Case Report

Rapidly growing mycobacteria as emerging pathogens in bloodstream and device-related infection: a case of pacemaker infection with *Mycobacterium neoaurum*

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Introduction: We present a case of pacemaker infection with a rapidly growing mycobacterium (RGM).

Case presentation: An 80-year-old woman presented with fever, weight loss and malaise for 2 months. *Mycobacterium neoaurum* was isolated from blood cultures and from cardiac pacing wires. She made an excellent recovery with combination antimicrobial therapy and removal of the device.

Conclusion: Such RGMs are encountered with increasing frequency in intravascular device-associated infections, posing challenges for both laboratory identification and clinical management.

Keywords: bloodstream infection; combination therapy, device-related infection; rapidly-growing mycobacteria.

Case report

An 80-year-old woman complained of weight loss, fatigue and night sweats for the preceding 2 months. She had a past medical history of mild asthma, managed with salbutamol inhaler only. She had a permanent pacemaker, inserted 9 years previously for complete heart block. This had been replaced 7 years later because of a pocket infection. She had received 3 weeks of treatment at that time with co-amoxiclav (culture results were not available to us), but the old wires had been left in situ.

Physical examination was normal except for a fever of 38.7 °C and a petechial rash on her shins, suggesting a vasculitic process. Blood tests, including a full blood count and serum electrophoresis, were within normal ranges other than a mild thrombocytopenia and a C-reactive protein level of 22 mg l⁻¹. There were no risk factors or clinical evidence of immunosuppression, so human immunodeficiency virus serology and other tests of immune suppression were not done.

Blood cultures taken on admission were positive after incubation for 4 days with Gram-variable bacilli in the aerobic bottle, which stained positively with a Ziehl–Neelsen stain (Fig. 1). Colonies on chocolate agar after 2 days of incubation were orange coloured (Fig. 2). An API Coryne (bioMerieux) suggested an identification of *Rhodococcus equi* (0150004, 97.7%). However, sensitivity tests were not in keeping with this identification, the organism being resistant to erythromycin and vancomycin (MIC 4 mg l⁻¹). Six sets of blood cultures taken over the following 2 weeks grew the same organism. The isolate was identified by the Public Health England Mycobacterial Reference Laboratory as *Mycobacterium neoaurum* using 16S rRNA gene sequencing. MICs (mg l⁻¹) determined by agar incorporation were as follows: daptomycin, 16; amikacin, 0.5; gentamicin, 0.5; ampicillin, 0.5; teicoplanin, 0.25; vancomycin, 2; clarithromycin, 4; clindamycin, 1; erythromycin, 16; linezolid, 0.25; ciprofloxacin, 0.016; moxifloxacin, 0.008; doxycycline, 0.064; tetracycline, 0.125; rifampicin, 1.0; meropenem, 0.25; augmentin, 0.25; and tobramycin, 0.5.

The patient continued to spike fevers and complain of night sweats but was haemodynamically stable. Transoesophageal
echocardiography revealed a mobile, globular structure, 0.8 cm in diameter, associated with one of the pacing leads in the right atrium (Fig. 3 and Supplementary video, available in the online Supplementary Material). The pacemaker system was removed, and *M. neoaurum* was also cultured from the right atrial and ventricular pacemaker tips.

The patient experienced a dramatic improvement in her symptoms after the start of antimicrobial therapy, initially with imipenem and amikacin. These were chosen pending identification of the isolate, as being active against *Mycobacterium chelonae* and *Mycobacterium abscessus* (Griffith et al., 2007), the mycobacterial species most frequently causing bloodstream infection in our practice. They were changed 23 days later, as susceptibility data became available and after pacemaker removal, to doxycycline and ciprofloxacin for 3 months together with linezolid for the first month. Blood cultures taken after extraction were negative and a new pacing system was inserted. Six months after extraction, the patient remains extremely well with negative blood cultures.

**Discussion**

*M. neoaurum*, a rapidly growing mycobacterium (RGM), was first isolated from soil and water in 1972 (Tsukamura & Mizuno, 1972). The first reported case of human disease was in 1988, a bacteraemia associated with a Hickman line in a patient with advanced ovarian cancer. There have since been a further 11 cases of line-related bacteraemia reported, all in immunosuppressed subjects but all with a favourable outcome (Brown-Elliott et al., 2010, Hawkins et al., 2008). In addition, this organism has been isolated from intravenous drug users with prosthetic valve endocarditis (van Duin et al., 2010, Kumar et al., 2014), and cultured from lung tissue in a patient with asthma and gastro-oesophageal reflux disease. (Morimoto et al., 2007). Two case reports have implicated *M. neoaurum* in skin infection, causing a skin nodule at the site of trauma in one case (Omoruyi et al., 2012) and scarring alopecia in another (Martin et al., 2007).

RGMs such as *M. neoaurum* are isolated with increasing frequency from clinical specimens (Bush et al., 2010), and are emerging as important pathogens in intravascular device-related infections, in part due to their propensity to form biofilms (El Helou et al., 2013a). *Mycobacterium mucogenicum*, *Mycobacterium fortuitum* and *M. abscessus* are the most common isolates in this setting. As the use...
of immunomodulatory agents becomes more widespread and medical prosthetics and intravascular devices more commonplace, we can expect to encounter an increasing number of these infections. We hypothesize that our patient’s pacemaker system became infected 2 years before presentation when there were signs consistent with pocket infection requiring replacement of the device. The old pacing wires were left in situ, acting as a nidus for the growth of this normally low-virulence organism.

Different species of RGM cause a diverse range of clinical syndromes. They present a challenge both to the routine laboratory and to the treating clinician. They may grow poorly on routine media and may easily be disregarded as a ‘diphtheroid’ contaminant in a blood culture. Growth only in the aerobic bottle, slow growth on solid media compared with other pathogens recovered from blood cultures and poor uptake of the Gram stain are clues that should prompt a Ziehl–Neelsen stain. Identification using phenotypic methods is slow because the organisms are unreactive. Differentiation of RGM from Nocardia and Rhodococcus equi can be difficult on routine media when cultures are young. The use of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry may be helpful, as identification of some RGM is rapid and reliable (Lotz et al., 2010). Precise identification is important, as it will assist the choice of empirical antimicrobial therapy (Brown-Elliott et al., 2012). Nevertheless, we lack good clinical outcome studies for treatment of most of these organisms. Molecular diagnostics for RGM such as M. abscessus have accelerated identification, and whole-genome sequencing may in the near future revolutionize the process, possibly incorporating markers of antimicrobial resistance and allowing epidemiological linkage studies (Bryant et al., 2013).

RGM are often resistant to multiple antimicrobials and the in vitro/in vivo correlation of susceptibilities is poorly established. Susceptibilities vary considerably among species. Several species possess an inducible macrolide resistance (erm) gene. For the unstable and/or immunocompromised patient with bacteraemia due to RGM, empirical therapy with amikacin plus a quinolone and a macrolide is suitable (El Helou et al., 2013b), until identification is available. Once the identity of the organism is known a two-drug combination is recommended (El Helou et al., 2013a). The optimum duration of therapy is undefined. Removal of the affected device is assumed to be a key, possibly essential, element of treatment (El Helou et al., 2013b).

Patients in these case series have presented with systemic symptoms, predominantly fever, and a notable absence of local signs suggestive of intravascular line infection. In this, our patient was typical. The propensity of such organisms to cause biofilm, and the increasing use of intravascular devices, means that we are likely to encounter these organisms increasingly frequently in clinical practice.

References


