Intravascular catheter-related bloodstream infection caused by *Abiotrophia defectiva* in a neutropenic child

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Bacteraemia and endocarditis are the most frequently reported clinical infections due to *Abiotrophia defectiva* species. This species has been rarely implicated in infections in neutropenic patients. We report a rare case of long-term venous catheter-related infection caused by *A. defectiva* that occurred in a febrile child who had neutropenia and Langerhans’ cell histiocytosis.

Introduction

*Abiotrophia* species have previously been referred to as nutritionally variant streptococci on the basis of growth characteristics such as nutrient requirements (pyridoxal hydrochloride) and satellitism around colonies of other bacteria. First isolated in 1961 by Frenkel & Hirsch (1961) from patients with endocarditis and otitis media, *Abiotrophia* species form part of the normal human flora in the oral cavity and the urogenital and intestinal mucosae. *Abiotrophia defectiva* and *Granulicatella adiacens*, another related nutritionally variant *Streptococcus*, are grouped into separate genera based on genetic and phylogenetic analysis of their 16S rRNA gene sequences, which revealed low DNA relatedness to other strains of *Streptococcus* (Kanamoto et al., 2000). Bacteraemia and endocarditis are the most frequently reported clinical infections due to *Abiotrophia* and *Granulicatella* species and account for 4.3–6% of all ‘streptococcal’ endocarditis cases (Brouqui & Raoult, 2001). They have been rarely implicated in infections in neutropenic patients (Lopardo et al., 2007; Murray et al., 2001). We report a case of long-term venous catheter-related infection caused by *A. defectiva* that occurred in a febrile child who had neutropenia and Langerhans’ cell histiocytosis (LCH) and who was receiving broad-spectrum antibiotics.

Case report

A 2-year-old boy presented with a 4-week history of fever, pain and a severe deterioration in his health. Clinical examination and biological analysis revealed skin lesions and an inflammatory syndrome. Initial radiographs showed several lytic bone lesions. The diagnosis of LCH was confirmed by biopsy of the skull lesions. Treatment consisted of an induction regimen of vinblastine and prednisolone, followed by maintenance therapy with the same drugs. The disease relapsed 1 year after the initial diagnosis, and was resistant to prednisone reinduction and an initial course of second-line treatment with 2-chlorodeoxyadenosine. The persistence of fever, anaemia and hypoalbuminaemia, and the appearance of new bony lesions, justified intensifying the treatment of this refractory LCH by adding high-dose cytarabine to the 2-chlorodeoxyadenosine.

A long-term intravascular catheter (port reservoir) was implanted in the patient’s right subclavian vein at the start of conventional chemotherapy and 6 months before starting high-dose chemotherapy.

Beginning from the first day of the first course of induction, the patient received prophylactic cotrimoxazole (given orally three times weekly). Piperacillin–tazobactam treatment was first administered for neutropenic fever on day 9 post-chemotherapy. Due to persistent neutropenic fever, a 2-day course of amikacin and fluconazole was added. Grade 2 mucositis occurred at day 13 and required opiate analgesia. Two blood cultures out of two performed on day 18 and 22 post-chemotherapy from the central venous catheter revealed, with a time to positivity of 42 h, growth of an *A. defectiva* strain which was resistant to several antibiotics (namely erythromycin, lincomycin, piperacillin–tazobactam and cotrimoxazole). Percutaneous peripheral blood cultures were negative. A Gram smear of blood culture broth initially showed a mixture of Gram-positive and Gram-negative cocci in chains, and species identification was obtained using a Vitek 2 GP card (bioMérieux) and confirmed by MALDI-TOF MS (Bruker Daltonik). Two days before normalization of the neutrophil
count, pain and inflammation were noted around the subcutaneous port. The catheter was removed on day 22 post-chemotherapy. Culture of the catheter tip grew *A. defectiva* (100 c.f.u. ml\(^{-1}\)). Vancomycin was added to the initial antimicrobial treatment. Transthoracic echocardiography revealed no vegetations and no valvular/septal abnormalities. In consultation with the clinical microbiologists, i.v. vancomycin was continued for 1 week and stopped 3 days after the neutrophil count reached 500 mm\(^{-3}\). No recurrence of fever was observed, the local subcutaneous infection healed within a week, and all cultures of peripheral blood samples remained negative.

**Discussion**

*A. defectiva* or *Streptococcus defectivus* can cause a variety of infections, including bacterial endocarditis, especially in the setting of negative blood cultures (Brouqui & Raoult, 2001). Isolated cases of keratitis (Abry et al., 2001) have also been reported. The presence of *Granulicatella* species in bacteraemic episodes in neutropenic patients was recently highlighted whereas *A. defectiva* was only isolated in cases of infectious endocarditis (Murray et al., 2001; Senn et al., 2006).

We report here what is to our knowledge the first case of *A. defectiva* catheter-related infection in a neutropenic child. The concomitant chemotherapy-induced mucositis might have predisposed to this infection. Indeed, as previously reported, *A. defectiva* and *Granulicatella* species bacteraemia may occur in the setting of chemotherapy-associated mucositis and neutropenia (Lopardo et al., 1997; Murray et al., 2001; Senn et al., 2006); however, this infection remains quite unusual. Over a 10-year period in our department of oncology for children and adolescents, no bacteraemia with *A. defectiva* was ever observed while *A. defectiva* and *Granulicatella* species bacteraemia occurred in 13 adult patients with solid tumours or haematological malignancies. Ohara-Nemoto et al. (1997) reported that the rates of oral colonization in healthy students were 11.8% and 87.1% for *A. defectiva* and *Granulicatella* species, respectively. The rarity of *A. defectiva* bacteraemia in neutropenic patients could reflect a low frequency of oral colonization by this species.

Debate has existed regarding the major route whereby microbes infect intravascular catheters. Most of the evidence suggests that an intraluminal source predominates in association with more prolonged catheter indwelling times (Mermel, 2011). In this case, an extraluminal entry route arising from a skin infection at the catheter insertion site, and predisposed to by the concomitant chemotherapy-induced mucositis, may explain the infection.

The diagnosis of *A. defectiva* infections is challenging because of the organism’s pleomorphic appearance, slow growth rate and growth requirements. The Gram stain appearance from blood culture broth can vary from Gram-variable cocci to Gram-variable pleomorphic bacillary forms (Murray et al., 2001). The addition of pyridoxal-containing medium or cross-inoculation of the inoculated plates with *Staphylococcus aureus* may increase the recovery of *A. defectiva* isolates in subcultures. Prolonged incubation for at least 72 h under 5–10% CO\(_2\) atmosphere is recommended (Ince et al., 2002).

According to the NCCLS interpretative criteria for *Streptococcus* species, the susceptibilities of *G. adiacens* and *A. defectiva* strains were, respectively: penicillin, 55% and 8%; amoxicillin, 81% and 92%; ceftriaxone, 63% and 83%; meropenem, 96% and 100%; and clindamycin, rifampicin, levofloxacin, ofloxacin and vancomycin, 100% for both species (Tuohy et al., 2000). Because of their unique growth requirements, relatively uncommon recovery from clinical specimens, and the lack of standardized testing methodology and interpretation, limited antimicrobial susceptibility data are available for these organisms. However, the emergence of macrolide resistance among *A. defectiva* and *Granulicatella* species isolates is also of great concern. Zheng et al. (2004) reported the results of antimicrobial susceptibility testing of 15 invasive paediatric *A. defectiva* and *Granulicatella* species isolates. The authors suggest that the prevalence of β-lactam and macrolide resistance is high among recent invasive isolates of nutritionally variant streptococci. In addition, they demonstrated that the macrolide efflux resistance mechanism encoded by mef(A) that is common in other streptococcal species is also found in these species. A strain of *A. defectiva* was reported that was resistant to erythromycin/clindamycin, causing sequential episodes of infective endocarditis in a child, the mechanism of resistance of which involved an erythromycin-resistance gene erm(B) homologue (Poyart et al., 2000). In our case, the central venous line infection with *A. defectiva* occurred while the child was treated with piperacillin–tazobactam and an aminoglycoside, and was eradicated by removal of the catheter and vancomycin administration.

This case and another case report (Lopardo et al., 2007) suggest that both *A. defectiva* and *Granulicatella* species should be regarded as possible causes of bacteraemia in immunocompromised patients.

**References**


