Idiopathic interstitial pneumonia with autoimmune features (IPAF)

Connective tissue disease-associated interstitial lung disease (CTD-ILD) is one of the most important considerations in a patient presenting with idiopathic interstitial pneumonia (IIP). CTD-ILD is associated with a better prognosis and survival than idiopathic pulmonary fibrosis (IPF), as the disease trajectory tends to be less aggressive due to a better immunosuppressive treatment response. However, 20 -30% of patients with IIP and some auto-immune features will not meet the criteria for a defined connective tissue disease.

This led to the development of the research construct of idiopathic pneumonia with autoimmune features (IPAF) in 2015 by the European Respiratory Society/American Thoracic Society (ERS/ATS).[1] The group proposed three overarching domains of diagnostic criteria: clinical, morphological, and serological - of which a patient should fulfil at least two of the three.

Most published literature on IPAF is retrospective and contradictory. The Prognostic Analysis of IIPs with Rheumatologic Features: PAIR cohort study[2] is the first to prospectively recruit patients with IIP and assess them on 63 individual items suggesting connective tissue disease in the three domains.

Of the 376 patients recruited with IIP, 70 (18.6%) met the criteria for IPAF. The most common CTD-related signs/symptoms were mucocutaneous lesions, namely, mechanic hands, Raynaud's phenomenon and periungal erythema/nail-fold capillary dilatation. Anti-nuclear antibody (ANA) positivity, high titre rheumatoid factor and anti-synthetase antibodies were the most identified serological abnormalities, while non-specific interstitial pneumonitis and organising pneumonia were the most common morphological characteristics. Usual interstitial pneumonia is not considered a diagnostic feature of IPAF and this is therefore not unexpected.

Patients who fulfilled the IPAF criteria were more likely to be younger, females and non-smokers. During the study period, 17 patients went on to develop defined systemic autoimmune disease, however this was six times more likely in the IPAF group. These 17 patients were excluded from the final survival analysis.

Patients fulfilling the IPAF criteria had a significantly longer survival than non-IPAF patients. Over the course of the three-year study period, 77 patients died of which only two had IPAF. Patients with IPAF also had a much lower risk of acute exacerbation than non-IPAF. These findings support the authors' previous retrospective research showing that an IPAF diagnosis is an independent predictor of improved outcomes.

An unclear aspect of the study is the seemingly interchangeable use of UIP and IPF, the former being a radiological pattern, while the latter a specific form of chronic, fibrosing interstitial pneumonia for which there is no identifiable cause. The author states that their data shows no prognostic benefit of an IPAF diagnosis in those patients with IPF, however the group consisted of only 6 patients. Further research is required to describe the prognosis of patients with IPAF-UIP.

A further limitation of the study is its design prior to the publication of the official ERS/ATS IPAF criteria, which resulted in palmar telangiectasia, anti-PM-Scl antibody and anti-MDA-5 antibody not being included in the study protocol.

Although an IPAF diagnosis infers a better outcome for patients, the question which remains unanswered is how these patients should be treated? Which immunosuppressant agents should be prescribed and for how long? Watch this space. As IPAF moves from a research construct to a clinical entity, we will hopefully have the answers soon.

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2. Enomoto N, Homma S, Inase N, et al. Prospective nationwide multicentre cohort study of the clinical significance of autoimmune features in idiopathic interstitial pneumonias. Thorax 2022;77(2):143-153. https://doi.org/10.1136/thoraxjnl-2020-216263