



A Case of Disseminated Sepsis Caused by an Unusual Microorganism in a Patient With Diabetes

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Patients with suboptimally controlled diabetes are susceptible to a higher frequency and severity of infections from common microorganisms (1). They are also at a higher risk of acquiring sepsis at unusual sites and from uncommon microbes (2). We report a patient with a background of longstanding type 2 diabetes, multiple comorbidities, and an intra-cardiac device, who had life-threatening disseminated sepsis caused by an unusual bacterium.

Case Presentation

A 54-year-old Caucasian man with a BMI of 39.7 kg/m², height of 177 cm (69.6 inches), weight of 124.4 kg (274.2 lb) and suboptimally controlled type 2 diabetes of >10 years' duration presented with 3–4 weeks' duration of a skin rash over his trunk and upper limbs that was mildly pruritic and painful to touch. During the next 2–3 weeks, the lesions over his trunk became more extensive and spread to his lower limbs, with evolution in some areas to 2-cm violaceous, painful, tender lumps and blisters with scant discharge.

For the past 4 years, the patient had been taking insulin glargine and glulisine. A recent A1C was 9.4%, and he had diabetic retinopathy and peripheral neuropathy. His medical history included chronic atrial fibrillation, ischaemic heart disease, and severe left ventricular systolic dysfunction, which required insertion of a cardiac resynchronization therapy defibrillator 3 years ago. He also had



■ **FIGURE 1.** Nodular skin lesion on patient's right arm (humerus).



■ **FIGURE 2.** Erythematous plaques of the skin with overlying necrotic crust and superficial ulceration on patient's left shin.

stage 3 chronic kidney disease and a history of previous cerebrovascular accident with good neurological recovery.

Physical examination revealed multiple itchy and mildly warm lesions over his trunk and all four extremities. The rash was at different stages of evolution and included maculopapular, vesicular, and nodular lesions. In some areas, it was eczematous with asteototic changes, whereas in other areas he had erythematous

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TABLE 1. Patient's Laboratory Test Results at Presentation

	Patient Values	Normal Values
Urea (mmol/L)	22.8	2.5–6.7
Serum creatinine (μmol/L)	125	70–150
Na (mmol/L)	134	135–145
K (mmol/L)	4.1	3.5–5
Glomerular filtration rate (mL/min/1.73 m ²)	56	>90
A1C (% [mmol/L])	9.4 (79)	<6.5 (<48)
Hemoglobin (g/L)	141	130–180 (men)
Total white blood cell count (10 ⁹ /L)	11	4–11
C-reactive protein (mg/L)	54	<10
Bilirubin (μmol/L)	30	3–17
Alanine transferase (IU/L)	41	5–35
Alkaline phosphatase (IU/L)	91	5–35

plaques with overlying necrotic crust and superficial ulceration. There was no lymphadenopathy, ulceration, abscess formation, or caseous necrosis (Figures 1 and 2). He was afebrile with normal vital parameters but looked unwell with bilateral leg edema, increased jugular venous pressure, and crackles over his lung bases. There were no cardiac murmurs.

Laboratory results on presentation are listed in Table 1. In view of the high C-reactive protein and suspicion of infection of the intracardiac device, multiple blood samples were collected for culture. The initial aerobic blood culture set (BacT/ALERT, bioMérieux, Marcy-l'Étoile, France) was positive at day 5 of incubation, with gram-positive bacilli seen by gram staining. This was subcultured onto blood agar and, after 48 hours of incubation at 37° C, grew colonies of variable morphology that on Ziehl-Neelsen stain showed acid-fast bacilli. This was subsequently identified as *Mycobacterium chelonae*. A mycobacterial blood culture (BACTEC MYCO/F Lytic, Becton Dickinson, Franklin Lakes, N.J.) was also positive for *M. chelonae* on day 9 of incubation. After an initial negative skin lesion biopsy, a repeat biopsy 20 days later showed granulomatous inflammation. Acid-fast bacilli were seen on microscopy, and *M. che-*

lonae was cultured after 25 days of incubation.

Initial management included high-dose diuretics for decompensated heart failure and insulin dose adjustment. Once the diagnosis of systemic sepsis with *M. chelonae* was made, the patient was started on a triple-therapy regimen of tobramycin, clarithromycin, and ciprofloxacin. In vitro susceptibility testing indicated resistance to tobramycin and ciprofloxacin, and these were replaced by tigecycline while continuing clarithromycin.

Transoesophageal echocardiogram (TOE) did not confirm the diagnosis of endocarditis. However, because there was a strong possibility of the pacemaker or its leads being a harboring site for the organism, a decision was made to remove the intracardiac device. This was supported by information downloaded from the device that suggested that the defibrillator had not been required on any occasion for the past 3 years. The risk of further deterioration in cardiac function was balanced against the need to eradicate mycobacterial infection, and the device was removed 3 weeks after confirmation of the infection with a plan to replace it with a new one after the infection was eradicated. Although on removal the device appeared clinically infected,

mycobacterial culture of the specimen was negative. Despite aggressive antibiotic therapy and removal of the device, the patient deteriorated with progressive sepsis and multiorgan failure during the next 3 weeks and passed away.

Questions

1. Was there a link between immunocompetence and generalized infection?
2. What was the role of the intracardiac device in the pathogenesis of infection with *M. chelonae*?
3. What were the unusual features of this case?

Commentary

M. chelonae is a rapidly growing mycobacterium belonging to the family of nontuberculous mycobacteria. It is ubiquitous in the environment and found in soil and water (3). It grows in 3–7 days at 25–40° C, and clinical suspicion of mycobacterium infection is usually required so that the correct culture media and conditions are used. However, in our case the organism grew from routine blood cultures.

In the majority of patients, *M. chelonae* infection manifests as localized cutaneous disease, which can occur after trauma (e.g., tattooing procedures [4,5]) or in the health care setting after cardiovascular, chest, abdominal, ophthalmic, otolaryngological, and orthopedic surgery or reconstructive or cosmetic procedures (1,6). Disseminated disease usually occurs in the context of immunosuppression (e.g., in the transplant setting or associated with chemotherapy) (7). Infections involving intravenous catheters, prostheses, or implantable devices (e.g., pacemakers and prosthetic valves) have been reported (8–10).

The case presented here has several interesting aspects. Our patient had disseminated *M. chelonae* infection despite being immunocompetent. Most reports in the literature describe disseminated infection in immunocompromised patients (11,12), and those reported in immunocompetent

patients with diabetes are examples of localized infection (e.g., insulin injection or jet injector site abscesses (13,14), suppurative hidradenitis (15), and post-bite hand infection (16)). It is likely that our patient, who had longstanding and suboptimally controlled diabetes, advanced cardiac failure, and chronic kidney disease, was predisposed to dissemination of sepsis, and the probable infection of the intracardiac device was responsible for its persistence and resistance to treatment.

The initial portal of entry of our patient's infection remains unclear. Introduction of the microorganism during pacemaker insertion is a possibility. However, because *M. chelonae* is a rapidly growing, virulent bacterium, the likelihood that it remained dormant for ~3 years is low. The infection may have been transmitted through a break in the skin that went unrecognized by the patient, or it may have been introduced by insulin self-injection. The latter is supported by case reports in which *M. chelonae* abscesses formed at insulin injection sites (2).

The importance of the intracardiac device in the pathogenesis of the infection and the eventual outcome is another interesting aspect of this case. There have been two other case reports of pacemaker lead endocarditis caused by *M. chelonae* infection; in one, the patient had diabetes (9,17). An infected device is usually suspected on the basis of local signs at the device pocket site, although its diagnosis can be challenging in patients presenting with no local signs. Device removal is essential for eradication of the infection, and careful planning is needed to provide alternative cardiac management strategies during the time the patient is without the device. After removal of the device, it is also essential to manage the wound with attention to detail, while keeping future access requirements in mind. Reimplantation, if required, needs to

be deferred for several weeks to allow for eradication of the infection.

There is a lack of evidence for the treatment of *M. chelonae* infection. Successful treatment of disseminated infection in an immunosuppressed host has been described using monotherapy (18), but combination therapy, as was done in our patient, is more commonly used. Before the availability of susceptibility results, we used an empirical combination of tobramycin and ciprofloxacin in addition to clarithromycin to reduce the risk of resistance to clarithromycin, which is known to occur with monotherapy. Results of in vitro susceptibility testing indicated that the organism was resistant to both of the additional agents, which were then replaced with tigecycline.

Our patient eventually succumbed to this infection despite his immunocompetent status, the use of a combination therapy regimen, removal of the intracardiac device, and optimized medical management. Two reported deaths from *M. chelonae* sepsis have been in immunocompromised patients, and there have been no reports of mortality in an immunocompetent patient with or without diabetes (19,20). There are a few possible explanations for this adverse outcome in our patient. There was a delay between initial presentation and removal of the intra-cardiac device. This was caused by the time taken to grow the organism, the dilemma posed by the normal TOE, and the importance of cardiac support in this high-risk patient, which needed to be weighed against the possible benefit of device removal. It is also possible that in vitro resistance to two of the three agents used in the initial empirical regimen may have led to acquired resistance to the third agent, leading to failure of the modified regimen. Finally, the presence of comorbidity may have played a major role in the patient's eventual demise.

Clinical Pearls

- *M. chelonae* is an exceptional and

opportunistic human pathogen and usually presents as localized infection. However, disseminated infection can occur in immunocompromised patients and, much less commonly, in immunocompetent predisposed individuals.

- There is no standard antimicrobial therapy for nontuberculous mycobacterial infection, and the management strategy is based on the use of an antibiotic combination directed by in vitro sensitivities. Timely removal of any foreign device is imperative.
- This case emphasizes the ability of *M. chelonae* to be an invader that should not be underestimated, especially in a patient with significant comorbidity and an indwelling device.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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