Case Report

Genomic species identification is important to delineate the pathological characteristics of *Acinetobacter* in tunnelled, cuffed haemodialysis catheter-related bacteraemia

Te-Li Chen¹, Chiao-Lin Chuang², Leung-Kei Siu³, Chang-Phone Fung⁴ and Wen-Long Cho⁴

¹Section of General Medicine and Section of Infectious Diseases, Taipei Veterans General Hospital, ²Section of General Medicine and Section of Nephrology, Taipei Veterans General Hospital, ³Division of Clinical Research, National Health Research Institute and ⁴Institute of Tropical Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan.

Keywords: *Acinetobacter*; bacteraemia; cuffed haemodialysis catheter; tunnelled

A tunnelled, cuffed haemodialysis catheter (TCHC) is used for vascular access in haemodialysis patients who are awaiting implantation or maturation of arteriovenous access, or who do not have other options. Catheter-related infection, especially bacteraemia, is a common cause of catheter failure [1]. In 3–10.5% of the bacteraemic episodes, the causative pathogens involved is *Acinetobacter* spp. [1–3]. Routine phenotypic methods for identifying *Acinetobacter* do not normally determine the species of the bacterium involved [4]. For this reason, in the literature, infections caused by *Acinetobacter* often do not report on the species. However, different *Acinetobacter* spp. vary in the clinical problems they cause and antibiotic susceptibility [5]. Therefore, identification of *Acinetobacter* to species is required in TCHC-related bacteraemia, to enable the selection of an appropriate antibiotic therapy. In addition, the clinical characteristics and management of this type of *Acinetobacter* bacteraemia have not previously been considered.

Here we present two cases of TCHC bacteraemia caused by *Acinetobacter* spp, which were identified to the genomic species level by sequence analysis of an internal fragment of recA gene [6]. Briefly, polymerase chain reaction (PCR) amplification of the recA gene was performed by using forward primer rAI (5′-CCTGAATCTTCTGGTAAAAC) and reverse primer rA2 (5′-GTTTCTGGGCTGCCAAACCATTAC). The program of PCR was: 94°C 5 min, 1 cycle; 94°C 30 s, 55°C 30 s, 72°C 30 s, 30 cycles; and a final extension cycle was 72°C 10 min. The amplicon was then purified, cloned and sequenced. The species identification was determined by means of sequence analysis using the Basic Local Alignment Search Tool (BLAST) available on the National Center for Biotechnological Information (NCBI) website for comparison with NCBI nucleotide databases.

Our report shows that the identification of *Acinetobacter* using the phenotypic method might prevent or delay correct clinical management, including appropriate antibiotic therapy.

Case report

Case 1

A 63-year-old male was referred from an out-patient haemodialysis unit because of intermittent fever and chills over a week, associated with haemodialysis. He had suffered from hypertension for years, and 5 months previously, he had reached end-stage renal disease. A left radio-cephalic arteriovenous fistula and a dual lumen, tunnel, cuffed, silastic central venous catheter was created (via the right jugular vein) while he was hospitalized for his renal disease. He was dialysed 3 times a week through the catheter up to the maturation of the fistula.

In addition to fever and chills, he also presented nausea, vomiting and ill appearance. His body temperature was 39.2°C, blood pressure 112/69 mmHg and his pulse rate was 140 beats/min. Physical examination failed to reveal a site of infection. There was no evidence of exit-site or tunnel infection. The results of chest radiography and urinalysis were normal. His white blood cell (WBC) count was 1.8 x 10⁹/l and the C-reactive protein (CRP) level was 12.71 mg/dl. Based on a presumptive diagnosis of catheter-related infections, empirical antibiotic therapy with intravenous vancomycin (1g) and levofloxacin...
(250 mg) was initiated. No fever was noted for the following 3 days. Unfortunately, fever developed shortly after haemodialysis on the 4th day of hospitalization. Isolates from blood cultures taken via the catheter port and peripheral vein were both phenotypically identified as *Acinetobacter calcoaceticus–Acinetobacter baumannii* (Ac–Ab) complex using the API ID 32 GN system (bioMérieux, Marcy l’Etoile, France). The isolates were resistant to amikacin, cefazolin, chloramphenicol, but susceptible to gentamicin, cefuroxime, cefotaxime, cefepime, imipenem, ampicillin/sulbactam, ciprofloxacin, tetracycline and trimethoprim-sulfamethoxazole. Unexpectedly, the isolates were genotypically identified as *Acinetobacter haemolyticus*. The catheter was removed, antibiotic therapy was changed to moxifloxacin and the patient was dialysed via a temporal femoral catheter. Fever subsided over the next day. An echocardiogram revealed no evidence of endocarditis. The tip culture was negative for bacteria. Intravenous antibiotic therapy with moxifloxacin was continued for 1 week. He was discharged with another 1 week of oral moxifloxacin, and was free of recurrent bacteraemia throughout the following year.

**Case 2**

A 72-year-old male had been admitted to a local hospital due to *Escherichia coli* sepsis. He was initially cured, but fever and chills recurred 3 days before he was transferred to our hospital. He had underlying diseases of hypertensive cardiovascular disease, gout and pulmonary tuberculosis, which had been treated. He had received open cholecystectomy due to stone-induced cholecystitis and gall bladder haemorrhage. He had been undergoing haemodialysis 3 times weekly for 3 years. The haemodialysis was performed via a right jugular catheter because he had no other options for vascular access.

On arrival, he looked ill and complained of abdominal pain and vomiting. His body temperature was 38.3°C and his blood pressure was 110/70 mmHg. The infectious focus could not be elicited by physical, chest radiographic and laboratory examinations. WBC count was 23.5 x 10⁹/l, with 8% band form. CRP level was 18.65 mg/dl. He received empiric antibiotic therapy with cefazolin (1g, q.d.) and gentamicin (80 mg, t.i.w.), but intermittent low-graded fever persisted. Blood culture was positive for Ac–Ab complex, which was resistant to ampicillin, cefazolin, cefuroxime, aztreonam, chloramphenicol and trimethoprim-sulfamethoxazole, but was susceptible to gentamicin, amikacin, ceftazidine, cefepime, imipenem, ampicillin/sulbactam and ciprofloxacin. The isolates were identified as *Acinetobacter* genomic species 13 sensu Tjernberg and Ursing (13TU) by the aforementioned genotypic method. The antibiotic was changed to cefepime (1g, q.d.) and amikacin (375 mg, q.o.d.). Unfortunately, high fever (40.3°C) was noted after haemodialysis on the 5th hospitalization day (the day after changing antibiotics). Subsequently, the catheter was removed and his fever subsided 2 days later. Tip culture was also positive for the same pathogen. He received antibiotic therapy with cefepime and amikacin for a total 3 weeks. No recurrence of bacteraemia was noted throughout the following year.

**Discussion**

It is not normally possible to identify bacteria belonging to *Acinetobacter* genus to species level by their phenotypic properties, especially those bacteria of the Ac–Ab complex [4]. This complex includes at least four *Acinetobacter* genomic species: genomic species 1 (*A. calcoaceticus*), 2 (*A. baumannii*), 3 and 13 TU. In the clinical setting, bacteria identified as *A. baumannii* by a phenotypic method should be classified as Ac–Ab complex. In a large study of 123 episodes of TCHC-related bacteraemia, five causative pathogens were identified as *A. baumannii* [2]. However, the identification method used in this study was not reported and therefore the genomic species could not be assigned with confidence as *A. baumannii*. Several genotypic methods have been developed for the genomic identification of *Acinetobacter* spp, including the sequence analysis of the *recA* gene used in this report [6]. This is the first time that the causative *Acinetobacter* of TCHC-related bacteraemia has been identified to the genomic species level. Initially, the presumptive identification of the isolates obtained from the two patients by phenotypic method was Ac–Ab complex. However, they had a relatively susceptible antibiogram compared with those of other clinical isolates of *A. baumannii*. The discrepancy between species identification and antibiogram prompted us to perform a genomic identification. Although *A. baumannii* is the main genomic species isolated from clinical specimens, including those from nosocomial pneumonia and non-haemodialysis catheter-related bacteraemia [4], the causative pathogen was *A. haemolyticus* in our first case and *Acinetobacter* 13 TU in the second case. Therefore, the significance and prevalence of *A. baumannii* in TCHC-related bacteraemia remained to be determined. Based on this result, correct identification of *Acinetobacter* to the species level by genotypic methods is necessary, to obtain an insight into the importance of the different *Acinetobacter* spp. in TCHC-related bacteraemia.

* A. *haemolyticus* is usually isolated from activated sludge, clinical specimens, the hospital environment [4] and human skin [7]. *Acinetobacter* 13 TU can also be found colonizing the skin of patients and even healthy persons [7], and it has been reported to cause nosocomial outbreaks [8]. Although the origins and entry routes of bacteria were undetermined in our patients, the results reinforced the importance of basic disinfection procedures during routine haemodialysis. *Acinetobacter* spp. are considered as microorganisms with a relatively low virulence [4]. However, the two patients in our cases presented high fever and other
systemic signs of infection, which were indistinguishable from those caused by other virulent bacteria, such as *Staphylococcus aureus*. Despite prompt antibiotic therapy, these patients experienced intermittent or persistent fever for 4–5 days. It has been reported that *Acinetobacter* has the ability to produce a biofilm [9], and this structure might hinder the efficacy of antibiotic penetration. Hence removal of the catheter was warranted, for a better response to the antibiotics. Although *Acinetobacter* endocarditis and osteomyelitis have been reported [4], none of our cases experienced these complications. In general, the recommended duration of an antibiotic therapy for the TCHC-related bacteraemia is 3–4 weeks [2,10]. In our first case, the *A. haemolyticus* infection was also effectively cured after the removal of the catheter plus a shorter course of antibiotic therapy.

In conclusion, the correct genomic identification should be performed to delineate the pathological characteristics of different *Acinetobacter* spp. in TCHC-related bacteraemia. Catheter removal is required for a better outcome. For bacteraemia caused by *A. haemolyticus*, our experience is that a shorter course of oral antibiotic therapy may be sufficient.

Acknowledgement. We thank Prof. Stephen Phillips (Division of Infection and Immunity, University of Glasgow, UK) for his critical reading of the manuscript.

Conflict of interest statement. None declared.

References


Received for publication: 25.10.06
Accepted in revised form: 4.12.06