Case Report

Human infection with *Delftia tsuruhatensis* isolated from a central venous catheter

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We present the case of a patient with catheter-related infection caused by *Delftia tsuruhatensis*, a newly described species closely related to *Delftia acidovorans* (formerly *Comamonas acidovorans*). To date, *D. tsuruhatensis* has not been described as a pathogen. To the best of our knowledge, this is the first report describing *D. tsuruhatensis* as the causative agent of a human infection.

Case report

A 53-year-old woman with severe idiopathic pulmonary hypertension presented with flu-like symptoms, chills and a reduced general condition at our outpatient clinic. She had been treated for the past 18 months with continuous intravenous iloprost via a non-tunnelled central venous catheter (CVC) lying in the right vena subclavia. Her body temperature was 37.1 °C, heart rate was 86 beats min⁻¹, blood pressure was 140/83 mmHg, the respiratory rate was 15 breaths min⁻¹ and the arterial oxygen saturation was 96 % while breathing 2 l oxygen min⁻¹ via a transtracheal catheter. The lungs were clear on auscultation and there was no heart murmur. There was no erythema, pus or tenderness at the site of the CVC. Routine blood analyses were initially normal except for mild leukocytosis; the C-reactive protein rose to a maximum of 47 mg l⁻¹ within 3 days and declined thereafter. Blood cultures were obtained through the CVC and a peripheral line. The CVC was subsequently removed and its tip was sent for culture. Blood cultures drawn into BacT/ALERT FA/FN bottles were processed with the BacT/ALERT 3D system (bioMérieux). Aerobic bottles inoculated with blood from the catheter became positive after 11 h and those inoculated with blood from the peripheral line became positive after 28 h. Anaerobic bottles remained negative. A differential time to positivity of 17 h clearly pointed to a catheter-related infection at that point. Subcultures as well as cultures from the removed CVC tip on 5 % sheep blood agar and MacConkey agar showed growth of oxidase-positive, nonpigmented, lactose-nonfermenting colonies.

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; CVC, central venous catheter.

The GenBank/EMBL/DDBJ accession number for the 16S rRNA gene sequence of *Delftia tsuruhatensis* strain IMM1 is GU591410.

Microscopy revealed long, straight, Gram-negative rods. Identification was attempted with the VITEK 2 colorimetric card (bioMérieux) and *Delftia acidovorans* was identified with a probability level of 98 %. To confirm identification according to in-house policies, 16S rRNA gene sequencing was done. The 5'-end of the 16S rRNA gene was amplified using universal bacterial 16S rRNA gene primers as described before (Bosshard *et al.*, 2004). The PCR product was sequenced and homology analysis was performed using SmartGene IDNS. A homology of >99 % with a minimum of 0.5 % difference with the second homologous species allows for identification at the species level according to Clinical and Laboratory Standards Institute (CLSI) approved guidelines for identification of bacteria by 16S rRNA gene target sequencing, which are widely used (Janda & Abbott, 2007). The obtained sequence of 747 bp located at the 5'-end of the 16S rRNA gene showed 100 % identity to the type strains of *Delftia tsuruhatensis* (GenBank accession no. AB075017) and *Delftia lacustris* (GenBank accession no. EU888308), which are closely related and undistinguishable by 16S rRNA gene sequence (Jørgensen *et al.*, 2009). The third most homologous species appeared to be *D. acidovorans* (GenBank accession no. CP000884.1) with a sequence identity of 99.3 % (five mismatches), enabling the identification of our strain as *D. tsuruhatensis* (Shigematsu *et al.*, 2003) or *D. lacustris* (Jørgensen *et al.*, 2009). Since our strain could not utilize D-mannitol or D-malic acid (API 20 NE and Vitek 2 colorimetric GN Card; bioMérieux) for growth, it was assigned as *D. tsuruhatensis* according to Jørgensen *et al.* (2009). The isolated strain was named IMM1 and the 16S rRNA gene sequence was submitted to GenBank under accession number GU591410. Antimicrobial susceptibility testing was conducted by the disc diffusion method. Since neither the CLSI nor the European Committee on

Antimicrobial Susceptibility Testing provide disc diffusion breakpoints for non-*Enterobacteriaceae* other than *Pseudomonas aeruginosa*, *Acinetobacter* species, *Stenotrophomonas maltophilia* and *Burkholderia cepacia*, the antibiogram was read visually. Large zones of inhibition were observed with amoxicillin-clavulanate, piperacillin-tazobactam, ceftriaxone, ceftazidime, cefotaxime, cefepime, ciprofloxacin, levofloxacin, imipenem, meropenem and ertapenem whereas the organism was judged resistant to ampicillin, cefalothin, cefuroxime, gentamicin, tobramycin, amikacin and colistin due to lack of an inhibition zone. Ciprofloxacin 750 mg per os b.i.d. was chosen empirically after microscopy from blood culture had shown Gram-negative rods, to enable outpatient treatment with oral therapy. The MIC of ciprofloxacin determined by Etest (AB Biodisk) was 0.25 mg l⁻¹. According to CLSI MIC breakpoints for non-*Enterobacteriaceae* other than *P. aeruginosa*, *Acinetobacter* species, *B. cepacia* and *S. maltophilia* (CLSI, 2010), the isolate was judged susceptible to ciprofloxacin. Therefore, therapy with oral ciprofloxacin was continued. The patient's condition rapidly improved and fever and chills disappeared. Blood results returned to normal range. A new CVC was inserted after 8 days of treatment into the left vena subclavia and the continuous iloprost therapy was switched from the peripheral line to the CVC for further home treatment. Antibiotic therapy was stopped after 14 days. A repetitive outpatient follow-up within the following 12 weeks showed a stable clinical condition without any complications.

Discussion

D. tsuruhatensis was first described in 2003 (Shigematsu *et al.*, 2003). The organism was isolated from activated sludge collected from a domestic wastewater treatment plant in Japan, is able to degrade various (hazardous) aromatic hydrogen carbon compounds and is closely related to *D. acidovorans* (formerly *Comamonas acidovorans*). Recently, *D. lacustris* was described as a novel species (Jørgensen *et al.*, 2009), based on physiological and biochemical characteristics which differentiate this species from its closest relative, *D. tsuruhatensis*. *D. tsuruhatensis/lacustris* and *D. acidovorans* form two distinct 16S rRNA gene sequence clusters within the genus *Delftia*, which divides them in two phylogenetic groups (Shigematsu *et al.*, 2003). Since our strain did not utilize D-mannitol or D-malic acid, it is concluded according to the characteristics described by Jørgensen *et al.* (2009) that our strain can be assigned as *D. tsuruhatensis*. This species has been described as a plant growth-promoting bacterium and was proposed as a potential biocontrol agent against plant pathogens (Han *et al.*, 2005; Validov *et al.*, 2007). To date, no reports of *D. tsuruhatensis* as a human pathogen are available to our knowledge. However, *D. acidovorans* has been reported to cause catheter-related bacteraemia, endocarditis and ocular and urinary tract infections (Castagnola *et al.*, 1994; del Mar Ojeda-Vargas *et al.*, 1999; Ender *et al.*, 1996; Horowitz *et al.*, 1990; Stonecipher

et al., 1991) as have other glucose-nonfermenting bacteria. Besides other species of this group such as *Comamonas*, *Brevundimonas*, *Acidovorax* and *Ralstonia* species, *S. maltophilia* and *B. cepacia* are increasingly recognized as nosocomial and opportunistic pathogens. For certain patient populations such as cystic fibrosis and lung-transplant patients or immunocompromised patients, colonization and infection with these organisms has become a serious threat (Enoch *et al.*, 2007).

Identification of non-fermentative Gram-negative rods poses a challenge to clinical laboratories since commercial biochemical systems frequently fail to provide an accurate result. Likewise in this case *D. tsuruhatensis* was misidentified by the VITEK 2 system as a closely related species, which in routine clinical laboratories can only be distinguished by molecular methods. Hence, if accurate identification is needed, 16S rRNA gene sequencing is recommended (Zbinden *et al.*, 2007). Antibiotic susceptibility patterns of non-fermentative Gram-negative rods are manifold due to a variety of intrinsic mechanisms that can cause rapid emergence of new resistances. As interpretative criteria for disc diffusion assays are still lacking, specific MIC testing is used to safeguard antimicrobial chemotherapy. Quinolones, namely ciprofloxacin, show broad-spectrum activity for aerobic Gram-negative organisms including glucose non-fermenting Gram-negative rods (Spangler *et al.*, 1996) and have successfully been used for *D. acidovorans* infections (Lema *et al.*, 2001). As *D. acidovorans* is frequently resistant to aminoglycosides as another antibiotic class used to treat systemic Gram-negative infections, we initially suspected *D. tsuruhatensis* to show this characteristic as well. This case shows that quinolones are a reasonable empirical treatment option for infections with Gram-negative glucose non-fermentative rods.

In conclusion, this case underlines the growing relevance of Gram-negative non-fermentative rods as pathogens in a clinical environment with an increasing frequency of immunocompromised individuals and patients with permanent indwelling devices. Identification increasingly relies on molecular methods in such cases since commercial and in-house systems that were originally directed to the family *Enterobacteriaceae* are not able to safely distinguish many of these species.

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