Letters to the Editor

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Early diagnosis of pyomyositis using clinic-based ultrasonography in a patient receiving infliximab therapy for Behçet’s disease

Sir, Behçet’s disease is a chronic, relapsing inflammatory disorder that causes ocular inflammation in up to 70% of patients [1, 2]. Despite intensive immunosuppressive therapy, relapsing ocular inflammation can lead to permanent loss of vision [2]. Infliximab, a monoclonal chimeric antibody to tumour necrosis factor (TNF), is a novel therapy used in the management of Behçet’s panuveitis that is unresponsive to established immunosuppressive treatment. Initial short-term experience in six patients with Behçet’s panuveitis has resulted in a rapid and effective resolution of ocular inflammation with no side-effects [3, 4]. Long-term safety data obtained in patients taking infliximab for rheumatoid arthritis (RA) and Crohn’s disease report an increase in the incidence of tuberculosis [5] and physicians should be vigilant in diagnosing infection in patients receiving infliximab [6]. Current practice guidelines recommend the discontinuation of infliximab during acute bacterial infections, but there is a paucity of data as to the safety and timing of recommencing infliximab on resolution of infection.

We report the case of an 18-yr-old man with Behçet’s panuveitis, choroiditis and retinal vasculitis which was inadequately controlled with conventional immunosuppression with mycophenolate, azathioprine and prednisolone. He had presented at age 14 with orogenital ulceration and retinal vasculitis and had previously been treated with methotrexate, cyclosporin, cyclophosphamide, α-interferon, thalidomide, tacrolimus and high-dose steroids in various combinations. Mycophenolate was continued and he commenced infliximab at a dose of 3 mg/kg on a 0, 2 and 6 weeks schedule. After the second dose a marked regression in the degree of retinal vasculitis was observed. Following the third dose of infliximab he reported atraumatic pain and swelling in his right upper arm, present for 3 days. On examination he was apyrexial but was noted to have tenderness over the middle third of the right biceps muscle with limitation of elbow extension. Musculoskeletal ultrasound was performed immediately in our rheumatology out-patient clinic using an ATL HDI 3000 machine with L 7–4 MHz probe. This demonstrated an anechoic collection lying posterior to the middle portion of the biceps muscle with hypoechoic changes within the adjacent biceps muscle (Fig. 1A) and increased power Doppler signal in the surrounding soft tissues (Fig. 1B). Under ultrasound guidance, 2 ml of pus was aspirated and Staphylococcus aureus was isolated on culture. Ziehl–Neelsen stain and tuberculosis culture of the aspirate was negative. Investigations subsequently demonstrated a white blood cell count (WCC) of 7.9 × 10^9/l and C-reactive protein (CRP) of 117 mg/l. Bone scintigraphy did not demonstrate increased uptake in the humerus and a diagnosis of pyomyositis was made. Infliximab was discontinued and treatment with fluoroaxilin and gentamicin for 12 days resulted in complete resolution of clinical and ultrasound signs (Fig. 1C) with normalization of the CRP. Fluoroaxilin and fusidic acid were continued for a further 4 weeks.

Three weeks after completing the course of antibiotics there was no evidence of recurrence of infection. The patient now complained of further deterioration in visual acuity and ophthalmological examination confirmed a recurrence of retinal vasculitis. Treatment with infliximab was recommened at 3 mg/kg on a 0, 2, 6, 12 and 20 weeks schedule with prompt resolution of ocular inflammation after the first infusion. At 22 weeks of follow-up, clinical and ultrasound examination of the right upper arm did not demonstrate evidence of recurrence of pyomyositis.

This case highlights the effectiveness of anti-TNF therapy in patients with Behçet’s panuveitis who have not adequately responded to conventional treatment with corticosteroids and multiple immunosuppressive agents. There are reasonable concerns regarding the long-term safety of anti-TNF therapy when given to a young man, but it is important to note that this patient had already developed severe iatrogenic complications from other therapies by the age of 18. These included avascular necrosis of both femoral heads and both knee joints and hypertension and diabetes mellitus secondary to high doses of steroids required to control ocular inflammation. In patients requiring high-dose cortico-steroid and immunosuppressive therapy, administration of infliximab at an earlier stage of disease may have less long-term toxicity owing to steroid-sparing effects.

Musculoskeletal bacterial infection has been reported in patients with RA and Crohn’s disease receiving infliximab, though pre- and post-licensing data suggest that this is not increased [7]. To date, seven cases of myositis in patients receiving infliximab have been reported to the UK distributor [Personal communication from Schering-Plough Ltd]. Three cases were confirmed to be infective with one case of tuberculous pyomyositis of the thoracolumbar paravertebral musculature, one case of psoas abscess and one case of Streptococcus pyogenes myositis of the cervical spine musculature. All patients were treated with appropriate antibiotics and no mortality was reported. Given the frequency of musculoskeletal pain in the patient population receiving
infliximab, a high index of suspicion is required when assessing new or worsening musculoskeletal pain in order to make a diagnosis of infective myositis. The rapid diagnosis of pyomyositis was facilitated by the availability of musculoskeletal ultrasound in our rheumatology department and highlights the usefulness of ultrasound in detecting soft tissue fluid collections and in guiding aspiration [8, 9]. The ultrasound features of pyomyositis vary from focal areas of muscle oedema and disruption in the early stages of disease to larger, organized fluid collections when established. Ultrasound detection of the anechoic collection—performed in 5 min and giving a diagnosis prior to the availability of WCC or CRP results—allowed the operator to locate the fluid and to select a needle of sufficient diameter and length for aspiration. Ultrasound is more sensitive than clinical examination in the detection of fluid collections or effusions in a number of clinical settings, particularly in the diagnosis of musculoskeletal infection [10]. It can be rapidly performed by an experienced operator and is safe (uses no ionizing radiation), inexpensive and should be the initial investigation performed in the diagnosis of pyomyositis. Repeat ultrasound examination allowed for non-invasive monitoring of the musculature during antibiotic treatment and once infliximab was recommenced. Ultrasoundography of the spine and paravertebral musculature is limited to superficial soft tissues and magnetic resonance imaging (MRI) is preferred in this situation.

No recommendations exist on the issue of reintroducing infliximab after musculoskeletal or other bacterial infection. Infliximab was only definitely continued in one previously reported case of non-infective muscle cramps that resolved within 24 h. In our case we reintroduced infliximab on recurrence of severe panuveitis because other therapies had already proved ineffective. The absence of osteomyelitis on bone scintigraphy and the complete resolution of clinical and ultrasound findings supported this course of action and to date there is no clinical, laboratory or ultrasound evidence of recurrence at 22 weeks of follow-up. We propose that resolved musculoskeletal or other bacterial infection is not a contraindication to the readministration of infliximab, but individual cases must be considered carefully according to the balance of risks and benefits.

The patient detailed in this letter gave informed consent for the reproduction of case details and ultrasound imaging.

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