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Anti-TNFα therapy in rheumatoid arthritis and autoimmunity

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The purpose of the presented study was to evaluate the presence and evolution of the seric levels of autoantibodies in patients affected by rheumatoid arthritis (RA) treated with anti-TNFá blockers, to consider the differences between infliximab and etnarecept regarding the induction of autoantibodies and to describe the relationship between antinuclear antibody (ANA) titre, C-reactive protein (CRP) and Blys levels (a B-cell activating factor implicated in both animal and human autoimmune disorders).

The study included 54 patients (8 men, 46 women,mean age 51.4±12.4 years, mean duration of disease 13.6±8.8 years) with RA, diagnosed in agreement with ACR criteria, unresponsive to conventional therapy, who were treated with anti-TNFα blockers for 12 consecutive months. 43 patients were treated with infliximab and 11 with etanercept, using the conventional doses. The patients received also methotrexate (7.5 to 15 mg/ week), or azathioprine (methotrexate intolerance- 2 patients).

The patients were evaluated clinically every 2 months and biologically (full blood count, liver and kidney function) every month. ESR, CRP, C3 and C4 and TSH levels were evaluated every 4 months (or more frequently if needed). Autoantibody levels (rheumatoid factor, antinuclear, anti-ds DNA, anti-ENA, anti-mitochondrial, anti-thyroid and ANCA) were evaluated at baseline, then on the days of the fourth, sixth and eighth infusion of infliximab or at 4, 8 and 12 months in patients receiving etnarecept.

At baseline 37% of the patients were ANA positive (37, 2% in the infliximab subgroup and 36, 3% in the etnarecept subgroup). During treatment with infliximab, 95,3% patients showed ANA positivity at least at one determination, with progressive increase of ANA levels. At the 8^{th} and 12^{th} month, the levels were significantly higher than at baseline and at the 4^{th} month ($p<0.001$), with no significant differences between 8^{th} and 12^{th} month ($p=0.477$) and baseline and 4^{th} month ($p=0.215$). During treatment with etnarecept 54, 5% patients showed ANA positivity at least at one determination, but with no significant difference in ANA levels during the 1 year follow-up period. At baseline only one subject (in infliximab group) had very high ANA levels (higher than 1:1.280). During the treatment period, 46.5% of the subjects treated with infliximab presented at least one very high value of ANA levels, whereas 0% of the etnarecept groups presented such values.

No significant correlation was found between ANA titres and CRP levels at each time of the study period either in infliximab or in etanercept subgroup.

Other antibodies did not present any significant evolution.

The Blys level measured at baseline and after 1 year of treatment (in patients with ANA levels higher than 1: 1.280, which were detected only in the infliximab group) did not evidence an homogeneous trend.

The study confirms the induction of autoantibodies (mainly ANA), in an important number of RA patients treated with infliximab, almost half of the cases having very high titres of ANA. RA patients treated with etnarecept present ANA positivity in a lower percentage and at lower titres, probably due to the different mechanism of TNF inhibition. Both serum level variations of CRP and Blys production do not seem to participate in ANA induction after administration of TNFa blockers.The presence of other autoantibodies is insignificant and the mechanism of their induction is unknown.

Comment on the paper:

Paola Caramaschi, Domenico Biasi, Marco Colombatti et al – Anti-TNFα therapy in rheumatoid arthritis and autoimmunity. *Rheumatology International* 2006; 26: 209-214