Case Report

Cellulosimicrobium cellulans isolated from a patient with acute renal failure

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Introduction: *Cellulosimicrobium cellulans* is a rare human pathogen that is associated with chronic immunosuppression, such as human immunodeficiency virus infection, post-transplantation or end-stage renal disease.

Case presentation: A 59-year old man with a past medical history of significant cardiovascular, cerebrovascular and peripheral vascular disease was admitted to the intensive care unit (ICU) with intractable seizures. Physical examination, radiographic imaging and culture results suggested the patient had developed metabolic encephalopathy due to pneumonia caused by *Staphylococcus aureus* and *Moraxella catarrhalis*. The patient recovered neurologically with the use of broad-spectrum antibiotics but developed acute renal failure during his stay. Seven days later, he relapsed into seizure activity and two separate blood cultures grew *Cellulosimicrobium cellulans*. Despite maximal antibiotic therapy, the patient continued to deteriorate. After 16 days, the patient's family withdrew care and he subsequently died.

Conclusion: We report the isolation of *Cellulosimicrobium cellulans* from a patient who developed acute renal failure following a prolonged stay in the ICU for sepsis encephalopathy.

Keywords: 16S rRNA sequencing; acute renal failure; antimicrobial therapy; *Cellulosimicrobium cellulans*.

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Case report

A 59-year-old man was admitted to the intensive care unit (ICU) with intractable seizures. His past medical history was significant for ischaemic heart disease with two previous myocardial infarctions, peripheral vascular disease requiring a left femoral–femoral bypass and a right femoral–popliteal bypass surgery, chronic obstructive pulmonary disease, dyslipidemia, and a prior admission to the ICU for pneumonia and septicemia. Four months earlier, he had suffered a stroke in the left middle cerebral artery region, leaving him with word-finding difficulties and confusion.

On physical examination, the patient was confused, tachycardic (heart rate 120) and tachypneic (respiratory rate of 40). He had decreased air entry and crackles on auscultation of both lungs, and the rest of his physical examination was unremarkable. Laboratory tests showed a normal blood cell count, electrolytes, urea and creatinine. The patient's venous blood gas analysis pH was 7.04, with a partial CO₂ pressure of 96 and an elevated anion gap of 16. He was intubated and underwent a computed tomography scan of his head, which showed old cerebral infarcts in both hemispheres, generalized atrophy of the brain, and no abscess or haemorrhage. A chest X-ray demonstrated diffuse pulmonary oedema with possible underlying pneumonia. Electroencephalogram recordings revealed moderate metabolic encephalopathy without a clear seizure focus. A lumbar puncture yielded normal results.

Empirical treatment with intravenous piperacillin-tazobactam (4.5 g every 6 h) and acyclovir (1500 mg initial

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Abbreviations: ICU, intensive care unit; IV, intravenously; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.

dose and then 200 mg every 12 h) was started. One day after admission, Gram-positive and Gram-negative cocci grew in respiratory cultures and were subsequently identified as *Moraxella catarrhalis* and *Staphylococcus aureus*. Identification was initially made by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics), and was >2.0 on several repeats, including the formic acid extraction method, which yielded a score of >2.3 . The *S. aureus* isolate was susceptible to vancomycin (MIC $1 \mu\text{g ml}^{-1}$), cloxacillin (MIC $0.5 \mu\text{g ml}^{-1}$), clindamycin (MIC $<0.25 \mu\text{g ml}^{-1}$), erythromycin (MIC $<0.25 \mu\text{g ml}^{-1}$) and sulfamethoxazole-trimethoprim (MIC $<10 \mu\text{g ml}^{-1}$). At this time, the patient's creatinine rose significantly to $160 \mu\text{mol l}^{-1}$ (normal $62\text{--}120 \mu\text{mol l}^{-1}$). Acyclovir was discontinued and the dosage of piperacillin-tazobactam [2.25 g intravenously (IV) every 12 h] was reduced because of the patient's poor creatinine clearance. Vancomycin (1 g IV every 24 h) was also added based on the lack of response to treatment and suspicion of methicillin-resistant *Staphylococcus aureus* as a cause of the infection.

Seven days later, the patient developed fever, hypotension and tachycardia, and an increased frequency of seizures despite IV anti-epileptic treatment with phenytoin (100 mg every 6 h). Repeat lumbar puncture and respiratory cultures were negative. However, two sets of blood cultures drawn 6 h apart from a peripheral vein and the left internal jugular central venous catheter grew Gram-positive rods, which were identified as *Cellulosimicrobium cellulans* by MALDI-TOF MS. The catheter was replaced, and the patient remained on antimicrobial therapy with piperacillin-tazobactam and vancomycin. The patient did not recover his renal function and required daily haemodialysis. He could not be weaned off mechanical ventilation, and began requiring inotropic support to maintain his blood pressure. After 16 days in the ICU, the family elected to withdraw care, and the patient died.

Cell morphology obtained from both sets of blood culture bottles showed Gram-positive rods. After overnight incubation at 37°C in aerobic conditions on BBL Trypticase Soy Agar II plus 5 % sheep blood plates (Becton Dickinson and Co.), colonies were 1 mm in size, non-haemolytic, grey, smooth and convex (Fig. 1). A culture grown in aerobic tryptic soy broth (TSB; Becton Dickinson and Co.) demonstrated easily decolorized Gram-positive coccobacillary morphology during the stationary phase as seen in Fig. 2(a), and slender, long, Gram-positive rods in the exponential phase as demonstrated in Fig. 2(b). PCR of the 16S rRNA gene was performed on DNA isolated from cultures grown in TSB (forward primer: 5'-AGAGTTTGATCCTGGCTCAG-3'; reverse primer: 5'-AAGGAGGTGATCCAGCCGCA-3'; Invitrogen). Sequencing of the purified PCR product (Robarts Research Institute Sequencing Facility, London, Ontario, Canada) and a BLAST search of related sequences

in GenBank showed that the sequence matched the type strains of *C. cellulans* at 100 % nucleotide identity, *Cellulosimicrobium funkei* at 100 % nucleotide identity and *Cellulomonas* sp. at 100 % nucleotide identity.

The genus *Cellulosimicrobium* is composed of three species: *C. cellulans*, *C. funkei* and *C. terreum*. *Cellulosimicrobium* spp. are non-acid-fast, catalase-positive, Gram-positive bacilli belonging to the suborder *Micrococccineae*, order *Actinomycetales* and class *Actinobacteria* (Brown *et al.*, 2006; Rowlinson *et al.*, 2006; Yoon *et al.*, 2007). *C. cellulans*, formerly known as *Cellulomonas cellulans* or *Oerskovia xanthineolytica*, is an uncommon human pathogen that has been isolated from soil, grass cuttings, decaying plant materials and sewage facilities (Brown *et al.*, 2006; Yoon *et al.*, 2007).

Infections due to *Cellulosimicrobium* spp. have been reported in almost 30 cases, including bacteremia (Casanova-Roman *et al.*, 2010), endocarditis (Urbina *et al.*, 2003), intra-abdominal sepsis (Borra & Kleinfeld, 1996; Lujan-Zilbermann *et al.*, 1999; Thomas *et al.*, 2007), meningitis (Kailath *et al.*, 1988; Yilmaz *et al.*, 2006), keratitis (Shah *et al.*, 1996), endophthalmitis (Jarupornpan *et al.*, 2011) and septic arthritis (Magro-Checa *et al.*, 2011) and in association with bone-marrow transplantation (Ellerbroek *et al.*, 1998). In most of the cases, infection was secondary to a medical device or foreign body, and removal of the latter was required for resolution of the infection (Harrington *et al.*, 1996; Kailath *et al.*, 1988). Although two cases have been reported in previously healthy patients (Casanova-Roman *et al.*, 2010; Tucker *et al.*, 2008), infection with *C. cellulans* has typically been described in immunocompromised patients with human immunodeficiency virus infection (Heym *et al.*, 2005), tumor-induced immunosuppression, post-transplant

Fig. 1. *C. cellulans* growth at 37°C under aerobic conditions on BBL Trypticase Soy Agar II plus 5 % sheep blood plates after 12 h growth.

Fig. 2. Gram stain of *C. cellulans* from colony isolated on sheep blood agar demonstrated easily decolorized Gram-positive coccobacillary morphology during the stationary phase (a), and slender, long, Gram-positive rods in the exponential phase (b).

patients and patients with end-stage renal disease (Ellerbroek *et al.*, 1998; Urbina *et al.*, 2003). The latter was the most frequent underlying condition associated with *C. cellulans* infections (Rihs *et al.*, 1990), although our patient developed an infection after sustaining acute renal failure, an occurrence that has not been reported elsewhere.

Similar to a previous study (Magro-Checa *et al.*, 2011), our sequencing results demonstrated that 16S rRNA sequencing alone may not be able to distinguish between the three closely related species, although the differentiation may not necessarily affect treatment (Brown *et al.*, 2006). *C. cellulans* has been reported as being resistant to erythromycin and other macrolides but is considered susceptible to vancomycin, which was the therapy of choice in most of the reported cases. Other treatment options such as linezolid or rifampin may be associated with a higher rate of cure (Magro-Checa *et al.*, 2011; Tucker *et al.*, 2008).

To our knowledge, this case represents the first documented case of *C. cellulans* infection following acute renal failure. While *C. cellulans* can cause infections in healthy patients (Casanova-Roman *et al.*, 2010; Tucker *et al.*, 2008), our case demonstrates its role as an opportunistic pathogen in the context of a patient who sustained renal injury and had a prolonged stay in the ICU.

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