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Successful use of rituximab in a patient with recalcitrant Churg-Strauss syndrome

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Churg-Strauss syndrome (CSS) is a disorder characterised by hypereosinophilia and systemic vasculitis occurring in people with asthma and allergic rhinitis. Corticosteroids in combination with a cytotoxic agent are the most effective treatment for CSS. Rituximab, a genetically engineered chimeric anti-CD20 monoclonal antibody has recently been tried with favourable responses in chronic immunological diseases.[1] Several published reports have shown its effectiveness in ANCA mediated vasculitides.[2 3] We present a patient with CSS who responded well to rituximab after conventional treatments had failed.

A 49 year old, white male patient with a long history of asthma presented in 2000 with inflammatory polyarthritis, bilateral scleritis, and negative autoantibodies. He was managed as a patient with seronegative RA but was intolerant to methotrexate and sulfasalazine. His symptoms settled, only to recur in 2004 with polyarthralgia, vasculitic skin rash (fig 1), dyspnoea, microscopic haematuria, and mild proteinuria.

Repeat investigations showed a high absolute eosinophil count of 4×10^9/l, raised erythrocyte sedimentation rate (ESR) of 120 mm/1st h, and C reactive protein (CRP) of 181 mg/l, mildly raised creatinine, and a positive cANCA (anti-proteinase 3 (PR3) titre of 30 (normal <2)). High resolution computed tomography of his chest showed pulmonary infiltrates consistent with pulmonary vasculitis. A nasal biopsy showed chronic inflammation, with some areas suggestive of vasculitis, and eosinophilic infiltration. His skin biopsy showed leucocytoclastic vasculitis, and a renal biopsy disclosed minimal non-specific abnormalities. Based on the above,[4] a diagnosis of CSS was made and treatment was started with prednisolone 40 mg and azathioprine.

His initial response was not sustained, requiring a change to cyclophosphamide in January 2005. Despite fortnightly pulses of cyclophosphamide (15 mg/kg) for 5 months, his condition continued to deteriorate. At this point, after reviewing the available publications on the use of rituximab in ANCA associated vasculitis,[2 3] treatment was started with this drug. Although it was planned as a 4 week regimen at 700 mg/week (375 mg/m^2 body surface area) with 100 mg intravenous methylprednisolone,[2] he required hospital admission after the second infusion, with bronchopneumonia and herpes zoster. This was treated appropriately, and his third infusion was given as a bolus on the 4th week (1 g). After this, his skin vasculitis cleared completely (fig 1) with normal ESR, CRP, absolute eosinophil count, anti-PR3 titres (fig 2), and undetectable B cells with normal T cell markers. He has been seen fortnightly since then (nearly 3 months), with no recurrence of skin vasculitis. Small increases in his eosinophil count ($(0.5–1.5)\times10^9$/l) have occurred and treatment with oral prednisolone at a dose of 30 mg a day is continuing.

Based on the above, rituximab appears to be a promising treatment for induction of remission in CSS. The rationale behind the use of rituximab is based on three assumptions[5]: (*a*) ANCA has an important role in the pathogenesis of ANCA associated vasculitides; (*b*) treatment with rituximab can effectively deplete CD20 expressing precursors of ANCA-producing plasma cells; and (*c*) plasma cells producing ANCA are short lived, and transient depletion of their CD20+

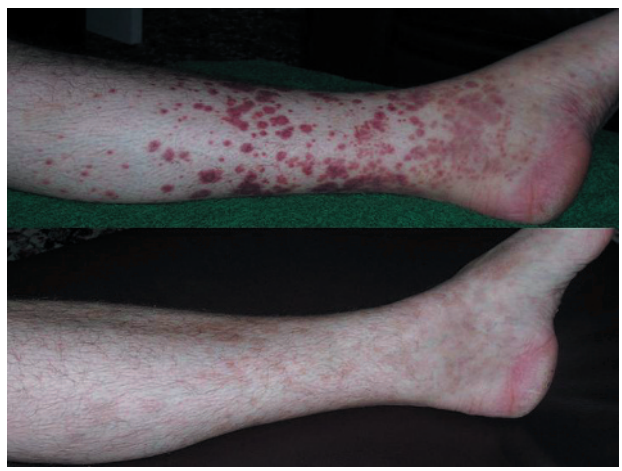

Figure 1 Skin vasculitic changes before (above) and after (below) treatment with rituximab.

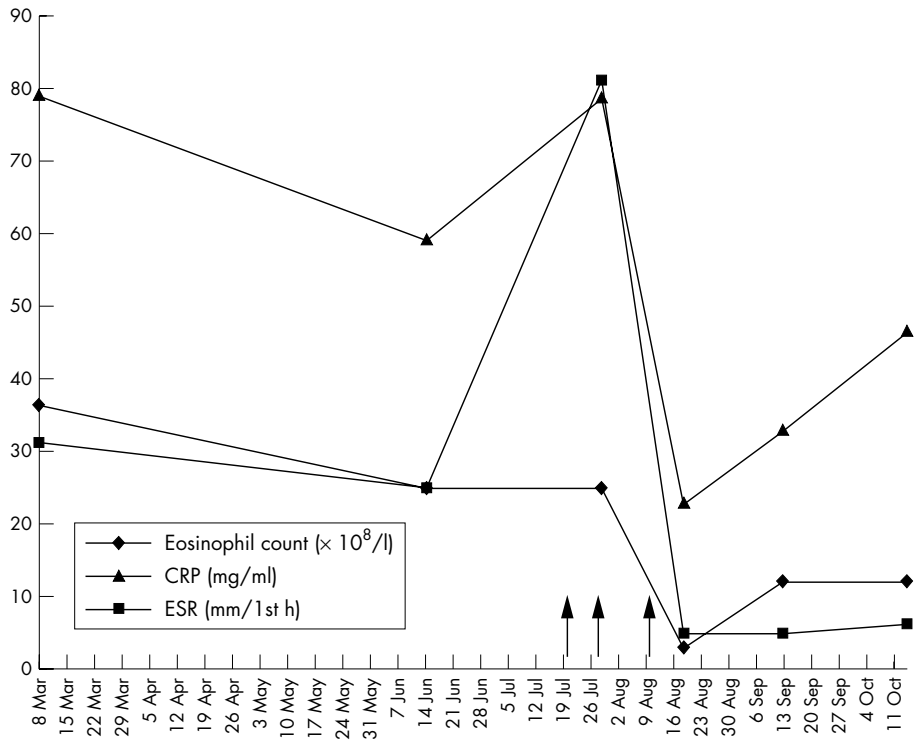

Figure 2 Changes to inflammatory markers and eosinophil count with rituximab (indicated by arrows)

precursors will abrogate ANCA production. However, we need to be aware of the concurrent risks of robust immunosuppression and predisposition to serious infections. Further research is warranted into the maintenance of remission and the long term safety with rituximab use.

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Successful treatment of refractory adult onset Still's disease with rituximab

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We read with interest the article by Aarntzen *et al*[1] reporting the inefficacy of anti-tumour necrosis factor (TNF) α inhibitor treatment with etanercept in adult onset Still's disease (AOSD).

We found that etanercept and also infliximab were ineffective in two patients with AOSD. Both patients were subsequently successfully treated with the monoclonal anti-CD20 antibody rituximab, targeting B cells. In both cases AOSD was diagnosed according to American College of Rheumatology criteria. Major symptoms were polyarthritis, fever, and typical skin lesions. Despite successive treatment with prednisolone and methotrexate (MTX), ciclosporin, leflunomide, cyclophosphamide po, and intravenous immunoglobulin, the patients' AOSD remained active, with recurrent febrile episodes, rash, synovitis, a serum ferritin level of 6400 μg/l (normal $\leqslant$200), and a mean C reactive protein level of 82 mg/l (normal $<$8). Use of the TNFα inhibitors etanercept and infliximab (5 mg/kg intravenously (IV)) in one patient and etanercept in the other was also ineffective after treatment in combination with MTX for an adequate time. The average dosage of concomitant prednisolone required was $>$30 mg daily.