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Letter to the Editor

Rheumatoid arthritis-associated interstitial lung disease (RA-ILD): Systemic disease activity correlates with lung inflammation

Enfermedad pulmonar intersticial asociada a la artritis reumatoide (EPI-AR): La actividad sistémica de la enfermedad correlaciona con la inflamación pulmonar

Dear Editor,

It is known that interstitial lung diseases (ILD) are a group of lung disorders characterized by inflammation and/or fibrosis of lung parenchyma manifested with progressive dyspnea and high risk of end-stage respiratory failure.[1] ILD is one of the main systemic manifestations of rheumatoid arthritis (RA-ILD) and the second cause of death in patients with this autoimmune disease.[2] However, it is unknown if an association between RA disease activity and interstitial lung damage in RA-ILD exists. In this report, we hypothesized that in RA-ILD, the bronchoalveolar lavage (BAL) cell profile may correlate with the CDAI index, a validated index to measure RA disease activity. The hypothesis is based in the concept that in RA-ILD, an inflammatory insult may be responsible at least in part, of the damage observed in the interstitial lung tissue, and the inflammation is secondary to RA disease activity.[3] In order to test our hypothesis, we developed a protocol in which 18 patients who fulfil ACR/EULAR 2010 criteria with interstitial lung disease diagnosed by high resolution computed tomography (HRCT) were enrolled. Patients had a BAL as a part of the standard diagnostic procedure; the BAL cell profile was correlated with a CDAI index measured within 5 days apart of the BAL. The patients had a median age of 58 (IQR 53–64) years old and 83% were female. Usual interstitial pneumonia (UIP) pattern was the most common tomographic pattern in 44% of the patients, followed by lymphocytic pneumonia pattern in 16% of the patients. 44% of the patients had mixed tomographic patterns. Patients had a median CDAI index of 29 (IQR 5–38). There were no differences in the CDAI index values between patients with likely tomographic usual pattern vs. other tomographic patterns, median of 12.5 (IQR: 4–37.5) vs. median 29.5 (IQR: 21–33.5), $p < 0.17$ neither in the % of lymphocytes in BAL: $p < 0.38$ (median 17% (IQR: 6–57%) vs. median 35.5 (IQR: 32.5–65.5%), $p < 0.19$. Finally, association between disease activity and inflammation in lung disease was analyzed with Spearmen correlation analysis and we found a significant correlation between CDAI and the percentage of lymphocytes (rs: 0.528; CI: 0.04, 0.82) in BAL (Fig. 1). The UIP tomographic pattern is characterized by fibrosis elements characterized by reticular opacities of basal predominance, subpleural location involvement, presence of honeycombing and traction bronchiectasis; due to the extensive presence of fibrosis, this type of tomographic pattern is associated with a poor prognosis[4]; Nevertheless, Matson et al. have shown that it is possible to stop disease activity due to immunosuppressive treatment in patients with UIP RA-ILD pattern, demonstrating the

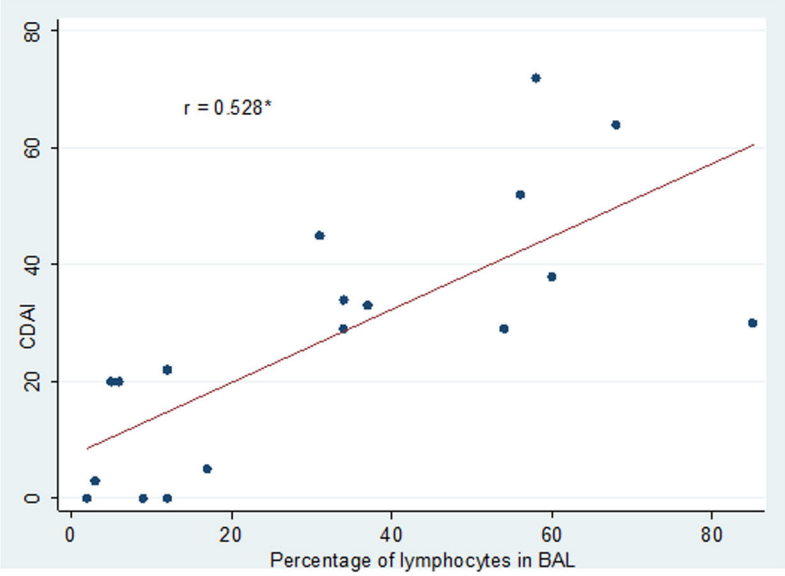

Fig. 1. Estimated correlation between the percentage of lymphocytes quantified in BAL and the CDAI.

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importance of the local inflammatory phenomenon of the lungs.[5] It has been documented that lymphocytes are the population with the highest presence in patients with AR-ILD; in addition, in the UIP pattern an increase in the number of neutrophils present in BAL has been observed.[6] Although previously documented findings on cell populations found in BAL have been considered non-specific, in this report we showed a significant correlation between lymphocyte count and CDAI calculated by expert rheumatologists. This finding is related to previously documented information from histological analysis of surgical lung biopsies, which describes that these patients present concurrently with follicular bronchiolitis, rheumatoid nodules or chronic pleuritis with an increase in CD4+ lymphocytes compared to lesions developed in patients with idiopathic pulmonary fibrosis.[7] This finding made demonstrates that systemic inflammation is a reflection of local inflammatory phenomena that are difficult to appreciate by conventional diagnostic tests. This knowledge could be used to establish a treatment plan according to the clinical phenotype of RA.

Ethics approval

The local ethical institutional review board approved the study protocol (approval code number: C20-14).

Consent for publication

Prior to participation, all participants were informed of the objective, scope of the research and subsequent publication of the project.

Consent to participate

Informed consent was given to all patients to participate in the study.

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This study did not receive any support or funding.

Data availability

Authors confirm the raw data to support this study's conclusions are included in the manuscript. The corresponding author will provide more information, upon reasonable request, to any qualified researcher.

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