Teaching Point
(Section Editor: A Meyrier)

An immunocompromised dialysis patient with skin and bone lesions

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Keywords: atypical mycobacterial disease; immunosuppression; Mycobacterium chelonae; renal transplant

Introduction

Patients with chronic kidney failure have disturbances of immune function involving both innate and adaptive systems. These result in both immunodepression which increases susceptibility to infection and immunooactivation leading to a chronic inflammatory state [1]. Dialysis treatment may further aggravate aspects of this, especially the induction of inflammation. In addition, there is a growing number of patients who have returned to dialysis programmes following transplant failure. Many of these will have been intensively immunosuppressed, often over years or decades. These patients are at particular risk.

Case report

A 60-year-old haemodialysis (HD) patient was admitted for investigation of a papulo-nodular rash predominantly affecting the extensor aspects of both arms (Figure 1). He had adult polycystic kidney disease and had developed end-stage renal failure 15 years previously, at which point he had commenced on HD. He had received a cadaveric renal transplant 12 years ago which had functioned for 10 years. For the past 2 years, he had been back on HD. Other past medical history included ischaemic heart disease, post-transplant diabetes mellitus and hypoadrenalism secondary to long-term steroid treatment. He had undergone splenectomy following abdominal trauma in the past. Two months prior to this admission, he had been hospitalized with abdominal pain and found to have a right paracolic abscess. This had been treated with drainage and antibiotics. At the time of this admission, he was receiving replacement doses of hydrocortisone, tacrolimus having been discontinued 18 months previously.

Shortly after admission, he sustained a fall. Subsequent radiographs showed pathological fractures of the right ankle and of the middle phalanx of the left fifth finger (Figure 2). A little later, he developed severe rectal bleeding which failed to respond to medical management. Oesophagastroduodenoscopy was unremarkable, but flexible sigmoidoscopy revealed fresh blood extending to the splenic flexure, suggesting a colonic cause. A mesenteric angiogram did not demonstrate active bleeding. He subsequently underwent subtotal colectomy with resolution of the bleeding.

Biopsies of the skin lesions showed non-caseating granulomata with central microabscesses and rod-like bacteria which were positive for Ziehl–Neelsen staining. A mycobacterial species was isolated after 5 days from a skin biopsy, suggestive of a rapidly growing atypical mycobacterium. The mycobacterium was subsequently identified as Mycobacterium chelonae. Histology of the appendix also demonstrated granulomatous inflammation, but staining for mycobacteria was negative. The radiographs of the right ankle and left hand were interpreted as compatible with mycobacterial infection of the bone causing pathological fracture of the ankle and dactylitis of the fifth middle finger. A diagnosis of disseminated atypical mycobacterial disease was made based on proven

Fig. 1. Skin involvement of disseminated disease with M.chelonae manifesting in papulo-nodular lesions on the forearm.
clearly demonstrated granuloma with Ziehl
Neelsen positive rods, and M. chelonae was isolated from two speci-
mens. However, the appendiceal biopsies only showed granuloma, with the stains being negative for acid-fast bacilli. This may be explained by the prior exposure of the tissue to formalin. Indeed, atypical mycobacteria appear to be more sensitive to decontaminating agents than tuberculous mycobacteria [5]. Although microbiological or histological evidence for bone involvement cannot be provided, there is radiological evidence supporting this hypothesis. The lucencies in the right ankle and left little finger were described as atypical of brown tumours and in keeping with mycobacterial osteomyelitis. Despite the limited microbiological evidence for gut and bone involvement, we still feel this is a distinct possibility, though we think that the severe haemorrhagic colitis in this patient was probably related to co-existent CMV infection. To our knowledge, this would be the first re-
port of infection with M. chelonae affecting these three organ systems concomitantly.

The risk factors for disseminated infection with atypical mycobacteria are treatment with immunosuppressant medica-
tion, steroid use and organ transplantation [4], all of which were present in the patient presented. Further contributing factors included post-transplant diabetes and previous splenectomy. The concurrent infection with CMV further reflects the immunocompromised state of our patient.

The mode of infection can only be speculated upon. There are several reports of infections with atypical mycobacteria occurring as a consequence of surgical and non-
surgical procedures [6]. In immunocompetent individuals, infection may occur at the site of trauma or surgery, suggesting reduced local immunity. In our patient, the involve-
ment of the appendix several weeks after radiologically guided drainage of a paracolic abscess may be attributable to inoculation with this ubiquitous pathogen which may then have spread from there.

Antimicrobial treatment of atypical mycobacterial dis-
eease is difficult, particularly in an HD patient. Clarithro-
mycin is the only antibiotic which has been tested in a clinical trial and shown to be effective in treating disseminated cutaneous disease, albeit with a risk of developing resistance [7]. Isolates of M. chelonae are generally reported to be highly susceptible to clarithromycin [8] and tobramycin [9] and less susceptible to imipenem and cipro-

doxacin [10]. The optimal duration of therapy for infec-
tions with atypical mycobacterial bacteria has not been established. However, the recommended minimal duration of combination antimicrobial therapy is 4 months for dissem-
nated cutaneous disease and 6 months for osteomyelitis [11]. In patients on HD, the antimicrobial treatment is further complicated by pharmacokinetic alterations which can influence the efficacy and the duration of the treatment course and necessitate close monitoring of the clinical response to ensure effective treatment and monitoring of antibiotic levels to avoid toxicity.

**Teaching points**

(1) M. chelonae is a rapidly growing mycobacterium, associated with disseminated soft tissue infections and osteomyelitis.

**Discussion**

Infections with atypical mycobacteria, also known as non-
tuberculous mycobacteria, are caused by a wide spectrum of ubiquitous acid-fast organisms, many of which have only recently been identified as pathogenic [3]. Infections with atypical mycobacteria commonly occur in the immunocom-

promised host, but can also manifest in immunocompetent individuals. The clinical picture varies depending on the species and includes soft tissue infections, chronic pulmo-

nary and osteo-articular infections as well as disseminated disease. For many species, there is limited data on which to base treatment recommendations and the role of antimicro-

bial susceptibility tests is controversial [2]. Multi-drug combinations are often recommended to avoid emergence of resistance.

**M. chelonae** has been associated with disseminated soft tissue infections, localized cellulitis, osteomyelitis and catheter infections and appears to have a proclivity for renal transplant patients [4]. Skin biopsies from our patient clearly demonstrated granuloma with Ziehl–Neelsen posi-

tive rods, and M. chelonae was isolated from two speci-
mens. However, the appendiceal biopsies only showed granuloma, with the stains being negative for acid-fast bacilli. This may be explained by the prior exposure of the tissue to formalin. Indeed, atypical mycobacteria appear to be more sensitive to decontaminating agents than tuberculous mycobacteria [5]. Although microbiological or histological evidence for bone involvement cannot be provided, there is radiological evidence supporting this hypothesis. The lucencies in the right ankle and left little finger were described as atypical of brown tumours and in keeping with mycobacterial osteomyelitis. Despite the limited microbiological evidence for gut and bone involvement, we still feel this is a distinct possibility, though we think that the severe haemorrhagic colitis in this patient was probably related to co-existent CMV infection. To our knowledge, this would be the first report of infection with M. chelonae affecting these three organ systems concomitantly.

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**Teaching points**

(1) M. chelonae is a rapidly growing mycobacterium, associated with disseminated soft tissue infections and osteomyelitis.
(2) Risk factors for disseminated infection with atypical mycobacteria include long-term steroid use and organ transplantation. In the immunocompetent host, local infection may be found following trauma or surgery.

(3) Adverse consequences of long-term immunosuppression may extend for months and even years following its cessation.

(4) Co-existent opportunistic infections are common. The finding of one such infection in a patient should alert to the potential presence of others.

Acknowledgement. I would like to thank Dr Gabriele Behrendt from the Department of Pathology at Queen Elizabeth Hospital, Welwyn Garden City, for the constructive discussion of the histopathological results.

Conflict of interest statement. None declared.

References


Received for publication: 1.11.09; Accepted in revised form: 25.1.10