LETTERS

Successful treatment of severe rheumatoid vasculitis by infliximab

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Rheumatoid vasculitis (RV) is a severe complication of rheumatoid arthritis (RA), which like a primary necrotising vasculitis can affect any organ but characteristically presents with painful cutaneous ulcers and systemic inflammation.[1 2] Usually patients with refractory RA are affected who, therefore, had already undergone extensive immunosuppressive treatment. The prognosis is poor and most patients die from infectious complications, cardiac failure, or cerebral insult.[3–6] Cyclophosphamide (CYC) is the preferred treatment but is often not well tolerated and does not contain the synovitis.[3] We report the cases of three patients with RV who could not sufficiently be treated by CYC and steroids but responded very well to infliximab infusion therapy.

CASE REPORTS

Case 1

A 48 year old male patient with longlasting RA was admitted because of general malaise, dyspnoea, oedema, pleural and pericardial effusions, increased creatinine and liver enzymes, leucocytopenia, thrombocytopenia, decreased C4 and CH_{50}, and increased levels of circulating immune complexes. The diagnosis of RV was established. The patient's condition did not sufficiently improve after treatment with steroid pulses, high dose CYC, or even plasmapheresis. He developed a life threatening heart failure caused by a "swinging heart" due to the pericardial effusion, which required immediate and repeated drainage (fig 1). As a last resort we decided to start infliximab treatment at 3 mg/kg. After the first infusion his condition improved rapidly and the pericardial effusion, in particular, disappeared within two weeks. All laboratory findings returned to normal. He continues to receive infliximab every eight weeks and is in good clinical condition. Even the activity of his RA, previously not sufficiently controlled by methotrexate alone, has decreased significantly.

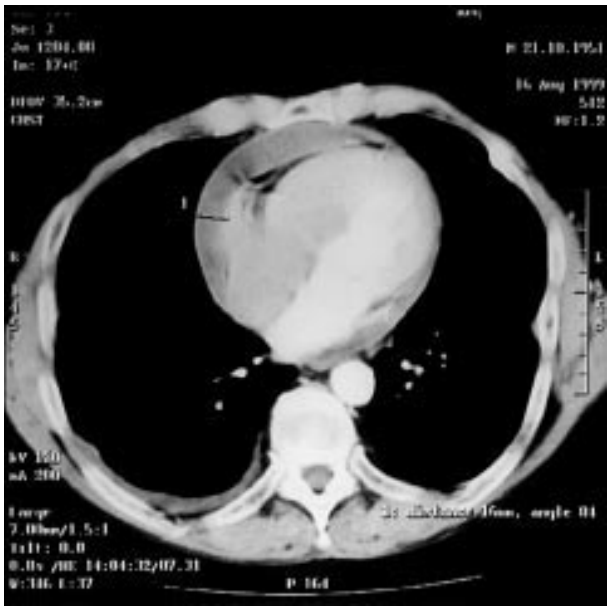

Figure 1 Case 1: chest computed tomographic scan showing the pericardial effusion due to RV.

Case 2

A 60 year old woman with a history of aggressive seropositive RA for 36 years suddenly developed painful ulcers on her left leg. The diagnosis of RV was established by biopsy from the ulcer rim. CYC bolus therapy was started and steroids also had to be increased. She responded partially to CYC, but the ulcers did not heal completely. Because of infections and leucopenia the dose and interval of the infusions often had to be adjusted. After 17 boli within 22 months the CYC therapy was stopped because of severe leucopenia. The lesions worsened after an ineffective trial of cyclosporin A (fig 2A). Infliximab was given at 3 mg /kg in weeks 0, 2, and 6 and thereafter every eight

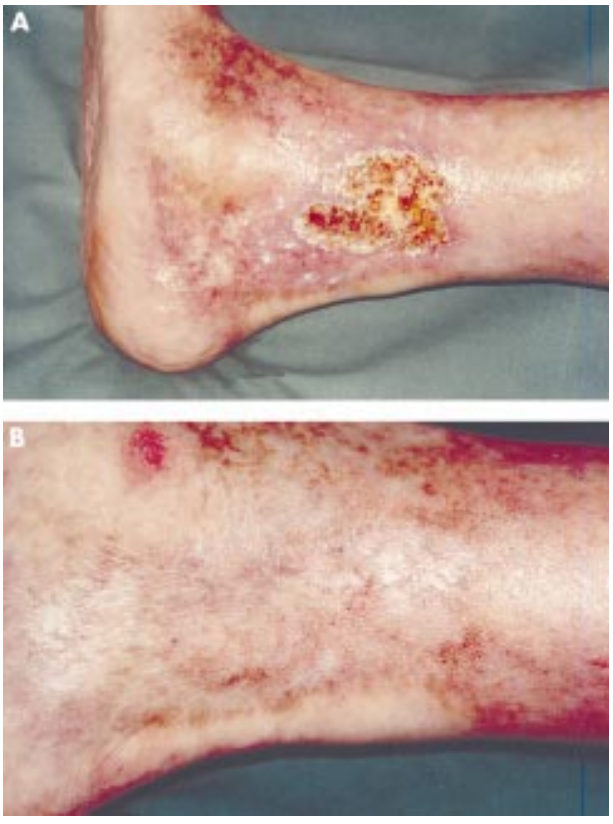

Figure 2 Case 2: leg ulcer before infliximab treatment was started (A) and the same lesion after seven infliximab infusions (B).

weeks. The ulcers improved soon after the second infusion and were completely healed after nine months (fig 2B). Her RA activity also improved greatly.

Case 3

A 64 year old male patient with RA was admitted to our hospital with a fistula between the colon and the urine bladder, which required immediate surgery because of imminent perforation. After surgery the wound did not heal. In addition, painful ulcers appeared on both legs, the scrotum, and other skin areas. All biopsies including that from the fistula, revealed necrotising vasculitis. CYC bolus therapy was started. The scrotal ulcer healed and the belly wound gradually improved, but the leg ulcers remained unchanged and his RA activity increased sharply. CYC had to be stopped because of leucopenia. Infliximab was started at 3 mg/kg at weeks 0, 2, and 6, and thereafter every eight weeks. The treatment was immediately effective for his synovitis and after a while the belly wound and the leg ulcers healed also.

CONCLUSION

These cases demonstrate a very rapid and sustained improvement not only of the vasculitic symptoms but also of the inflammatory joint activity, suggesting that infliximab may be a valuable alternative to standard CYC/steroid therapy for severe RV.

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Low dose methotrexate osteopathy in a patient with polyarticular juvenile idiopathic arthritis

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Low dose methotrexate (MTX) is widely used in the treatment of rheumatoid arthritis (RA) and various rheumatic disorders, including juvenile idiopathic arthritis (JIA). MTX is a folate antagonist, and its main adverse effects, which include haematological and hepatic toxicities, are well known. Used in high dosages in paediatric oncology, MTX has been associated with an osteopathy which is characterised by bone pain, osteoporosis, and insufficiency fractures of the legs.[1] The occurrence of MTX osteopathy in patients treated with low dose MTX has been reported but is still debated.[2–4]

CASE REPORT

A 36 year old woman presented with severe polyarthralgias lasting for the past two months. She had a 27 year history of polyarticular type JIA, and had received prednisone up to 10 mg/day for the past 25 years. She had no history of osteoporotic or insufficiency fractures. Physical examination showed multiple synovitis of hands, wrists, knees, and ankles. Laboratory investigations showed a slight increase of C reactive protein of 20 mg/l, and a strongly positive rheumatoid factor. Low dose oral MTX was started at an initial weekly dose of 7.5 mg (weight 56 kg, height 156 cm, albumin 42 g/l, serum creatinine 60 μmol/l).

In the absence of significant improvement, two months later, the weekly dose of MTX was increased to 10 mg. One month later, while she had a persistent active polyarthritis, and after having received a cumulative dose of 97.5 mg of MTX, she complained of sudden and spontaneous onset of right groin pain that was relieved by rest. Standard radiographs showed a fracture of both inferior and superior right pubic ramus. Serum calcium and 25-hydroxycholecalciferol levels were normal. Pain resolved with rest in a few weeks. Treatment with MTX was maintained.

Two months later, the patient presented with bilateral leg pain increased by weight bearing and relieved by rest. At that time, the received cumulative dose of MTX was 137.5 mg. Standard radiographs were normal but bone scanning with technetium-99m disclosed multiple areas of increased uptake (superior and inferior right pubic ramus, pubic symphysis, left hip, bilateral femoral condyles, right calcaneum) characteristic of multiple new insufficiency fractures (fig 1). MTX osteopathy was suspected and the treatment was discontinued.

DISCUSSION

MTX osteopathy was initially reported in children with acute leukaemia treated with a high dose of MTX.[1] Patients present with severe leg pain, osteopenia, and insufficiency fractures. Several reports have also suggested that the occurrence of spontaneous insufficiency fractures is more common than expected in patients with inflammatory rheumatism treated with low dose MTX.[3–6] The effect of MTX on bone mineral density has been rarely studied. In patients with RA, low dose MTX treatment was not associated with increased bone loss in the lumbar spine or the femoral neck at three years.[7] However, among the patients who were also receiving prednisone (⩾5 mg/day), MTX use was associated with greater bone loss