Letters to the Editors

Interstitial lung disease is associated to infections of lower respiratory tract in immunocompromised rheumatoid arthritis patients

Sirs,

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterised by synovial joint swelling and tenderness (1, 2). A high frequency of infections complicating RA has been reported during the last years; in particular, septic arthritis and pulmonary infections (3).

The aim of the study was to investigate the possible association between demographic, serological and clinical RA features and the lower respiratory tract (LRT) infections.

The study retrospectively evaluated clinical data, including comorbidities and different treatments of 563 RA patients satisfying the 2010 ACR/EULAR classification criteria (female/male ratio 3.43, mean age 64.8±13.6SD years, mean disease duration 11.5±9.4SD years) (1).

During a mean follow-up of 138.9±131.3SD months, we observed 47 patients with at least one episode of LRT infection.

The presence of RA-associated interstitial lung disease (ILD) (p=0.016), steroids ($p \leq 0.001$), and biological disease-modifying anti-rheumatic drugs (b-DMARDs) (p=0.01) were significantly associated to LRT infections. All variables remained independently associated to infections of LRT also at logistic regression analysis; while no differences were observed with regard to the kind of the b-DMARDs, namely anti-tumour necrosis factors-α (anti-TNF-α), rituximab, abatacept, tocilizumab. Age, smoke, disease duration, rheumatoid factor, anti-citrullinated protein antibodies, disease activity score, conventional DMARDs, and comorbidities were not associated to LRT infections. The presence of ILD was associated to more severe LRT infectious complications, requiring hospitalisation in 55.6% of patients, compared to 27.8% of patients without ILD; aspergillosis and legionellosis were the most serious recorded infections.

Since patients with ILD showed a risk to develop an infection of LRT 4.5 times higher of patients without ILD (33.3% *vs*. 7.3% in patients with and without ILD, respectively), we further analysed the possible relationships between demographic, serological and clinical features and LRT infections in this sub-group of patients.

Among 33/563 (5.9%) patients with ILD, diagnosed on the basis of high-resolution computerised tomography (HRCT) (female/male ratio 2/1, mean age 71.8±10.6 years, mean disease duration 16.1±13.0 years), only b-DMARDs were associated to infections of LRT (p=0.002). Of interest, a combination therapy with b-DMARDs, methotrexate, and corticosteroids was significantly more frequently recorded in RA-ILD patients with infections compared to those without LRT infections (81.8% *vs*. 13.6% of patients; p=0.001).

A radiological ILD pattern of usual interstitial pneumonia (UIP) was not associated to infections; although not significant, bronchiectasias, frequently observed in RA-ILD and possible infectious site (4), were twofold more frequent in patients with LRT infections.

ILD is an important extra-articular complication of RA, clinically involving about 5–10% of patients (5). Respiratory complications due to RA-ILD, as well as cardiovascular diseases, are the most significant causes of death in RA patients (5, 6).

Although the pathogenesis of RA-ILD remains to be further investigated, its presence may influence the choice of systemic therapies (7). It is still controversial if some DMARDs, such as methotrexate, might induce the ILD occurrence or progression (6, 8). On the other hand, current therapeutic approach for RA-ILD is still under debate, in particular, the possible beneficial effects of different treatments on both joint and lung involvement (5, 9). Currently, no controlled studies and no evidences are available, about efficacy of immunosuppressive drugs on both arthritis and ILD (5, 6, 9, 10)

Our data confirm, with the limit of a low number of patients analysed, that immunosuppressive treatment increase the risk of LRT infections particularly in RA-ILD patients, suggesting a more careful surveillance in this subgroup of patients (3).

We can conclude that in patients with RA-ILD it is necessary to balance the control of joint inflammation with the risk of drug-related LRT infections; this latter could be significantly reduced by tailoring both drug combination and doses (corticosteroids, traditional, and b-DMARDs) on individual patients.

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Competing interests: none declared.

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