Pleuroparenchymal fibroelastosis in interstitial lung disease with antineutrophil cytoplasmic antibody-associated vasculitis

Sirs,

We read with great interest the recent review on the epidemiology and management of interstitial lung disease (ILD) in patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), a group of systemic vasculitis that predominantly affect small vessels, including granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (1). The authors describe the clinical, radiological and histological features of ILD-AAV, establishing a 23% prevalence of ILD in GPA patients and 45% in MPA patients. The different radiological patterns of ILD-AAV are discussed. In MPA patients, high resolution computed tomography (HRCT) of the chest may reveal interstitial lung involvement with ground glass opacities, reticulations, interlobular septal thickening and bronchiectasis (2). In about 50% of MPA patients, usual interstitial pneumonia (UIP) pattern is described, while non-specific interstitial pneumonia (NSIP) and desquamative interstitial pneumonia (DIP) are observed in fewer cases (3). Combined pulmonary fibrosis and emphysema as well as unclassifiable fibrotic radiological patterns are even less frequent. The association of pleuroparenchymal fibroelastosis (PPFE) with ILD-AAV is not mentioned in this interesting review, and in order to contribute to the definition of PPFE as a distinct phenotype of ILD-AAV, we reviewed our population of 300 ILD patients from the previous year.

PPFE is a rare form of progressive upper-lobe-predominant ILD characterised by collagenous fibrotic thickening of sub pleural and parenchymal areas and sub pleural elastosis. This new form of ILD, with no clear relationship to smoking, can be idiopathic or secondary to organ transplants, drugs, lung infections or rheumatic disorders (4, 5).

A single case report by Japanese colleagues (6) described PPFE histological features in a patient positive for myeloperoxidase (MPO), without any definite parenchymal involvement, while Kinoshita *et al*. described radiological PPFE retrospectively in a single MPO-positive ILD-AAV patient (7).

We observed a subgroup of 4 ILD-AAV patients with PPFE. The diagnosis of PPFE in ILD-AAV patients was performed at Siena Referral Centre for ILDs and Siena Rheumatology Unit according to international diagnostic criteria (8-10). HRCT features were analysed retrospectively by radiologists experienced in interstitial lung diseases.

The demographic, clinical, immunological and functional features of our four patients with PPFE ILD-AAV are summarised in Table I. All our patients with interstitial lung involvement in the ambitus of ANCA-associated vasculitis showed renal and lung involvement. Two patients showed peripheral nervous system and a single patient a cardiac involvement. Chest auscultation did not detect any sounds except in two patients who manifested wheezing and bilateral crackles. Half the patients were positive for MPO- ANCA; the others were positive for PR3-ANCA antibodies. Lung function tests (LFT) showed that one patient had obstructive respiratory deficit; the other three had restrictive deficit associated with a moderate reduction in DLCO percentages (Table I). HRCT showed upper lung reticulations and nodules associated with diffuse areas of ground-glass opacities in all patients. One patient showed a radiological pattern of peribronchovascular fibrosis. In all patients PPFE showed a predominantly upper-lobe distribution with focal pleural and subpleural thickenings and bilateral dense apical consolidations.

All patients were treated with high-dose corticosteroids associated with immunosuppressants (Table I) and interestingly, all had been treated with Rituximab (1g i.v. repeated after 14 days every six months) and showed clinical-functional and radiological stabilisation of lung involvement, as demonstrated by HRCT and LFT at six-month follow-up. One patient showed HRCT evidence of improvement after 1 year of rituximab treatment.

In conclusion, patients with ILD-AAV (MPO- and anti PR3-positive) may present PPFE as a radiological pattern of ILD, associated with vasculitis. Very few papers have investigated the prevalence of PPFE in patients with vasculitis, our contribution suggests the need of radiological and functional monitoring of these patients, assuming a potential precocious use of Rituximab in halting disease progression.

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Table I. The main characteristics of population including age, lung function test parameters, main symptoms at onset, comorbidities BVAS and FFS score. All data were expresses as median (interquartile range).

Parameters	n=4
Age (median, IQR)	60 (55-74)
Gender (M/F)	4/0
Caucasian/others	4
Smoking habit, (never/former)	3/1
ANCA (MPO/PR3)	3/1
Diagnosis (GPA/MPA)	2/2
Main symptoms at onset	
Fever	25%
Renal failure	50%
Haemosperma	25%
Arthralgias	25%
Comorbidities	
0**BVAS at onset**	21 (17.5-23.7)
FFS	
0	25%
≥1	75%
Lung function test parameters (median, IQR)	
FVC ml	3130 (3020-3130)
FVC %	80 (75-80)
FEV1 ml	2030 (2030-2185)
FEV1 %	62 (62-68)
DLCO %	84 (82-85)
FEV1/FVC	76 (70-78)

FFS: per five factors score; BVAS: Birmingham vasculitis activity score.

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