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## Is there a link between the use of etanercept and Henoch-Schönlein purpura? Commentary on: Henoch-Schönlein purpura in a patient with rheumatoid arthritis receiving etanercept (*Eur J Dermatol* 2010; 20: 521-2)

We read with great interest the recent contribution by Asahina *et al.* [1]. They reported a case of Henoch-Schönlein purpura (HSP) that occurred in a patient with rheumatoid arthritis (RA) receiving etanercept, and speculated that anti-tumor necrosis factor (TNF)- $\alpha$ -TNF- $\alpha$  immune complexes and interferon (IFN)- $\alpha$  might be possible factors in the development of HSP. Duffy *et al.* also suggested transforming growth factor (TGF)- $\beta$  as a central cytokine in the development of HSP following etanercept treatment [2]. Wu *et al.* postulated a pathogenic role of TNF- $\alpha$  in the development of HSP [3]. However, we would like to add a possible consideration on the mechanism of HSP related to the use of etanercept. Saulsbury *et al.* previously reported that IgA rheumatoid factor (RF) might be closely related to the pathogenesis of HSP. In their study, IgA RF was found in 13 (54%) of the 24 HSP sera, while none of the patients with HSP had RF of the IgG or IgM isotypes, and the mean serum IgA concentration was higher in IgA RF positive patients ( $245 \pm 92$  mg/dL) than in IgA RF negative patients ( $171 \pm 69$  mg/dL) ( $P < 0.05$ ) [4]. There was also a positive correlation between the IgA RF concentration and the serum IgA level, and IgA RF concentration tended to be highest during the acute phase of the illness. These results suggest that IgA RF production may be linked to the development of HSP.

Recently, Yazdani-Biuki *et al.* [5] reported the effect of etanercept on the humoral immune system in the long term treatment of patients with RA. Although no significant changes in serum levels of total immunoglobulin and specific autoantibodies such as anti-cyclic citrullinated peptide, antinuclear, and ds DNA antibodies were seen in their study, serum IgA RF increased significantly after 9 months' etanercept treatment ( $P < 0.01$ ). These results indicate that the blockade of TNF- $\alpha$  with etanercept seems to have a pivotal effect on increasing the serum IgA RF levels through altering RF-producing B cells in patients with RA. Although the exact role of B cells and T cells in HSP

still remains controversial [6], B cells appear to play an important role in the pathogenesis of HSP.

Therefore, we speculate that the increased IgA RF level during etanercept treatment might have a causal relation to the development of HSP. However, further studies are necessary to elucidate which cells, post-switch cells or RF-producing memory B cells, are responsible for the raised RF isotypes, and the precise role of IgA RF in the formation of IgA-containing immune complexes in HSP. The sequential measurement of IgA RF during etanercept treatment and the effect of TNF blocking agents on IgA RF-producing B cells should also further evaluated in the future. ■

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