LETTERS

Peptostreptococcal pericarditis complicating anti-tumour necrosis factor α treatment in rheumatoid arthritis

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Ann Rheum Dis 2002;**61**:653–654

Rheumatoid arthritis (RA) is a common cause of disability and deformity for which treatment is often of limited value in controlling the disease process and outcome.[1]

Infliximab (chimeric antibody to tumour necrosis factor α (TNFα)) is clearly efficacious in up to 70% of patients, but treatment may be complicated by the development of infections that are occasionally serious and life threatening. Pooled analysis reported a 21% incidence of infection among 453 patients treated with infliximab compared with an 11% incidence in 109 placebo recipients.[2] Infections considered serious occurred in 3.4% and 1.8% of patients, respectively. As of August 2001, 84 of 170 000 patients treated with infliximab world wide had developed active tuberculosis, including 14 deaths.

CASE REPORT

Here we present the case of a 57 year old man with a five year history of RA who was admitted with a two week history of anorexia and nausea accompanied by pale stools and dark urine. Previous treatment for RA had included Salazopyrin (3 g/day), methotrexate (20 mg/week), cyclosporin (5 mg/kg), and a matrix metalloproteinase inhibitor (Trocade), with inadequate response to each of these agents..

Treatment with infliximab at a dose of 3 mg/kg was started in combination with methotrexate 7.5 mg/week and Deltacortril 5 mg/day. He responded well to this treatment regimen. Three weeks before his admission, he reported feeling very well. He had low grade synovitis in his metacarpophalangeal joints only, both erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) were normal, as were full blood count and liver function studies. The patient's occupation was that of a distributor of farm equipment.

On admission, he was apyrexial, tachycardiac, and normotensive. He was icteric with a 5 cm hepatomegaly. Clinical examination, including cardiovascular and respiratory systems, was normal. Poor oral hygiene was noted. Initial investigations showed a raised white cell count of 13.5×10^9/l with a neutrophilia; ESR 78 mm/1st h, CRP 159 mg/l, and transaminases were grossly abnormal with an aspartate aminotransferase of 1558 U/l and an alanine aminotransferase of 1525 U/l. An electrocardiogram was normal and a chest radiograph was also normal apart from showing cardiomegaly. Abdominal ultrasound showed hepatomegaly with minimal ascites. The initial diagnosis was drug induced hepatitis. He admitted to consumption of 20–25 units of alcohol weekly.

The day after admission, the patient collapsed and became hypotensive. An echocardiogram showed a large pericardial effusion. A computed tomographic (CT) scan of the thorax (fig 1) confirmed the effusion and also showed bilateral pleural effusions. He proceeded to pericardiocentesis and one litre of purulent fluid was drained. Treatment was started empirically with teicoplanin and gentamicin. Pericardial fluid subsequently grew peptostreptococci, and the antibiotics were changed to amoxycillin 2 g four times a day based on sensitivities. A repeat echocardiogram and CT scan at two weeks showed a residual pericardial effusion, and a fenestration procedure was carried out before the patient's discharge. Three months after discharge a further echocardiogram showed pericardial thickening, but no effusion was present.

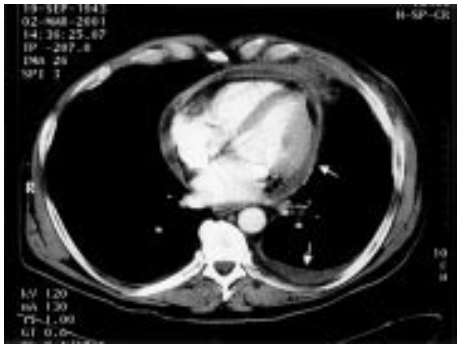

Figure 1 CT scan of the thorax showing marked pericardial effusion (arrow) and bilateral pleural effusions (left greater than right) (arrow): mediastinal windows.

Treatment with infliximab and methotrexate was withheld at the time of the patients' presentation with purulent pericarditis, but within two months his arthritis flared, necessitating an increase in steroids and the introduction of leflunomide.

His presentation initially suggested a drug-induced hepatitis. The subsequent development of pericardial tamponade was fortunately promptly recognised and treated, leading to a satisfactory outcome in this patient.

DISCUSSION

Peptostreptococcus is a rare anaerobe most commonly isolated from peritoneal fluid, followed by joint fluid, abscess and endometrial materials, soft tissue biopsy, and draining material.[3] To date, no cases of pericarditis caused by this organism have been reported. Although poor oral hygiene was evident, it is possible that this patient's occupation exposed him to the organism.

With increased use of anti-TNFα treatment, serious infections have been increasingly recorded. Although treatment successfully controlled the infection, this serious adverse event further highlights concerns about anti-TNFα treatment and emphasises the need for vigilance and prompt treatment.

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Accepted 18 December 2001

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Alopecia in Wegener's granulomatosis

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Ann Rheum Dis 2002;**61**:654–655

Alopecia is not a distinctive clinical sign in Wegener's granulomatosis and, as far as we know, to date no cases have been published describing this phenomenon.

CASE REPORT

We present the case of a 54 year old woman diagnosed with Wegener's granulomatosis, who in the first stage of her disease had alopecia and improved after treatment with cyclophosphamide and prednisone.

Nine months before her admission to our service, she had had paraesthesias, and leg pain and dysfunction. Electromyography showed some signs of sensorimotor polyneuropathy. She was given prednisone for 10 days (90 mg/day) and improved partially. Five months later, she started coughing up haemoptysic sputum, and had arthralgias in both hands, constitutional symptoms, and intense and diffuse hair loss (traction positive). Her temperature was 36.5ºC, blood pressure 130/60 mm Hg, respirations 16, pulse 80 beats/min, and her weight was 44 kg.

Physical examination showed 2 cm abdomen hepatomegaly and leg distal muscular atrophy. 4/5 upper limb distal weakness, normal positional and vibratory sensitivity, paretic-spastic walk, and deep tendon reflexes increased diffusely with clonic reply. The erythrocyte sedimentation rate was 91 mm/1st h, platelets 678×10^9/l, C reactive protein 229 mg/l, rheumatoid factor 1 U/ml. A chest *x* ray examination showed a bilateral interstitial pattern with multiple fibre tracts of hilar origin and ulterior segment atelectasis. Chest computed tomography showed three small nodules located in the front segment of the right upper lobe and right middle lobe—one was 5 cm and the other two were 1 cm. We also noted scarring fibre tracts in the left upper lobe and lower lobe back basal regions. The antineutrophil cytoplasmic antibody cANCA titre was 1/160 U/ml (normal range 0–20), proteinase 3 was 133 U/l, and myeloperoxidase, antinuclear antibodies, SSA/Ro, SSB/La, RNP, and Scl-70 were negative. ECA was 23 U/l (normal range 8–55).

A diagnosis of Wegener's granulomatosis was made. The patient was treated with prednisone (60 mg/day) with normal tapering and 10 monthly cyclophosphamide pulses (each 500 mg/m^2 each). The patient's symptoms, including respiratory, neurological involvement, and alopecia, improved. As Langford *et al* have described,[1] after the last pulse of cyclophosphamide we added methotrexate (10 mg/week); the patient's condition deteriorated and she had mild atrophy on her right leg lateral side and slight alopecia, and the proteinase 3 level reached 100 U/l. We stopped methotrexate and gave oral cyclophosphamide (2 mg/kg/day); the neurological symptoms and alopecia then improved (traction negative) and proteinase 3 became normal.

DISCUSSION

Wegener's granulomatosis is one type of vasculitis whose mortality rate, if not treated, can be high (82%) with a survival rate of 5–12 months.[2] Treatment of this disease with cyclophosphamide has increased the survival rate of patients,[3] and the daily combination of high doses of prednisone and oral cyclophosphamide has proved to be very effective in more than 90% of cases, especially when used from its initial stage to its remission,.[1] Because this combination has many side effects (in 42% of cases), other alternatives may need to be used, such as high doses of daily prednisone and monthly cyclophosphamide pulses, which have a higher degree of remission with fewer side effects, but also more relapses.[4] The use of methotrexate for maintenance of remission is a successful alternative to oral cyclophosphamide with a lower percentage of relapses (16%),[1] but in our patient that regimen was ineffective. Cyclophosphamide is an alkylating agent with cytotoxicity and immunosuppressive activity. Its main side effects are leucopenia, infections, vomiting[5] and haemorrhagic cystitis.[6] Alopecia is deemed to be one of the most common side effects of cyclophosphamide.[5] The side effects are directly related to the doses given, so that these can be reduced with a weekly dose of a 500 mg pulse given for three months[2]; the length of exposure to the drug may be another factor to take into account.[1] In our patient, alopecia appeared during the active stage of the disease. Once corticosteroids and cyclophosphamide were given, we were able to control the disease activity and cranial hair loss. We believe that the pilose follicle is another organ which nay be affected in Wegener's granulomatosis by a vasculitis of the scalp vessels; and although we did not perform a scalp biopsy, it seems likely that this disease might have caused the patient's hair loss.

The interesting aspect of this case is that the patient had Wegener's granulomatosis and alopecia and she improved with a treatment which included prednisone and cyclophosphamide.

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Accepted 18 December 2001

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