Case Report

Bloodstream infection caused by *Acinetobacter junii* in a patient with acute lymphoblastic leukaemia after allogenic haematopoietic cell transplantation

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Acinetobacter junii is a rare human pathogen associated with bacteraemia in neonates and paediatric oncology patients. We present a case of *A. junii* causing bacteraemia in an adult transplant patient with leukaemia. The correct identification of *Acinetobacter* species can highlight the clinical significance of the different species of this genus.

Introduction

Acinetobacter junii (genomic species 5) is a rare human pathogen, being particularly associated with outbreaks of septicaemia in neonates and paediatric oncology patients (Bernards *et al.*, 1997; de Beaufort *et al.*, 1999; Kappstein *et al.*, 2000). Rare cases of meningitis (Chang *et al.*, 2000), peritonitis (Borràs *et al.*, 2007), ocular infection (Prashanth *et al.*, 2000) and septicaemia in an adult oncology patient (Linde *et al.*, 2002) caused by *A. junii* have also been described. Although *Acinetobacter baumannii* is the most important and prevalent species involved in nosocomial infections (Bergogne-Bérézin & Towner, 1996), the real incidence and the roles of the other members of the genus *Acinetobacter* as human pathogens can be masked, since reliable phenotypical identification is time-consuming and labour-intensive (Gerner-Smidt *et al.*, 1991). The precise identification of *Acinetobacter* species requires the application of molecular methods (Vanechoutte *et al.*, 1995; La Scola *et al.*, 2006). Unfortunately, the latter approach is not generally applicable in clinical microbiology practice, which makes the delineation of *Acinetobacter* species often problematic and difficult. Here we present what is to our knowledge the first case of bacteraemia caused by *A. junii*

in a patient with acute leukaemia treated with allogenic haematopoietic cell transplantation (HCT).

Case report

A 43-year-old female diagnosed with acute lymphoblastic leukaemia type B in 2004 finished her chemotherapy treatment in June 2006. In February 2009, the patient presented a late relapse with bone marrow and central nervous system involvement. After achieving a second complete remission, the patient was treated with an HCT from a mismatched unrelated donor. In the first month after the HCT, the patient developed acute cutaneous graft-versus-host disease grade 2 (GVHD), resolved after treatment with prednisone (1 mg kg⁻¹ per day). The patient was discharged with a good status performance. On day +36 after the HCT, the patient was readmitted because of fever without neutropenia. Empirical therapy, initially with piperacillin/tazobactam (4/0.5 g every 8 h, i.v.) and oral levofloxacin (500 mg every 24 h) and later with meropenem (1 g every 8 h), teicoplanin (10 mg kg⁻¹ every 24 h) and oral posaconazole (200 mg every 8 h), was unsuccessful. Treatment with intravenous co-trimoxazole (trimethoprim 20 mg kg⁻¹ every 24 h and sulfamethoxazole 100 mg kg⁻¹ every 24 h divided into four doses) was added because of suspected toxoplasmosis, which was not confirmed by investigating *Toxoplasma* DNA in the blood

Abbreviations: GVHD, graft-versus-host disease; HCT, haematopoietic cell transplantation.

by PCR. The patient developed pancytopenia, laboratory signs of thrombotic thrombocytopenic purpura and clinical features of GVHD progression. Prednisone was increased to 2 mg kg⁻¹ per day and finally fever disappeared.

On day +63 after the HCT, the patient presented a new episode of fever (39.5 °C). At this time, she presented with 2700 leukocytes mm⁻³ with 40% neutrophils, haemoglobin 7.8 g dl⁻¹ and platelet count of 3000 mm⁻³ and she was receiving piperacillin/tazobactam (4/0.5 g every 8 h, i.v.). Three sets of blood cultures were drawn in a 30 min period. In the first two blood cultures, the isolates appeared as Gram-negative, strictly aerobic, non-fermenting, non-motile, catalase-positive, oxidase-negative coccobacilli, with the times to detection of 24.6 h and 25.3 h (BACTEC 9240 Blood Culture System; Becton Dickinson Diagnostic Instrument Systems). No growth was observed in the third set of blood cultures.

The isolate was identified as *Acinetobacter lwoffii* by the MicroScan Walk-Away system (Siemens Healthcare Diagnostic), with 98.7% presumptive identification. To confirm the species identification, amplified rDNA restriction analysis (ARDRA; Vaneechoutte *et al.*, 1995) was performed using firstly the enzymes *CfoI*, *AluI*, *MboI*, *RsaI* and *MspI*. The ARDRA profile 12123 compatible with both *A. junii* (genomic species 5) and unnamed genomic species 17 was obtained. To differentiate between these two options, a further restriction analysis was made with the enzyme *BfaI*. A restriction pattern 3 was obtained, confirming the identification of the isolate as *A. junii*. Antibiotic susceptibility was determined by Etest strips (AB Biodisk), according to the manufacturer's recommendations. According to Clinical and Laboratory Standards Institute breakpoints (CLSI, 2010), the isolate was susceptible to piperacillin-tazobactam (MIC ≤0.015 µg ml⁻¹), imipenem (MIC 0.125 µg ml⁻¹), meropenem (MIC 0.125 µg ml⁻¹), trimethoprim-sulfamethoxazole (MIC 0.25 µg ml⁻¹), minocycline (MIC 0.25 µg ml⁻¹), ampicillin-sulbactam (MIC 0.50 µg ml⁻¹), cefepime (MIC 1 µg ml⁻¹), doxycycline (MIC 1 µg ml⁻¹), gentamicin (MIC 1 µg ml⁻¹), amikacin (MIC 2 µg ml⁻¹), ceftazidime (MIC 2 µg ml⁻¹), tetracycline (MIC 4 µg ml⁻¹) and levofloxacin (MIC 2 µg ml⁻¹), and resistant to ciprofloxacin (MIC 4 µg ml⁻¹). In addition, the following antimicrobial agents (for which breakpoints from the Clinical and Laboratory Standards Institute are not available) were also tested: cephalothin (MIC 1 µg ml⁻¹), tigecycline (MIC 1 µg ml⁻¹), amoxicillin-clavulanate (MIC 2 µg ml⁻¹), aztreonam (MIC 4 µg ml⁻¹), chloramphenicol (MIC 4 µg ml⁻¹), cefoxitin (MIC 8 µg ml⁻¹) and ampicillin (MIC 128 µg ml⁻¹). No subsequent *A. junii* strain was isolated from the patient.

After the susceptibility testing results were obtained, therapy with piperacillin/tazobactam (4/0.5 g every 8 h i.v.) was maintained. The central venous catheter, without any signs of local infection, was removed 2 days after

obtaining the blood cultures. No further complications due to *A. junii* infection were observed in the course of 8 days of treatment with piperacillin/tazobactam. A resolution of the signs and symptoms was observed, especially after the catheter removal, and clearance of infection was confirmed by the subsequent blood cultures realized in the next 2 weeks. The patient died 1 month later because of an unfavourable evolution of GVHD, associated with thrombotic thrombocytopenic purpura and cytomegalovirus infection.

Discussion

Although the immediate source of the infection could not be identified in this case as the removed central catheter was not sent for microbiological culture, the significant improvement observed in the clinical course of the infection after catheter withdrawal probably indicates that this device was associated with the episode of bacteraemia as the pathogen was isolated even after appropriate antibiotic therapy. Seifert *et al.* (1997) showed that human skin appears to be a natural habitat of some *Acinetobacter* species, especially *A. lwoffii*, *Acinetobacter johnsonii* and *Acinetobacter* genospecies 3. The other species found, including *A. junii*, were described as colonizers only in hospitalized patients. They observed that these species have also been recovered from blood cultures from patients with catheter-related bacteraemia. Interestingly, *A. baumannii* and *Acinetobacter* genospecies 13TU were rarely found on human skin.

A few reports of nosocomial outbreaks caused by *A. junii* have been described (de Beaufort *et al.*, 1999; Kappstein *et al.*, 2000). Kappstein *et al.* (2000) reported an outbreak of bacteraemia in paediatric oncology patients for whom aerators may act as reservoir for this pathogen. They also described that the water system was contaminated with *A. junii* and recommended that, for high-risk areas, aerators should be avoided. In another study, de Beaufort *et al.* (1999) described six cases of sepsis in a neonatal unit, and concluded that intravenous fat emulsion was implicated as a possible source of the infection. However, community-acquired infections associated with *A. junii* have also been reported (Chang *et al.*, 2000; Prashanth *et al.*, 2000; Borràs *et al.*, 2007), showing the potential of this opportunistic pathogen to cause infection in humans.

A previous study evaluating the clinical characteristics of patients with *A. junii* infections reported that this pathogen mainly affected patients who have had prior antimicrobial therapy, invasive procedures or malignancy (Hung *et al.*, 2009). The study also showed that infections caused by this pathogen were primarily bacteraemia and the isolates remained susceptible to the majority of the antimicrobial agents tested. These high rates of bacteraemia observed are probably associated with the fact that, in general, the group of patients susceptible to acquired infection by *A. junii* show serious underlying diseases and therefore need invasive procedures, which act as reservoirs and a port of

entry for the infection, as previously described. Higgins *et al.* (2001) tested rare non-fermenting Gram-negative bacteria, including *A. junii* isolates, against different antibiotics and biocides, and concluded that despite being susceptible to certain antimicrobial agents *in vitro*, some isolates were still able to cause bacteraemia after antibiotic therapy. Our case is in accordance with this observation, as the patient was treated with piperacillin/tazobactam as empirical therapy, and subsequently developed a blood-stream infection caused by an organism susceptible to this antimicrobial agent. However, it should be considered that at the time of the episode of bacteraemia, the patient was receiving corticosteroid therapy.

Although *A. junii* is capable of causing serious infections, they are generally non-fatal because the micro-organism is commonly susceptible to antimicrobial agents (Bernards *et al.*, 1997). However, Peleg *et al.* (2006) identified a carbapenem-resistant *A. junii* blood culture isolate producing OXA-58 and IMP-4. In another study, Marqué *et al.* (2005) described the spread of the plasmid-borne OXA-58 in *Acinetobacter* clinical isolates from southern Europe, including an *A. junii* isolate carrying a 150 kb plasmid harbouring OXA-23 and OXA-58. The acquisition of resistance genes, typically associated with *A. baumannii*, by *A. junii* clinical isolates is a concern, since the therapeutic options for treating these infections become limited. A retrospective study described by van den Broek *et al.* (2009) demonstrated in a university hospital, under endemic conditions, the importance of other non-*baumannii* *Acinetobacter* species as a cause of nosocomial infection. The frequency of *Acinetobacter* genomic species 3 was the same as that obtained for *A. baumannii*. Surprisingly, *A. lwoffii* represented 11 % of the 359 strains evaluated in the study. Among the 20 different species identified, *Acinetobacter ursingii*, *A. johnsonii* and *A. junii* were also frequent, presenting 13, 13 and 12 isolates, respectively.

Although therapy is guided primarily by the susceptibility pattern of the isolate and not by the species identification, special attention should be given to the correct identification of *Acinetobacter* non-*baumannii* species, which will contribute to a better understanding of the epidemiology and the real clinical impact of these species as a cause of infections in humans. The majority of the reports describing infections caused by *A. junii* used a molecular method as a confirmatory identification test, especially 16S rRNA gene sequencing (Seifert *et al.*, 1997; Linde *et al.*, 2002; Borràs *et al.*, 2007; Hung *et al.*, 2009), showing the importance of molecular methods in the correct identification of species included in the genus *Acinetobacter*.

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