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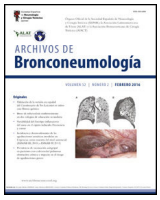

Editorial

Autoimmunity in the Study of Interstitial Lung Disease: Are Serological Test Enough?

Interstitial lung disease (ILD) are a large and heterogeneous group of diseases with known and unknown causes.[1] In some cases the clinical course of ILD is progressive and does not always require the same therapeutic approach.[2,3] ILD is a frequent cause of major morbidity and mortality in multi-system disorders, especially in patients with connective tissue diseases (CTDs), with an estimated prevalence of 30.2 cases per 100,000.[4] One of the hallmarks of CTD is the presence of autoantibodies (Ab), being the elevated titration of antinuclear antibodies (ANA) or the presence of autoantibodies against extractable nuclear antigens (ENA) useful as serological biomarkers of these kind of diseases. ILD usually occurs concomitantly or after the onset of CTDs, but in some patients ILD may be the first manifestation of an underlying CTD. Moreover a percentage of ILD patients have features of an autoimmune process in the absence of a defined CTD.[5] But it is important to highlight that the absence of ENA or other specific Ab in blood does not exclude the existence of an underlying CTD. It seems reasonable to think that the study of Ab presence in biological samples other than serum could improve their diagnostic profitability. A study carried out in 56 patients with pleural effusion showed that an ANA titer in pleural fluid > 1/160 presented a sensitivity and specificity of 91.67% and 83.3% respectively for the diagnosis of lupus pleuritis compared to other causes of pleural effusion.[6] However, studies that have attempted to associate the ratio of pleural fluid ANA/serum ANA show conflicting results.[7–9] In addition the presence of ANA in pleural fluid has been also found in other pathologies like neoplasms.[9,10]

Bronchoalveolar lavage (BAL) is useful to study different lung diseases and some authors have shown its prognostic value in some CTD-ILD as well as in the detection of their complications.[11–13] Currently BAL analysis in CTDs has been focused basically on the determination of different cellular products, such as inflammatory mediators or biomarkers of cell damage. But it is also possible to determine immunoglobulins in BAL.[14] This fact is particularly interesting in CTDs because these patients usually present increased numbers of cells that can produce Ab.

Salvador-Corres et al. analyzed the presence of different ENA in BAL samples from 155 patients with suspected ILD.[15] Interestingly they found several ENA Ab in 19 patients, 7 of them having more than one ENA. It is also noteworthy that after the analysis of Ab in BAL, the percentage of patients categorized as CTD-ILD or IPAF increased from 23% to 39.5% of the patients, showing the potential usefulness of ENA determination in bronchoalveolar fluid. Undoubtedly this finding may have consequences in the approachment of the study of these patients. Another remarkable result of BAL analysis revealed that in 7 patients (37%) ENAs found in BAL were not detected in the serum of the same patients, being ENA positive in BAL and negative in the serum from 3 of them. This finding also may be very important in our patients with CTD-ILD due to the different prognostic implications caused by the presence of several Ab together.

The study of ENA in BAL of patients with suspected CTD-ILD has not been addressed before and, according to these findings, it could expand the diagnostic sensitivity in non-filiated ILD. However, despite being an interesting line of research, additional studies are needed to validate the usefulness of determining CTDs' specific Ab in BAL. First, it is important to establish the pathogenic role of these antibodies in patients who only present ENA in BAL and not in blood test. It is known that the presence specific CTD autoantibodies is not sufficient to diagnose as autoimmune disease. In this way, when Salvador-Corres et al. compared the clinical and pulmonary functional test findings of CTD patients with and without ENA in BAL, they did not find relevant differences. The follow-up of these groups of patients can help to clarify questions and to reveal the diagnostic and prognostic role that ENA in BAL can play in this group of patients. Another important point is that authors did not study all Ab associated with CTD-ILD and we do not know whether other Ab in BAL could be comparable. For example, the technique of determining antibodies against neutrophil cytoplasm (ANCA) and its specificities is not globally standardized. Finally, we cannot guarantee that the secretion of these antibodies has been in situ and their presence is rather due to the damage of the alveolo-capillary membrane as a result of ILD. These and another uknowns need to be clarified taking into consideration that BAL is an invasive procedure. Nevertheless, the authors certainly opened an interesting approach to study of CTDs Ab in BAL deeply. Future works in this line could validate the usefulness of this technique in the management of CTD-ILD.

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