Case Report

Olecranon bursitis secondary to *Mycobacterium kansasii* infection in a patient receiving infliximab for Behçet's disease

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We present a case of *Mycobacterium kansasii* olecranon bursitis in a woman with known immunosuppression secondary to the treatment received for her Behçet's disease. We found only one other case report of olecranon bursitis caused by *M. kansasii* in the literature, which, unlike our case, presented in an immunocompetent adult following trauma. This case extends the range of opportunistic mycobacterial infections that are associated with anti-tumour necrosis factor therapy.

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Case report

A 53-year-old female with Behçet's disease complained of a 2 month history of swelling and discomfort over the back of her right elbow in November 2005 during a routine follow-up by the Department of Immunology, Leicester Royal Infirmary. Initial symptoms included a discharging pustule with mild pain, which gradually progressed to a red, tender, fluctuant soft tissue swelling involving the back of the right elbow. There was no enlargement of the draining lymph nodes and the left elbow looked clinically normal. There was neither fever, a raised white cell count nor a raised C-reactive protein level. Examination of her organ systems did not reveal any significant abnormalities.

She had been under the care of the Department of Immunology, Leicester Royal Infirmary, since being diagnosed with Behçet's disease in the 1980s. Her Behçet's disease was well controlled with infliximab infusions (5 mg kg⁻¹) every 8 weeks, 15 mg methotrexate weekly and variable doses of deflazacort (6–18 mg once a day – equivalent to 5–15 mg prednisolone once a day).

A clinical diagnosis of right olecranon bursitis was made and treatment with 500 mg oral flucloxacillin four times a day for 6 weeks was commenced. The pain and discomfort improved with the treatment but some residual soft tissue

swelling persisted. In July 2006 she presented again with increasing swelling and discomfort of the right elbow, together with swelling of the left elbow. Examination of the elbows confirmed bilateral olecranon bursitis.

Fluid from the bursae was aspirated and sent to the microbiology laboratory (Clinical Microbiology, Leicester Royal Infirmary). Direct microscopy revealed a white cell count $<100 \times 10^6$ cells l⁻¹. Gram staining of the fluid showed no organisms and Ziehl–Neelsen staining was negative for acid-fast bacilli. Fluid from the right and left bursae was cultured separately for bacterial, fungal and mycobacterial pathogens. There was no bacterial or fungal growth on primary culture and subculture. Growth was detected in the mycobacterial growth indicator tube, and on the glycerol Löwenstein–Jensen slope on day 12 and day 42, respectively, from the right bursa fluid. Both isolates were sent to the Regional Centre for Mycobacteriology, Health Protection Agency, Birmingham, UK, for identification and sensitivity testing. The mycobacterium was identified as *Mycobacterium kansasii* by GenoType Mycobacterium DNA strip (Hain Lifescience) and was demonstrated to be sensitive to ciprofloxacin, clarithromycin, ethambutol and rifampicin. A repeat aspiration of both bursae was performed a month later, on receipt of the above result, and confirmed *M. kansasii* infection in the right bursa.

Treatment with clarithromycin, ethambutol and rifampicin commenced in October 2006 on receipt of the second

Abbreviations: anti-TNF, anti-tumour necrosis factor; ATS, American Thoracic Society; BTS, British Thoracic Society; NTM, non-tuberculous mycobacteria.

positive culture result. Clarithromycin was changed to ciprofloxacin after 2 weeks due to nausea that persisted despite anti-emetics. Ciprofloxacin was stopped after 2 months of treatment (as a consequence of Achilles tendinitis), and ethambutol and rifampicin were continued. Redness and pain improved completely but she continued to have problems with swelling of both elbows. The offending bursae were therefore excised in January 2007. Histological examination of the excised tissue confirmed bilateral olecranon bursitis but no granulomata or acid-fast bacilli were seen. She was reviewed in the Orthopaedic Outpatients Department, Leicester Royal Infirmary, 2 weeks post-surgery. Both wounds had healed well but seromas had formed over both elbows. On aspiration, 30 ml bloodstained fluid was obtained from the left elbow and 5 ml of similar fluid from the right elbow. This fluid was not sent to the microbiology laboratory (Clinical Microbiology, Leicester Royal Infirmary) for culture as the seromas were considered to be a consequence of the surgery and not infection related. There were no further problems with seroma formation. She has now successfully finished a 19 month course of antituberculous medication with ethambutol and rifampicin.

Discussion

Bacteria are the most common cause of infective olecranon bursitis (*Staphylococcus aureus* and *Streptococcus* spp. accounting for the majority of cases), and this wristitis usually follows direct inoculation of organisms (Weinstein *et al.*, 1984). Non-tuberculous mycobacteria (NTM) rarely cause olecranon bursitis. The limited number of case reports in the literature include reports of infections by *Mycobacterium xenopi* (Rutten *et al.*, 1998), *Mycobacterium asiaticum* (Dawson *et al.*, 1995), *Mycobacterium szulgai* (Maloney *et al.*, 1987) and *Mycobacterium goodii* (Friedman & Sexton, 2001). *M. kansasii* is an NTM that commonly causes pulmonary infections in both immunocompetent and immunosuppressed hosts following inhalation of infected droplets into the lungs, and is clinically indistinguishable from tuberculosis. Disseminated infection to the lungs, reticuloendothelial system, bone, joints and skin has been reported in immunosuppressed hosts.

We found only one case report of *M. kansasii* olecranon bursitis in the literature (Barham & Hargreaves, 2006); this case followed a laceration acquired in a swimming pool. In our patient there was no history suggestive of direct inoculation of the organism into the bursa; however, she did have immunosuppression due to therapy for Behçet's disease. Clinically, both bursae were inflamed, although microbiological confirmation was made only for the right side. The possibility of disseminated infection could not be ruled out, and the primary focus of infection could not be established. Unfortunately, no extra clinical material was available from the left bursa to perform molecular analysis such as 16S rDNA PCR.

Due to the rarity of these infections, there have been no randomized controlled trials comparing different treatment regimens or treatment versus no treatment for *M. kansasii* non-pulmonary infections. The recommendations of both the British Thoracic Society (BTS) and American Thoracic Society (ATS) are therefore based on several retrospective and prospective studies of various treatment regimens. The ATS recommends 18 months of isoniazid, ethambutol and rifampicin treatment (ATS, 1997), whereas the BTS recommends 9 months of ethambutol and rifampicin treatment for immunocompetent patients, but a longer treatment time of 15–24 months for immunosuppressed patients (BTS, 2000).

Excision is recommended by both societies as the treatment of choice for infected lymph nodes. Our patient was treated in accordance with the BTS guidelines (BTS, 2000).

Patients undergoing treatment with anti-tumour necrosis factor (anti-TNF) therapy are known to be at risk of severe bacterial infections, as well as opportunistic infections; these include patients with documented cases of *Pneumocystis jirovecii* pneumonia, histoplasmosis, listeriosis and systemic candidiasis (Slifman *et al.*, 2003). Screening and, if appropriate, treatment for latent tuberculosis infection is recommended prior to commencement of anti-TNF therapy (Chang & Girgis, 2007).

There have been several reports of NTM infections associated with infliximab therapy over the last 3 years. A recent review (Salvana *et al.*, 2007) noted four NTM infections caused by *Mycobacterium peregrinum* in patients receiving infliximab therapy (Marie *et al.*, 2005), *Mycobacterium avium* (Okubo *et al.*, 2005), *Mycobacterium abscessus* (Mufti *et al.*, 2005) and *Mycobacterium fortuitum* (Boulman *et al.*, 2006). Since this review there have been three further case reports of NTM infections in patients receiving infliximab, two involving *Mycobacterium marinum* (Rallis *et al.*, 2007; Fallon *et al.*, 2008) and a further case in which *Mycobacterium aurum* was confirmed as the aetiological agent (Martín-Aspas *et al.*, 2008).

Conclusion

This case highlights a rare manifestation of an opportunistic infection in a patient receiving treatment with infliximab. It is unusual because of the bilateral involvement of the olecranon bursae, which raises concerns of dissemination amongst patients with immunosuppression, although, in this case, a definite association could not be established. The need for early aspiration and appropriate microbiological investigations, including the use of molecular methods where necessary, cannot be over-emphasized. Patients should be treated for at least 9 months with a minimum of rifampicin and ethambutol with or without surgery. This case increases the reported number of opportunistic mycobacterial infections associated with anti-TNF therapy.

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