

LETTER

Ichiro Nakamura · Makoto Tanno · Shin-Ichi Katsumata  
Katsumi Ito

## A lupus-like butterfly rash following infliximab therapy

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*To the Editor:*

Infliximab is a chimeric mouse-human monoclonal antibody recently approved for the treatment of both rheumatoid arthritis and Crohn's disease. By directly targeting tumor necrosis factor- $\alpha$  (TNF $\alpha$ ), this new agent has allowed a reduction in steroid doses and has led to improvement in the clinical signs and symptoms of inflammation. We report the development of a lupus-like butterfly rash after two infusions of infliximab in a patient with rheumatoid arthritis.

A 57-year-old man with a 1-year history of rheumatoid arthritis experienced a flare-up despite maintenance therapy with prednisone (10mg/day) and methotrexate (6mg/week). The C-reactive protein (CRP) concentration was 4.4mg/dl, and the erythrocyte sedimentation rate was 48mm/h. The patient began receiving infliximab, 3mg/kg body weight, at days 0 and 14. He had an initial complete response after two well-tolerated infusions. The CRP concentration decreased to 1.6mg/dl. However, before the third infusion, at day 28, he developed a papulosquamous butterfly rash (Fig. 1) with mild inflammatory arthritis involving his hands, wrists, and knees, suggesting drug-induced systemic lupus erythematosus. The concentration of CRP at this point was 2.0mg/dl. Interestingly, serologic examination revealed no elevation of anti-double-stranded DNA immunoglobulin G (IgG) and IgM antibodies (<5IU/ml and <8U/ml, respectively), negative anti-nuclear antibodies, and a weakly positive anti-infliximab antibody at a low titer of 1:10 (normal <1:10). Complement concentra-



**Fig. 1.** A 58-year-old man with rheumatoid arthritis developed a lupus-like papulosquamous butterfly rash induced by infliximab therapy

tions were normal (C3 was 143 mg/dl, and C4 was 21 mg/dl); anti-histone antibodies were not assayed. Further infusions of infliximab were discontinued, resulting in resolution of his rash within a week. Unfortunately, the discontinuation of infliximab therapy caused a flare-up of rheumatoid arthritis including in his wrist and knee joints.

Tumor necrosis factor- $\alpha$  seems to play a key role in host defense and immune surveillance.<sup>1</sup> Clinically relevant systemic lupus erythematosus is rare, although the development of antibodies to double-stranded DNA has been reported in up to 14%–16% of RA patients treated with infliximab.<sup>2,3</sup> In placebo-controlled trials of infliximab, 5 of 2292 patients (0.22%) receiving infliximab (3 with Crohn's

I. Nakamura (✉) · M. Tanno · S. Katsumata · K. Ito  
Department of Rheumatology, Yugawara Kosei-Nenkin Hospital,  
438 Miyakami, Yugawara, Ashigara-shimo, Kanagawa 259-0314,  
Japan  
Tel. +81-465-63-2211; Fax +81-465-62-3704  
e-mail: Ichiclast@aol.com

disease and 2 with rheumatoid arthritis) developed a lupus-like syndrome that resolved after discontinuing therapy with the drug.<sup>3</sup> Compared with previous reports,<sup>4-8</sup> the unusual feature of the case presented here is the lupus-like butterfly rash that was not associated with elevated anti-double-stranded DNA IgG and IgM. Further investigation and an accumulation of cases are necessary to clarify this discrepancy between our case and those previously reported. This is the first case report of infliximab-induced lupus-like rash in Japanese rheumatoid arthritis patients.

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