Lupus erythematosus manifestations exacerbated by etanercept therapy in a patient with mixed connective tissue disease

Sir,

Several authors have discussed the potential benefit of TNF-α blockers in systemic lupus erythematosus (SLE), a condition in which new therapeutic agents are needed (1-3). Nevertheless, the induction of anti-DNA antibodies in patients with rheumatoid arthritis (RA) treated with TNF-α blockers has been noted since the earliest clinical trials with etanercept and infliximab, a phenomenon emphasized in two recent papers (4, 5). However, although these biological abnormalities frequently occur in 20 to 60% (6), only a few lupus-like syndromes have been reported in patients treated with TNF-α antagonists (3, 7-11). Thus, it remains unclear whether the appearance of antinuclear antibodies (ANA) in RA patients treated with TNF-α blockers could compromise the use of such agents in SLE patients. We report the case of a patient presenting with a mixed connective tissue disease (MCTD) according to the criteria of Amigues et al. (12) who was treated by TNF-α antagonists which precipitated manifestations of SLE.

A 27-year-old woman was admitted because of symmetrical destructive polyarthropathy, Raynaud’s phenomenon, sclerodactyly and pericarditis. Immunological investigations revealed positive ANAs (titer 1:8000), anti-double-stranded DNA antibodies (anti-dsDNA, 21.5 Units/ml; negative < 7) (IgG isotype), anti-nRNP antibodies and anti- Ro antibodies, but no rheumatoid factor. There were no antineutrophil cytoplasmic antibodies (ANCA) or cryoglobulinaemia. She was unsuccessfully given hydroxychloroquine, then leflunomide (20 mg/day) and finally methotrexate (up to 20 mg/week IM). Considering the severity of the polyarthritides and the lack of efficacy of the corticosteroids (up to 20 mg/day prednisolone), she was given etanercept 25 mg twice a week.

One month later, she presented with polyarthritides and a generalized urticarial skin eruption suggesting a lupus-like syndrome. Laboratory results disclosed the following results: erythrocyte sedimentation rate 46 mm/hour, elevated C-reactive protein (45 mg/l; normal < 10), low lymphocyte count (0.3 x 10⁹/l; normal 1.5 – 4 x 10⁹) and a relevant increase in ANAs (titer 1:64000) and anti-DNA antibodies (41 U/ml) (IgG isotypes CH50 was low (59 U/ml; normal 63-90 U/ml), and anti-DNA antibodies (41 U/ml) (IgG isotypes CH50 was low (59 U/ml; normal 63-90 U/ml) and mycophenolate mofetil 2000 mg/day was started. One month later, she was symptom-free. No relapse of clinical SLE symptoms had occurred after one year of follow-up and immunological parameters including ANAs and anti-DNA antibodies had improved.

MCTD may overlap rheumatoid arthritis and SLE and could be an interesting model for studying the impact of TNF-antagonists in the treatment of such diseases, because it can naturally evolve into SLE as well as RA. Interestingly, under etanercept therapy, which was justified considering the severity of the rheumatologic manifestations, our patient added clinical symptoms strongly suggestive of SLE (13), and worsened biological abnormalities. In this cases, anti-TNF treatment have not induced lupus but have exacerbated the SLE symptoms of the MCTD. Because TNF blockers have been proposed for treating lupus patients (1-3), the present case highlights the need to establish the subgroup of SLE patients in whom it could represent a valuable tool. Moreover, MCTD with features of SLE at disease onset may not represent a suitable indication for TNF antagonists.

C. RICHEZ, MD, P. BLANCOC, MD, C. DUMOULIN, MD, T. SCHAVERREK®E, MD, PhD

References