Eosinophilic fasciitis induced by certolizumab pegol: association or coincidence?

Sirs,

We read the article by Debusschere *et al*. with great interest (1). The authors described a young patient with ankylosing spondylitis who developed eosinophilic fasciitis (EF) during treatment with certolizumab pegol (CZP). As the authors explained, CZP and physical stress may play an important triggering role in the development of EF. However, TNF-α inhibition has been found to be a chemotactic agent for eosinophils and downregulates eosinophil apoptosis, hence it appears counterintuitive that it would cause eosinophilia and EF (2, 3). This may require further explanation.

In recent years, the use of TNF-α inhibitors in rheumatologic, gastroenterological and dermatologic diseases has increased significantly and the adverse drug reactions that occur during their treatment have been described several times, but EF has been rarely reported. Hariman *et al*. reported a case of EF during infliximab therapy for psoriatic arthritis (4). Mpitouli *et al*. also reported a case of EF that occurred during infliximab treatment for Crohn's disease (5). Vester *et al*. reported a patient with recurrent transient blood eosinophilia during treatment with adalimumab, and normalisation of blood eosinophil levels after discontinuation of adalimumab treatment or reduction of drug dose use by half (6). One study showed that certolizumab developed eosinophilia in up to 10 of 1000 patients (6). Similar cases have been reported regarding etanercept (7). It can be seen that most of the TNF-α inhibitors have the adverse effect of causing eosinophilia. And EF may be the result of the eosinophil-mediated release of toxic granular proteins (*e.g*. eosinophil peroxidase, eosinophilic cationic protein, eosinophil-derived neurotoxin and eosinophil major basic protein) leading to skin and muscle organ damage (8). It seems paradoxical that TNF-α inhibitors have been reported to downregulate eosinophil apoptosis and also to be able to induce eosinophilia and EF (2, 3). Although the underlying mechanisms are unclear, the potential heterogeneity of allergic constitution between patients, the repercussions of antibody formation against these foreign proteins in different bodies, and the off-target effects of these drugs may explain this association (4). One study revealed that 30–46% of EF patients have a history of intense physical exertion or trauma before the onset of the disease. Therefore, physical stress and muscle trauma may play an important triggering role in this patient (9).

In conclusion, TNF-α inhibitors are increasingly used as maintenance therapy for rheumatic diseases, and the above-mentioned studies support the growing concern about the rare adverse effects of TNF-α inhibitors.

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