Brevibacterium otitidis: an elusive cause of neurosurgical infection

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Coryneform bacteria are usually considered as non-pathogenic when isolated from clinical specimens. We present a case of Brevibacterium otitidis neurosurgical infection in an immunocompetent patient, and highlight the difficulty with identification and interpretation of antimicrobial susceptibility results for this unusual pathogen.

Introduction

Coryneform bacteria isolated from clinical specimens are frequently considered non-pathogenic or possible contaminants as they are part of the normal human skin microbiota. Brevibacterium spp. were first described in 1953 (Breed, 1953) and are non-motile, non-haemolytic, catalase-positive, Gram-positive rods that are usually identified as diphtheroids or misidentified as Corynebacterium sp. These organisms colonize human skin and are found in dairy products such as cheese. In the last decade, there have been several case reports of clinical infections caused by these organisms (Pascual et al., 1996; Wauters et al., 2000; Dass et al., 2002; Gruner et al., 1994; Brazzola et al., 2000). This is, to our knowledge, the first reported case of Brevibacterium otitidis neurosurgical site infection and highlights the difficulty with identification and interpretation of antimicrobial susceptibility results.

Case report

A 54-year-old woman, who had a L4-5 microdiscectomy 3 weeks prior to admission, was admitted with swelling and severe pain at the surgical site. The patient was otherwise well, with no significant past medical history and she was not using immunomodulatory agents such as corticosteroids. Two weeks previously, she had noted a non-tender, fluctuant swelling at the surgical site. A day prior to admission, she reported severe surgical site pain associated with rigors. Physical examination on admission was remarkable for erythema around the surgical site with a fluctuant swelling. Laboratory studies upon admission revealed an elevated peripheral white cell count of 14.07 × 10^9 cells l^{-1} (normal range 4.00–11.00 × 10^9 cells l^{-1}), a neutrophil count of 10.69 × 10^9 cells l^{-1} (normal range 2.00–7.50 × 10^9 cells l^{-1}) and a C-reactive protein level of 12 mg l^{-1} (normal range 0–10 mg l^{-1}). Renal function was within normal limits. Magnetic resonance imaging of the spine showed enhancing tissues extradurally at the level of the recent surgery, with a small area of low density that was thought to represent an epidural abscess. The patient was brought to the operating theatre for wound exploration. Intraoperatively, a subcutaneous and subfascial collection was observed where serosanguinous fluid was aspirated. The patient was empirically commenced on intravenous cefuroxime (1.5 g three times daily), flucloxacinil (1 g four times daily) and metronidazole (500 mg three times daily) to treat a presumptive epidural abscess with associated surgical site infection, with the first dose of these antibiotics given immediately prior to surgery.

Four specimens, which included fluid, tissues and a swab, were sent to the microbiology laboratory (Microbiology Laboratory, Beaumont Hospital, Dublin, Ireland). Microscopy of these specimens revealed occasional pus cells but no organisms were seen on Gram stain or auramine stain for acid-fast bacilli. Operative specimens were inoculated onto two Columbia blood agar plates (aerobic and anaerobic), MacConkey agar, chocolate agar and cooked meat broth, and cultured for mycobacteria (MGit; Becton Dickinson). After 48 h incubation, the aerobic cultures of all four specimens yielded pure growth of catalase-positive, Gram-positive rods initially identified as diphtheroids. API Coryne (bioMérieux) failed to identify the isolate using routine methods. Since there were no standardized susceptibility breakpoints for Corynebacterium spp., the isolate was standardized against known susceptibility breakpoints.
spp., susceptibilities were determined by ETest (AB Biodisk) for fastidious Gram-positive bacilli according to the manufacturer’s instructions. The MICs of the antibiotics were as follows: penicillin, 1 mg l⁻¹; vancomycin, 0.125 mg l⁻¹; cefotaxime, 4 mg l⁻¹; daptomycin, 0.064 mg l⁻¹; linezolid, 0.25 mg l⁻¹. Based on the ETest guidelines, the breakpoint for penicillin susceptibility was 0.125 mg l⁻¹. However, due to the uncertainty of the identification of the isolate and the potential implications of altering antibiotic therapy inappropriately, the isolate was referred to the reference laboratory (Laboratory of Healthcare Associated Infections, Health Protection Agency, Colindale, London, England, UK) for further identification and antimicrobial susceptibility testing.

On clinical review of the patient with the neurosurgical team 2 days after surgery, the patient’s symptoms had improved significantly. As no other cultures were positive and the patient was clinically well, empiric antibiotics were discontinued and changed to intravenous daptomycin (4 mg kg⁻¹ daily) based on the low MIC.

At the reference laboratory the isolate was identified by sequencing the 16S rRNA gene. A partial sequence of 1224 bp was obtained (GenBank accession no. HQ402900). A BLAST search of GenBank (http://blast.ncbi.nlm.nih.gov) showed that the sequence matched the type strain of B. otitidis by 99.8%. Antimicrobial susceptibility testing confirmed resistance to penicillin, and susceptibility to vancomycin, linezolid and daptomycin (Table 1). Antibiotic therapy was changed to vancomycin (1 g twice daily). Our patient completed 6 weeks of antimicrobial therapy, her inflammatory markers improved and she was discharged home well after 2 months in hospital.

Discussion

Brevibacterium species, which may resemble Corynebacteria, were previously considered contaminants when isolated from clinical specimens. Though infrequently reported, Brevibacterium species are now well-recognized pathogens causing infections in immunocompetent and immunocompromised patients (Brazzola et al., 2000; Ulrich et al., 2006). These infections include sepsis, peritonitis, skin and soft tissue infections, and device-related infections, i.e. catheter-related blood stream infections and prosthetic valve endocarditis. Brevibacterium casei is the most commonly reported species of Brevibacterium isolated from clinical specimens (Gruner et al., 1994). We isolated B. otitidis in all operative specimens from our patient and given the presentation, we concluded that this was a pathogen requiring treatment, rather than a contaminant.

This species was first described in two patients with ear infections (Pascual et al., 1996). Subsequently, a case of peritonitis in a chronic ambulatory peritoneal dialysis patient (Wauters et al., 2000) and prosthetic valve endocarditis (Dass et al., 2002) due to B. otitidis were reported. This is to our knowledge the fifth case of significant infection caused by B. otitidis and the first case of a neurosurgical site infection in an immunocompetent patient.

Brevibacterium species can be differentiated from other coryneform bacteria by testing a wide array of biochemical reactions. The presence of meso-diaminopimelic acid in the peptidoglycan layer of the cell wall of Brevibacterium species and strong, rapid methane-thiol production are helpful in confirming identification of this genus but these tests are rarely available in the clinical diagnostic laboratory setting (Pitcher & Malnick, 1984). In the majority of reported cases, the isolates were sent to a reference laboratory for identification to species level through determination of cellular fatty acid composition and phenotypic characteristics. The identification can be further confirmed by 16S rRNA gene sequencing as was the case in our patient (Hoppe-Seyler et al., 2007).

Table 1. Antimicrobial susceptibility of B. otitidis isolated from operative neurosurgical specimens

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (mg l⁻¹)</th>
<th>S/I/R</th>
<th>Breakpoint (mg l⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime</td>
<td>1</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>Penicillin</td>
<td>1</td>
<td>R</td>
<td>0.125</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.125</td>
<td>S</td>
<td>4</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>8</td>
<td>R</td>
<td>0.5</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.125</td>
<td>S</td>
<td>0.5</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.25</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.25</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.25</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>0.25</td>
<td>NA*</td>
<td>NA*</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>≤ 0.002</td>
<td>S</td>
<td>1</td>
</tr>
</tbody>
</table>

I, Intermediate; R, resistant; S, susceptible.

*There are no agreed breakpoints for daptomycin.

Conclusion

We highlight this case due to: the unusual pathogen isolated, which was not previously recognized as a cause of discitis; the potential for dismissing this isolate as a contaminant; the importance of referring such isolates to a reference laboratory; and the challenge it presented to us in choosing appropriate antimicrobial therapy. In our everyday liaison with clinical teams, we advise on antimicrobial therapy after patient review and rely on the accuracy of the laboratory susceptibility results. The difficulty in accurate identification of these unusual pathogens, interpretation of their clinical significance and lack of standardized guidelines for interpretation of antimicrobial susceptibility tests may lead to inappropriate advice on antimicrobial therapy. This emphasizes the need for referring these clinical isolates to specialized laboratories for accurate results to enable the clinical microbiologist to offer appropriate advice.
References


Breed, R. S. (1953). The families developed from Bacteriaceae Cohn with a description of the family Brevibacteriaceae. VI Congresso Internazionale Microbiologia Roma 1, 10–15.


