
Treatment *C*	Prednisona 30 mg/day	Prednisona 30 mg/day	Prednisona 30 mg/day	Close monitoring	Home oxygen therapy	Home oxygen therapy	Lung transplantation	- Prednisona 30 mg/day - Home oxygen therapy

A: Velcro-like crackles and acropachies are not typical of PPFE, their presence suggests the existence of another disease. In these cases, due to the coexistence with a usual interstitial pneumonia (UIP) pattern and the findings in the physical examination, the diagnosis of PPFE associated with IPF was established.
B: **Definite pattern of PPFE:** Apical pleural thickening with subpleural fibrosis in upper lobes without involvement or less marked involvement in lower lobes. **Consistent pattern of PPFE:** Apical pleural thickening with subpleural fibrosis with predominant localization in lower lobes or association with lesions of other interstitial disease, three of the patients who presented this last pattern, in addition to apical thickening, had lesions compatible with UIP.
C: Only one case remains under clinical surveillance, being the only patient without symptoms and with normal PFTs.
All cases were presented to the multidisciplinary committee on interstitial lung diseases. The diagnosis was established by definitive radiologic pattern of PEFF. In case 1, case 2 and case 5 the differential with other interstitial diseases was considered, but the first two cases refused the biopsy, while the other one presented a rapid functional deterioration and died a few months later.
Our cases share similar characteristics to other series, such as a history of asbestos exposure, autoimmunity, and treatment with radiotherapy. Although most of the cases described have been in lung transplant recipients, one of our cases was in a liver transplant patient.

Informed consent

The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is held by the corresponding author.

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Authors' contributions

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Conflicts of interest

The authors state that they have no conflict of interests.

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