INTERSTITIAL LUNG DISEASE IS ASSOCIATED TO INFECTIONS OF LOWER RESPIRATORY TRACT IN IMMUNOCOMPROMISED RHEUMATOID ARTHRITIS PATIENTS

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Objectives. To investigate the possible association between demographic, serological and clinical features of rheumatoid arthritis (RA) and the lower respiratory tract (LRT) infections.
We further analyzed the possible relationships between demographic, serological and clinical features and LRT infections in a sub-group of patients with RA-associated interstitial lung disease (ILD).
Materials and Methods. Demographic, serological, clinical and therapeutic features of 563 RA patients were retrospectively analyzed (female/male ratio 3.43, mean age 64.8±13.6SD years, mean disease duration 11.5±9.4SD years).
Results. 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 ILD, therapy with steroids, and b-DMARDs were significantly associated to LRT infections (p=0.016, p=0.000, and p=0.01 for ILD, steroids and b-DMARDs, respectively).
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-tumor necrosis factors alpha inhibitors, rituximab, abatacept, tocilizumab. Moreover, the presence of ILD was associated to more severe LRT infectious complications, requiring hospitalization in 55.6% of patients, compared to 27.8% of patients without ILD (p=0.042). Since patients with ILD showed a risk to develop an infection of LRT 4.5 times higher of patients without ILD, we further analyzed this peculiar sub-group of patients. Among 33/563 (5.9%) patients with ILD (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 compared to those without LRT infections (81.8% vs 13.6% of patients; p=0.001).
Conclusions. ILD is an important extra-articular complication of RA, involving about 5-10% of patients, and its current therapeutic approach is still under debate, because the lack of evidences that immunosuppressants are effective both on joint and lung involvement. Idiopathic pulmonary fibrosis (IPF) is usually compared to RA-ILD for their similarity in radiological and histological features. In IPF patients, the PANTHER-IPF study showed an excess mortality due to pulmonary infection in azathioprine and prednisone treatment arm, and corticosteroids increase the risk of serious infection fourfold. Our data confirm, with the limit of a low number of patients analyzed, that immunosuppressive treatment increase the risk of LRT infections particularly in RA-ILD patients, suggesting a more careful surveillance in this sub-group of patients.
In conclusion, 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.

Keywords: *Rheumatoid arthritis, pulmonary infections, interstitial lung disease.*