In conclusion, infliximab can be used safely in daily clinical practice, but both doctors and patients should be aware of the (infection) risks, especially in patients receiving a higher dose (>3 mg/kg) of infliximab, in order to anticipate and minimise these risks.

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Fever and increasing cANCA titre after kidney and autologous stem cell transplantation for Wegener's granulomatosis

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Wegener's granulomatosis is a systemic vasculitis mainly affecting the lungs, nasal sinuses, and kidneys. Treatment usually consists of cyclophosphamide (Cy) and steroids.[1] High dose Cy with autologous stem cell support could be an alternative treatment for patients resistant to conventional treatment or requiring long term immunosuppression with the risk of secondary malignancy.[2]

CASE REPORT

We report on a 33 year old woman with chronic relapsing sinusitis, pulmonary granuloma, and proteinuria with progressive renal insufficiency since 1988. Renal biopsy showed necrotising glomerulonephritis, and biopsy of the nasal sinus showed granuloma with necrotising vasculitis. Proteinase-3-antineutrophil cytoplasmic antibodies (PR3-ANCA) were detectable with a titre of 1/280. Despite treatment with Cy (750 mg/m^2 every 3 weeks, later 100 mg/day orally) and steroids renal function deteriorated, and she underwent dialysis from April 1995 to December 1998. Live kidney transplantation from the patient's sister matched for HLA was performed in December 1998. Irrespective of ciclosporin A (CSA), which was given as prophylaxis for host versus graft reaction, she continuously needed immunosuppression with Cy (orally, 100 mg/day) because of persistent disease activity with relapsing pulmonary infiltrations. The transplanted kidney remained unaffected.

A cumulative Cy dose of over 100 g was reached and in view of the relapsing pulmonary granuloma and increasing PR3-ANCA titres, which in our patient correlated well with disease activity, stem cell mobilisation was performed in May 1999 with Cy 4 g/m^2 followed by granulocyte-colony stimulating factor 5 μg/kg for 10 days. Stem cell apheresis and selection of CD34+ stem cells was performed using the CliniMacs device on day 10. When PR3-ANCA titres increased from 1/128 to 1/500 after 4 months, high dose immunosuppression with Cy 50 mg/kg days 1–4 and ATG 5 mg/kg days 1–4, followed by retransfusion of 2.82×10^6 CD34+ cells/kg body weight was given. The conditioning regimen was chosen according to the protocol for aplastic anaemia.[3] Marked clinical improvement was seen with a regression of pulmonary infiltrates on chest *x* ray examination. Complete haematological reconstitution was achieved on day 12 after stem cell retransfusion. CSA was continued for renal graft protection.

Five months after high dose Cy, the patient was admitted with malaise, high grade fever, and pancytopenia. The PR3-ANCA titre was 1/1000, but computed tomography scans of the lungs and nasal sinuses were normal. An active Epstein-Barr virus (EBV) infection was diagnosed by serology (IgG and IgM). Polymerase chain reaction disclosed a high plasmatic viral load with 1 270 000 EBV transcripts per 100 ng genomic DNA. Treatment with intravenous ganciclovir and immunoglobulins led to resolution of all symptoms.

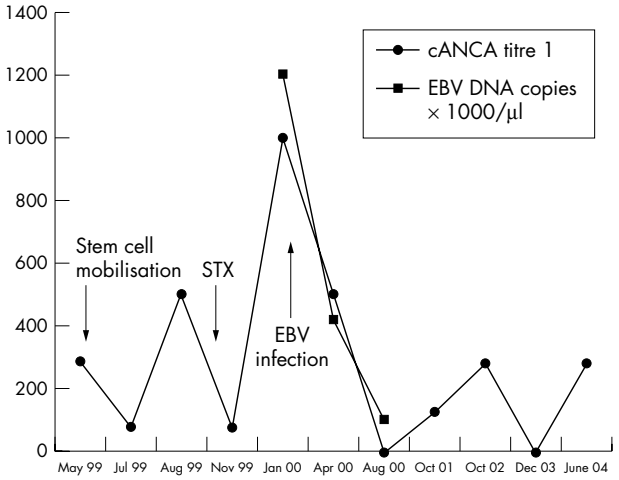

Figure 1 PR3-ANCA titre and the number of EBV DNA copies before stem cell mobilisation May 1999, before stem cell transplantation (STX) September 1999, and during EBV infection.

The PR3-ANCA titre fell in parallel with the EBV viral load in plasma (fig 1).

The patient remains in remission of Wegener's granulomatosis now 5 years after transplantation continuing treatment with low dose CSA (3 mg/kg body weight) and, later, mycophenolate mofetil (2×1 g) for host versus graft reaction prophylaxis. The CD3+, CD4+ T helper cells are still slightly lowered at 664×10^6 cells/l and the CD4/CD8 ratio is reduced to 0.63. PR3-ANCA titres vary between 0 and 1/280, but have not consistently been negative (fig 1).

DISCUSSION

High dose immunosuppression with in vitro and in vivo T cell purging followed by autologous stem cell support was effective in our patient with severe, refractory Wegener's granulomatosis. It remains to be seen if disease remission continues after complete immune reconstitution. To our knowledge, this is the first reported case of refractory Wegener's granulomatosis successfully treated with high dose immunosuppression and autologous stem cell support. Five cases (including this one) are registered in the European Group for Blood and Bone Marrow Transplantation database. Intensive T cell depletion bears an increased risk of opportunistic infections as seen in our patient with an unusual course of an EBV infection. The increase of the PR3-ANCA titre during EBV infection fits the hypothesis that Wegener's granulomatosis may be triggered by infectious agents[4] and is supported by the findings of Mayet *et al*,[5] who found cANCA production after transforming B cells in vitro with EBV.

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Refractory adult onset Still's disease successfully treated with anakinra

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Proinflammatory cytokines like tumour necrosis factor α (TNFα), interleukin (IL) 6, IL18, and IL1 have been implicated in the pathogenesis of several chronic rheumatic inflammatory diseases, including juvenile idiopathic arthritis and adult onset Still's disease (AOSD).[1–5] The treatment of these diseases includes non-steroidal anti-inflammatory drugs (NSAIDs), systemic corticosteroids and, in resistant cases, methotrexate (MTX), cyclophosphamide, sulfasalazine, and ciclosporin A[6–8] have been used. Over the past years, several cases of successful treatment with infliximab and etanercept in AOSD, refractory to conventional drugs, have been published.[8 9]

CASE REPORT

We report a favourable response to anakinra in a patient unresponsive to several disease modifying antirheumatic drugs (DMARDs) and TNFα blockers, requiring chronic high doses of steroids. The patient is a 32 year old woman diagnosed at the age 18 with AOSD, defined by the criteria of Yamaguchi *et al*.[10] She was treated with NSAIDs, systemic