Serial autoantibody detection in interstitial lung diseases: should they be repeated at follow-up?

Interstitial lung diseases (ILDs) are a heterogeneous group characterized by progressive thickening of the lungs; they include a wide variety of lung pathologies of known and unknown cause. Idiopathic pulmonary fibrosis (IPF) and non-specific idiopathic pneumonia (NSIP) are the most common idiopathic ILDs.[1] The 2018 ATS/ERS international guidelines for the diagnosis of IPF recommend analysis of autoantibodies to exclude ILDs associated with connective tissue lung diseases (CTD-ILD).[1] The diagnosis of IPF requires exclusion of other ILDs and serological evaluation of C-reactive protein, erythrocyte sedimentation rate, antinuclear antibodies, rheumatoid factor, myositis panel, and anti cyclic citrullinated peptide in newly diagnosed ILDs. Many biomarkers have been proposed in the literature for differential diagnosis but they are not yet approved for clinical use.[2] The guidelines also underline that there is no clear agreement on the serological tests to perform in the initial screening.[1] Autoantibody determination is mainly required in cases with atypical IPF features, including women under 60 years of age, where interstitial lung involvement may be the first manifestations of CTD-ILD.[3]

We therefore wondered whether autoantibody determination should be repeated regularly under specific conditions in patients with UIP pattern and negative serological test at onset, in order to verify the initial diagnosis of IPF, since some patients develop CTD manifestations months or years after the initial diagnosis.[3] The question mainly concerns UIP and NSIP radiological patterns, i.e. the most frequent radiological features associated with rheumatoid arthritis, systemic sclerosis and Sjogren syndrome.[4]

We retrospectively evaluated a cohort of 91 patients (71 males, age 68.46 ± 7.70 years) diagnosed with IPF and treated with pirfenidone between August 2011 and January 2019: we selected patients who had undergone assay of serum autoantibodies. Five of them (2 males, age $69{,}8 \pm 13{,}1$ years) developed clinically evident CTD (2 Sjogren syndrome and 3 rheumatoid arthritis), that was confirmed by rheumatological tests and clinical evaluation. Concerning systemic manifestations of CTD, two patients reported sicca syndrome, one patient showed rheumatic nodules of the elbow and two patients complained of diffuse joint pain and stiffness. Mean time to CTD onset after diagnosis of IPF was $25{,}8 \pm 33{,}7$ months. The three patients with RA-UIP died 60 ± 31.74 months after diagnosis of ILD, showing a prognosis similar to that of IPF patients treated with pirfenidone, as already reported in the literature.[5]

Our results are in line with the first paper reporting this subtype of ILD patient.[5] Homma et al. observed a mean latency of 24 months between IPF diagnosis and CTD, which is considerably shorter than our figure.[6] This discrepancy may be due to inclusion of patients with various radiological and ILD patterns, not focused on UIP features as in our study. In confirmation of these assumptions, Kono et al. reported similar results to ours in a cohort of 111 patients diagnosed with IPF, where 9% of patients developed CTD.[7]

Here we reported our cases, initially diagnosed with IPF, who subsequently developed CTD. This subgroup is estimated to make up 8–10% of all IPF patients, raising the question of follow-up and sustaining the utility of taking a working diagnosis approach to ILD. We first provided survival data on these patients treated with pirfenidone; it could be worth extracting the population with UIP prior to diagnosis of CTD in order to investigate the effect of antifibrotic treatment in this cohort and the usefulness of serial determination of autoantibodies.

Conflict of interest

The present research was performed at Siena University without funding sponsors. The authors have no conflict of interest to declare.

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