Interstitial lung disease in ANCA-associated vasculitides: another step forward

Sirs,

We thank Bargagli *et al*. for their interesting letter (1) and we would like to also congratulate with them, because they substantially expand the evidence on this topic with the description of their interstitial lung disease (ILD) population obtained from the previous year, showing a subgroup of 4 patients with a combination of ILD in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and pleuroparenchymal fibroelastosis (PPFE).

We did not include in our review this association, because of the extreme dearth of evidence regarding the combination of these two clinical entities, limited at two case reports, before this letter (2, 3).

Of course, this association need to be better characterised and various issues deserve to be better explored, including if this association is simply coincidental or a separate disease entity with distinct clinical, pulmonary functional characteristics and different prognosis compared to its individual components, eventually related to the interaction of specific genetic and/or environmental factors. A clue in favor of a causal association between ILD-AAV and PPFE may be considered previous reports showing the propensity of PPFE to be associated with connective tissue diseases (CTD)-ILD (4), including systemic sclerosis (5), suggesting a specific role for autoantibodies in the pathogenesis of these combined syndromes. In a similar manner, recent studies describing the clinical significance of PPFE in patients with idiopathic pulmonary fibrosis (IPF), showed that this association has important clinical, physiological and prognostic value compared to patients with IPF alone (6, 7). However, this limited evidence still suggests that the combination of PPFE with various types of pulmonary fibrosis may be a specific and independent disease entity responsible for PF, including ILD-AAV.

In particular, we believe that a specific issue in these patients is related to prognosis: although we do not know yet the prognosis of ILD-AAV when is combined with PPFE, we have evidence suggesting that the combination of PPFE with IPF and/or CTD-ILD is associated with a worse prognosis compared with IPF and/or CTD-ILD alone. Therefore, this evidence may suggest that a bad prognosis could occur also for patients with ILD-AAV when combined with PPFE. Finally, as we stated in our review (8), the standard treatment for AAV is considered also as a possible treatment in patients with concomitant ILD and includes mainly systemic glucocorticoids, cyclophosphamide, rituximab, mycophenolate mofetil, methotrexate and azathioprine.

However, two antifibrotic drugs, pirfenidone and nintedanib, have been recently approved for IPF treatment (9), and a recent trial (the INBUILD trial) showed that these antifibrotic drugs are also effective in reducing disease progression in patients with ILD other than IPF, including ILD secondary to autoimmune diseases (10). Recent evidence seems also to suggest a role for antifibrotic drugs in the treatment of PPFE (11), at least in combination to idiopathic pulmonary fibrosis (11), suggesting that nintedanib and pirfenidone may also be effective in the treatment of patients with ILD-AAV with or without PPFE.

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