Biological DMARDs-Induced Lupus in Patients with Rheumatoid Arthritis: A Single Centre Experience

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Purpose Autoimmune diseases arise from an abnormal immune response of the body against self-proteins leading to tissue and organ damage. The excessive production of harmful autoantibodies (AAB) is a hallmark of autoimmune diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and Sjögren’s syndrome (SjS). Also in cancer research, it has been recently shown that AABs are useful to characterise patients. The characterisation of patient subgroups by means of stratification is essential for the efficient development of therapies, but often difficult due to the lack of appropriate biomarkers. Personalised or precision medicine approaches rely on appropriate multivariate multiplexing technology and data analysis. AABs serve as diagnostic markers for the investigation of relationships and patterns, which can be related to relevant clinical variables.

Methods Here, we illustrate Luminex bead-based AAB assays using a set of 96 biomarker targets and their utility to characterise SLE and SSc as well as cancer study groups. For the investigation of relationships and patterns, which can be related to relevant clinical variables.

Results

Longitudinal observational study in 246 bionaive RA receiving their first bDMARD, anti-tumour necrosis factor (TNF) or non-TNF drugs, according to local treatment guidelines.

Disease activity, therapeutic response and serial autoantibody profiles (antinuclear (ANA), anti-dsDNA) were systematically assessed at baseline and every six months. Prevalence, clinical significance and therapeutic implications of ANA/anti-dsDNA specificities were further analysed (SPSS-19, p<0.05).

Results

214 RA received TNF inhibitors (56 infliximab, 65 adalimumab, 8 golimumab, 18 certolizumab, 67 etanercept) as first bDMADs and 32 different mechanism of action (10 rituximab, 7 abatacept, 15 tocilizumab). Overall, ANA seroconversion was demonstrated in 14.22% (35/246), while anti-dsDNA in 8.94% (22/246); no change in the immunological profile under golimumab, certolizumab, abatacept or rituximab.

Biological drugs (bDMARDs) have changed landscape and outcomes in various rheumatic conditions. Increased risk for infections, paradoxical reactions, autoimmunogenicity are widely acknowledged and may be responsible for treatment failure and switching among biologics.

Objectives To assess drug-induced autoimmunity (serology, clinical significance) in patients with rheumatoid arthritis (RA) treated with bDMARDs.

Patients and methods Longitudinal observational study in 246 bionaive RA receiving their first bDMARD, anti-tumour necrosis factor (TNF) or non-TNF drugs, according to local treatment guidelines.

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Significantly higher rates of ANA were reported in infliximab-treated RA (30.53%) as compared to adalimumab (18.46%), etanercept (7.46%) and tocilizumab (6.66%) (p<0.05); anti-dsDNA positivity was found in 10 infliximab (17.85%), 4 adalimumab (12.30%), 3 etanercept (4.47%) and one tocilizumab (6.66%), within an average of 36.5 (2-67) months.

ANA/anti-dsDNA positive status correlated with RA activity (DAS28-ESR) and loss of therapeutic response, concomitant DMARDs (leflunomide) and corticosteroids, administration adverse reactions (p<0.05).

Only four patients (1.62%; 4/246) were classified as drug-induced lupus. Three of them (infliximab, adalimumab, tocilizumab –induced) developed mild to moderate disease, with characteristic malar rash, serositis, haematological, elevated ANA and anti-dsDNA that normalised six months after bDMARD discontinuation; the fourth patient had adalimumab-induced lupus two months after drug initiation, with severe course (subacute extensive skin lesions, cytophenia, seraosis) and fatal outcome.

Conclusion Development of ANA with or without anti-dsDNA specificity is typically associated with loss of response to bDMARD in RA and infrequently responsible for drug-induced lupus. Systematic evaluation of ANA/dsDNA is not recommended in routine practice, but essential in certain specific clinical settings (secondary non-responders or lupus-like symptoms).