

Development of eosinophilic fasciitis during treatment with certolizumab pegol for ankylosing spondylitis

Sirs,

Eosinophilic fasciitis (EF) is a rare fibrosing disorder with poorly understood pathogenesis and unknown aetiology (1-2). We report a patient who developed EF undergoing treatment with certolizumab pegol (CZP) for ankylosing spondylitis (AS). This is the first report of EF arising during treatment with CZP, and second description of EF occurring during treatment with a tumour necrosis factor- α (TNF- α) blocker.

A 24-year-old man was referred to our centre with a 5-month history of stiffness and skin induration of the extremities. Two years earlier, AS was diagnosed based on inflammatory back pain, radiographic sacroiliitis, knee synovitis and HLA-B27 positivity. After initial therapy with NSAIDs and sulfasalazine, CZP was initiated. After CZP introduction he developed transient red, itchy 'bumps' on his extremities, together with peripheral blood eosinophilia. Because of suspected link with CZP, this was stopped. Around that time, as basketball player he experienced progressive limb stiffness and skin tightness during exercise. Secukinumab 150 mg monthly was then introduced, since persisting axial complaints. Further history revealed weight loss, partly because of change to vegan diet. Fever, night sweats and Raynaud's phenomenon were absent. Clinically, symmetrical skin induration of his limbs was visible with 'groove signs' (Fig. 1) and extension deficits of knees and elbows. Sclerodactyly was absent. Laboratory studies showed peripheral eosinophilia (970/ μ L), polyclonal hypergammaglobulinaemia, mild increased ESR and CRP, normal CK and negative antinuclear antibody assay. Capillaroscopy was normal. Contrast-enhanced MRI of the arm showed fascial inflammation with subcutaneous oedema. A full-thickness wedge biopsy including skin, subcutis, fascia and muscle of the left upper arm was performed. Histology showed a dense lymphocytic infiltrate in the fascia (without eosinophils), confirming the diagnosis of EF. Of note, eosinophils are not always present in the histopathology of EF (2). PET-CT scan revealed no underlying malignancy. Parasitic and haematological disorders were ruled out.

Prednisolone 60 mg daily, methotrexate 15 mg weekly and physiotherapy were initiated, with interruption of Secukinumab (since there were few axial complaints at that time). After rapid normalisation of the eosinophil count and inflammatory markers, prednisolone was tapered down and stopped after 4 months, whilst continuing methotrexate. Secukinumab was reintroduced upon relapse of inflammatory back pain, with good response. The patient is currently in remission for his AS and shows complete resolu-

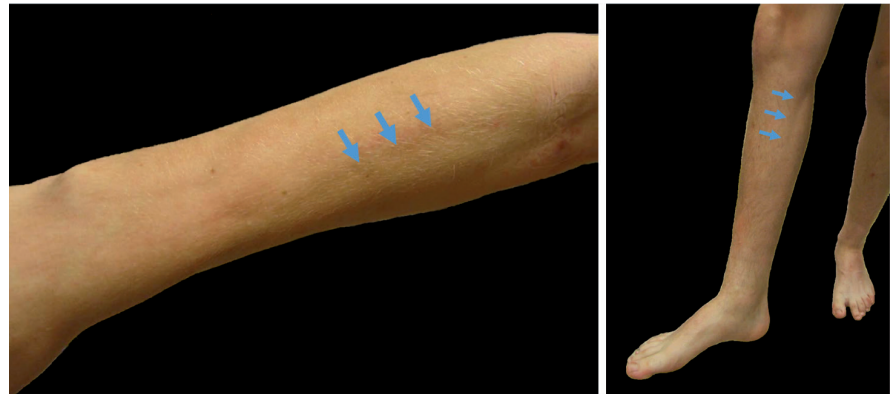


Fig. 1. The 'groove sign' on the lower arm (left) and on the lower leg (right).

tion of skin tightness at his arms, keeping mild residual induration in the legs. Peripheral eosinophil counts remain normal.

To our knowledge, EF has not been previously described during CZP treatment. Other drug-induced scleroderma has been described though (2). Hariman *et al.* reported an EF case during infliximab treatment for psoriatic arthritis (3).

We believe CZP had a triggering role in EF development in our case. First, the patient developed urticarial lesions shortly after CZP introduction, with subsequent evolution of skin tightness. Second, initially peripheral eosinophil counts were normal, whilst progressively rising shortly after CZP introduction.

EF is hypothesised to be an immune-allergic disorder (2, 4). Suggested EF triggers include strenuous exercise, physical factors, graft-versus-host disease, initiation of haemodialysis, *Borrelia burgdorferi* infection, exposure to certain drugs, autoimmune and haematologic disorders (2). As basketball player, physical stress might have played a triggering role in this case, in addition to CZP.

As stated by Hariman *et al.*, it seems contradictory that TNF- α inhibition would induce eosinophilia and EF, since TNF- α has been reported to be a chemotactic agent for eosinophils and downregulates eosinophil apoptosis (5, 6). Furthermore, a case series of steroid-resistant EF showed beneficial responses to infliximab (7). The mechanism by which CZP triggered EF in this case remains unclear.

Prospective follow-up of this rare disease through reference networks could enable achieving more disease insight and eventually result in clinical practice guidelines (8).

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