

Letters to the Editor

Henoch Schönlein purpura following etanercept treatment of rheumatoid arthritis

Sirs,

We report the case of a 60 year old woman with a 20 year history of seropositive erosive rheumatoid arthritis (RA) who developed a purpuric rash and microscopic haematuria, concurrent with an episode of sinusitis, three months after starting etanercept therapy. Investigation revealed a raised erythrocyte sedimentation rate (ESR) (80mm/h), normal C-reactive protein (CRP) (8 mg/L), full blood count and chemistry. IgM and IgA rheumatoid factors (RF) were present. Anti nuclear antibody (ANA) was positive (1/640 speckled), antibodies to double stranded DNA, extractable nuclear antigens (ENA) and anti neutrophil cytoplasmic antibody (ANCA) were negative. Antistreptolysin O was positive at 300/L (N:0-200). C3, C4, C3d levels were normal. There was polyclonal expansion of immunoglobulins and low level polyclonal cryoglobulinaemia. Circulating immune complexes were absent. Skin biopsy revealed leucocytoclastic vasculitis with C3 deposition. Renal biopsy revealed focal and segmental glomerular lesions with necrosis of glomerular capillary loops and cellular infiltration of Bowman's space (Fig. 1A). Cellular crescents were observed in 3 of 35 glomeruli associated with segmental mesangial and endocapillary hypercellularity. Immunohistochemistry revealed diffuse granular deposits of IgA and C3 localized within the mesangium of all the glomeruli (Fig. 1B). Electron microscopy revealed dense deposits in the mesangial and paramesangial areas. Henoch Schönlein purpura (HSP) was diagnosed on the basis of purpuric lesions, leucocytoclastic vasculitis and IgA glomerulonephritis associated with C3 deposition, fulfilling the ACR criteria (1). Treatment was commenced with intravenous methylprednisolone (3 x 500mg) followed by monthly infusions of cyclophosphamide permitting resolution of clinical signs, immunoglobulin levels, proteinuria and haematuria. Several months later Etanercept was recommenced due to active RA. She again developed sinusitis and a purpuric associated with an ESR of 50mm/h and microscopic haematuria and proteinuria. Blood work up and repeat renal biopsy were again consistent with a diagnosis of HSP.

While there are three published reports of HSP associated with RA in adults with two describing HSP occurring in the setting of pre-existing RA (2-4), this is the first report of HSP subsequent to TNF- α inhibition.

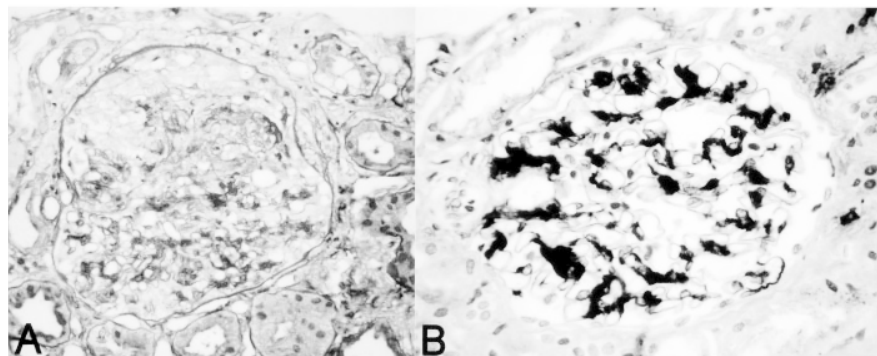


Fig. 1. A. Light microscopy demonstrating segmental and focal glomerulonephritis. At the top of this glomerulus, a cellular crescent occupies a segment of Bowman's space adjacent to a segmental mesangial and endocapillary proliferation. Some fibrin is also evident. (Trichrome x 200). B. Immunohistochemistry demonstrating deposits of IgA in the mesangium (Magnification x 200).

There are several reports of vasculitis following TNF- α inhibition but only one report of glomerulonephritis following etanercept treatment (5) and no reports of recurrence following rechallenge. Two patients with vasculitis following infliximab treatment had recurrent disease on switching to etanercept and one patient had a recurrence following switch from etanercept to infliximab, suggesting that the induction of vasculitis is a class effect of TNF- α inhibition. The recurrence of upper respiratory tract infection with positive antistreptolysin O test in the setting of TNF- α inhibition may explain the onset of HSP. Circulating immune complexes do not seem a likely explanation for vasculitis in our patient as levels were normal and the vasculitic lesions were not characterised by immune complex deposition. Cunnane and Jarrett comment on the switch in T-cell profile following TNF- α inhibition (6, 7). RA is a Th1 associated disease and evidence suggests HSP is Th2 associated. Reduced TNF- α effect may swing the balance of cytokine function in favour of uninhibited Th2 cytokines such as TGF- β . TGF- β producing T cells are increased in acute HSP when compared to levels of IFN- γ or IL-4 producing T cells (8). There is no known association between disease activity in HSP and levels of TNF- α or its soluble receptors and the activity of HSP (9).

We have described the first case of HSP with biopsy proven renal vasculitis following TNF- α inhibition in the setting of RA, which recurred on reintroduction of treatment.

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Reprints will not be available from the author.

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