

***Moraxella osloensis* bacteremia in a kidney transplant recipient**

doi:10.1111/j.1432-2277.2008.00727.x

The combination of contemporary potent immunosuppressive agents and antimicrobial prophylactic regimens are simultaneously increasing the susceptibility of organ transplant recipients to opportunistic infections and altering the range of causative microbial pathogens [1]. New molecular diagnostic methods are being increasingly used to identify previously unrecognized opportunistic pathogens [1,2]. *Moraxella* are aerobic, pleomorphic Gram negative bacteria that are common commensal organisms of the human upper respiratory tract. *Moraxella catarrhalis* is typically considered to have the greatest ability to act as a pathogen; other species such as *Moraxella osloensis* are considered to be rare pathogens in humans and most reported cases were found in immunocompromised patients [3,4]. Thus far no case of *M. osloensis* infection after solid organ transplantation (SOT) has been published. Of note, correlating clinical disease with other species such as *M. osloensis* has been hampered by the complexity of differentiating *Moraxella* by biochemical and phenotypic testing [3,4]. Therefore, *M. osloensis* may be an underappreciated pathogen.

A 60-year-old man underwent a living-unrelated kidney transplant for end-stage renal disease because of systemic sclerosis. His past medical history also included renal cell carcinoma, for which he underwent a left nephrectomy three years prior to the transplant. He required peritoneal dialysis from the time of the nephrectomy up to the transplant. The transplant was performed without complications. Immunosuppression included induction with antithymocyte globulin (ATG, 1.5 mg/kg on four consecutive days), mycophenolate mofetil (1.5 g/day), tacrolimus (trough levels 8–12 ng/ml) and a steroid taper. The peritoneal dialysis catheter and ureteral stent were removed three weeks after the transplant. Cultures of peritoneal fluid drawn before catheter removal were negative for bacterial growth. A urine culture obtained before stent removal grew vancomycin-resistant *Enterococcus faecium*, which was treated with a 3-day course of linezolid.

Ten days later, he presented with abdominal pain, nausea, vomiting, fever and chills of one day's duration. He had a temperature of 36.3 °C, pulse of 106/min, and

blood pressure of 179/122 mmHg. His physical exam was remarkable for abdominal distension, tenderness and reduced bowel sounds. Initial laboratory test results were notable for a white blood cell count at 16 900/µl with 89% neutrophils, creatinine of 1.3 mg/dl, and normal hepatic and pancreatic enzyme levels. Abdominal computed tomography scans revealed postoperative changes around the allograft, no ascites, and mild distension of the small bowel consistent with an ileus. Cultures were obtained before empirical treatment with vancomycin and cefepime was started. Urinalysis and urine culture were unremarkable. On day 2, a non-*catarrhalis* *Moraxella* species was isolated from a set of the admission blood cultures. PCR sequencing of genomic DNA using a set of 16S rDNA primers confirmed that the isolate was *Moraxella osloensis* (99% identity over 443 bp, *e*-value 0). Antimicrobial susceptibility testing was performed by the *E*-test (AB Biodisk, Solna, Sweden) and Kirby–Bauer disk diffusion methods. Using CLSI breakpoints for *Haemophilus influenzae* for interpretation, the isolate was sensitive to penicillin, cefotaxime, cefepime, ciprofloxacin, and trimethoprim-sulfamethoxazole and was resistant to tetracycline. Blood cultures obtained after the initiation of antibiotics were negative. The patient's abdominal pain progressively improved and his bowel function returned to normal with conservative management. He was discharged on the fourth day of the admission on a two-week course of oral ciprofloxacin. He recovered without further difficulties and was doing well on 9-month post-transplant clinic visit.

Genetic analysis has become an effective tool for the taxonomic identification of *Moraxella* species and may prove to be a powerful method to elucidate relationships between different species and clinical disease [5]. In addition to being a human respiratory tract saprophyte [3,4], *M. osloensis* has also been recovered from environmental samples and is a mutualist of *Phasmarhabditis hermaphrodita* (Nematoda: Rhabditidae), a parasitological roundworm that infects and kills terrestrial mollusks [6–11]. In garden slugs infected by *P. hermaphrodita*, *M. osloensis* is thought to act as the primary killing agent [7,12]. Historically *M. osloensis* has rarely been implicated in systemic disease

of humans, with only a dozen cases of clinical infection, including four cases of bacteremia, reported from 1969 to 2000 (summarized in [13]). While cases of exogenous infection have been reported, most infections are believed to have arisen endogenously [5,13,14]. A recent single-institution study reported that all ten episodes of *Moraxella*-associated bacteremia over an 18-month period were because of *M. osloensis* [5]. All patients had cancer, and nine had a central venous catheter infection. As species identification of *Moraxella* species other than *Moraxella catarrhalis* is rarely pursued by most clinical laboratories, *M. osloensis* may be a more common opportunistic pathogen than previously recognized, particularly of immunocompromised hosts including SOT recipients. Our patient did not have a central venous catheter or a history of mucosal compromise of the respiratory or upper gastrointestinal tracts, however, received ATG induction [5,13]. Whether his ileus represented a consequence of the *M. osloensis* bacteremia or its etiology was unclear. In addition, *M. osloensis* never was isolated from urine cultures, making infection of the stent most unlikely. As the patient enjoyed gardening before and after the transplant, environmental exposure may have occurred. We examined 50 g of soil from the patient's garden to determine whether *Phasmarhabditis* or similar nematodes were present in the soil. Using the nematode growth media agar capture method [15], we collected multiple isolates of a single nematode species that is most closely related to members of the *Panagrolaimus* genus (Nematoda: Panagrolaimidae), based on 18S rDNA sequence (90–91% identity over 781 bp, *e*-value 0). Nematodes of the Rhabditidae family were not recovered. While the *M. osloensis* isolate supported nematode growth and reproduction, the nematode did not prefer *M. osloensis* over other innocuous bacteria, like *Escherichia coli* and *Bacillus subtilis*.

In conclusion, we report the first case of *M. osloensis* bacteremia following SOT, which represents only the fifteenth case in humans. *M. osloensis* may be an underappreciated cause of infection in immunocompromised hosts arising from an endogenous source or from the environment. The origin of the bacteremia in our case is not clear but may have been associated with gardening. Additional studies, including the use of molecular diagnostics, are needed to understand the biology of *M. osloensis* and the incidence, pathogenesis, and optimal treatment of infections caused by non-*catarrhalis* *Moraxella* species, including *M. osloensis*.

Nucleotide sequence accession numbers

Partial sequences of the *Moraxella osloensis* 16S small subunit ribosomal RNA gene and the nematode 18S small subunit ribosomal RNA gene have been deposited in the

GenBank database under the accession numbers EU541351 and EU541352, respectively.

Acknowledgements

This work was supported in part by a Howard Hughes Medical Institute Early Career Award to C.D.S.

Costi D. Sifri,¹ Ann Karen C. Brassinga,¹
Tanya Flohr,² Jason M. Kinchen,³
Kevin C. Hazen,⁴ Robert G. Sawyer,²
Timothy L. Pruett² and Hugo Bonatti²

¹ Division of Infectious Diseases and International Health,
Department of Medicine,
University of Virginia Health System,
Charlottesville, VA, USA

² Department of Surgery,
University of Virginia Health System,
Charlottesville, VA, USA

³ Beirne Carter Center for Immunology Research,
University of Virginia Health System,
Charlottesville, VA, USA

⁴ Department of Pathology,
University of Virginia Health System,
Charlottesville, VA, USA

References

1. Fishman JA. Infection in solid-organ transplant recipients. *N Engl J Med* 2007; **357**: 2601.
2. Palacios G, Druce J, Du L, et al. A new arenavirus in a cluster of fatal transplant-associated diseases. *N Engl J Med* 2008; **358**: 991.
3. Berger U, Falsen E. Distribution of species of *Moraxella* and moraxella-like organisms in the nasopharynx of healthy human adults (author's transl). *Med Microbiol Immunol* 1976; **162**: 239.
4. Schreckenberger PC, von Graevenitz A. *Acinetobacter*, *Achromobacter*, *Alcaligenes*, *Moraxella*, *Methylobacterium*, and other nonfermentative Gram-negative rods. In: Murray PR, Baron EJ, Pfaffer MA, Tenover FC, Yolken RH, eds. *Manual of Clinical Microbiology*, 7th edn. Washington, DC: ASM Press, 1999: 539–60.
5. Han XY, Tarrand JJ. *Moraxella osloensis* blood and catheter infections during anticancer chemotherapy: clinical and microbiologic studies of 10 cases. *Am J Clin Pathol* 2004; **121**: 581.
6. Crawford RL, Hutton SW, Chapman PJ. Purification and properties of gentisate 1,2-dioxygenase from *Moraxella osloensis*. *J Bacteriol* 1975; **121**: 794.
7. Tan L, Grewal PS. Pathogenicity of *Moraxella osloensis*, a bacterium associated with the nematode *Phasmarhabditis hermaphrodita*, to the slug *Deroeras reticulatum*. *Appl Environ Microbiol* 2001; **67**: 5010.

8. Vaz-Moreira I, Silva ME, Manaia CM, Nunes OC. Diversity of bacterial isolates from commercial and homemade composts. *Microb Ecol* 2008; **55**: 714.
9. An R, Sreevatsan S, Grewal PS. *Moraxella osloensis* gene expression in the slug host *Deroceras reticulatum*. *BMC Microbiol* 2008; **8**: 19.
10. Watanabe K, Teramoto M, Harayama S. An outbreak of nonflocculating catabolic populations caused the breakdown of a phenol-digesting activated-sludge process. *Appl Environ Microbiol* 1999; **65**: 2813.
11. Miyake D, Kasahara Y, Morisaki H. Distribution and characterization of antibiotic resistant bacteria in the sediment of southern basin of Lake Biwa. *Microbes Environ* 2003; **18**: 24.
12. Tan L, Grewal PS. Endotoxin activity of *Moraxella osloensis* against the grey garden slug, *Deroceras reticulatum*. *Appl Environ Microbiol* 2002; **68**: 3943.
13. Shah SS, Ruth A, Coffin SE. Infection due to *Moraxella osloensis*: case report and review of the literature. *Clin Infect Dis* 2000; **30**: 179.
14. Bennett SN, McNeil MM, Bland LA, et al. Postoperative infections traced to contamination of an intravenous anesthetic, propofol. *N Engl J Med* 1995; **333**: 147.
15. Barriere A, Felix M-A. Isolation of *C. elegans* and related nematodes. In: The *C. elegans* Research Community, ed. WormBook. doi: 10.1895/wormbook.1.115.1. Available at: <http://www.wormbook.org> (last accessed on July 17, 2006).