### **CLINICAL CASE REPORT**

## Bacteremia and polyarticular septic arthritis secondary to *Moraxella bovis* in a pregnant patient with HIV who injects drugs

Brook Danger BSc, MSc, MD<sup>1</sup>, Christopher Ripplinger BSc, MD<sup>1</sup>, Joseph Blondeau BSc, MSc, PhD<sup>2</sup>, Leah Blondeau BSc, MSc<sup>3</sup>, Shaqil Peermohamed BSc, MD, MPH<sup>4</sup>

CASE PRESENTATION: We report a rare case of *Moraxella bovis* bacteremia and polyarticular septic arthritis in a 37-year-old pregnant woman with HIV who injects drugs. Two sets of blood cultures obtained 5 hours apart were positive for gram-negative bacilli, and purulent fluid was present intra-operatively from both her left knee and her right third MCP joints. **DIAGNOSIS:** Organism identification using ligation sequencing confirmed both her blood culture and synovial tissue isolates as *M. bovis*. Her infection was initially treated with third-generation cephalosporins and later changed to moxifloxacin because of a drug reaction; although she defervesced clinically with improvement in her C-reactive protein levels, she died most likely as a result of a non-traumatic fat embolism after an elective cesarean delivery. **DISCUSSION:** In contrast to *Moraxella catarrhalis*, other *Moraxella* species are rarely associated with disease in human hosts. *M. bovis* is classically associated with infectious bovine keratoconjunctivitis in cattle; interestingly, our patient denied significant animal exposure. To the authors' knowledge, this is the first case describing infection secondary to *M. bovis* in an adult host.

**KEYWORDS:** Moraxella, Moraxella bovis, PWID—persons who inject drugs, septic arthritis

PRÉSENTATION DU CAS: Les auteurs rendent compte d'un rare cas de bactériémie à Moraxella bovis et d'arthrite septique polyarticulaire chez une femme enceinte de 37 ans atteinte du VIH qui s'injectait des médicaments. Deux séries d'hémocultures obtenues à cinq heures d'intervalle étaient positives aux bacilles Gram négatif, et du liquide purulent a été observé dans le genou gauche et la troisième articulation métacarpophalangienne pendant la période peropératoire. DIAGNOSTIC: La détection des organismes au moyen du séquençage par ligature a confirmé que les isolats des hémocultures et des tissus synoviaux contenaient du M. bovis. L'infection a d'abord été soignée au moyen de céphalosporines de troisième génération, qui ont ensuite été remplacées par de la moxifloxacine en raison d'une réaction au médicament. Même si elle a présenté une défervescence sur le plan clinique et que les taux de protéine C-réactive se sont améliorés, la patiente est décédée, probablement à cause d'une embolie graisseuse d'origine non traumatique après une césarienne non urgente. DISCUSSION: Contrairement au Moraxella catarrhalis, les autres espèces de Moraxella sont rarement associées à des maladies chez les hôtes humains. Le M. bovis est normalement relié à une kératoconjonctivite bovine infectieuse chez le bétail. Fait intéressant, la patiente a nié une exposition importante à des animaux. À la connaissance des auteurs, il s'agit de la première description d'une infection secondaire au M. bovis chez un hôte adulte.

MOTS-CLÉS: arthrite septique, Moraxella, Moraxella bovis, PIM — personnes qui s'injectent des médicaments

<sup>1</sup>Internal Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; <sup>2</sup>Clinical Microbiology, Saskatchewan Health Authority, Saskatoon, Saskatchewan, Canada; <sup>3</sup>Pathology and Laboratory Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; <sup>4</sup>Internal Medicine/Infectious Disease, College of Medicine, University of Saskatchewan, Saskatchewan, Saskatoon, Canada

**Correspondence:** Shaqil Peermohamed, 103 Hospital Drive, Saskatoon, Saskatchewan S7N 0W8 Canada. Telephone: 306-655-6658. E-mail: shaqil.peermohamed@saskhealthauthority.ca



#### **INTRODUCTION**

Moraxella species are part of the normal commensal flora of the human upper respiratory tract. Whereas common clinical manifestations associated with Moraxella catarrhalis include otitis media and pneumonia, other Moraxella species are rarely pathogenic in human hosts. Polyarticular septic arthritis secondary to Moraxella species has previously been described in several case reports, but Moraxella bovis is almost exclusively associated with infectious bovine keratoconjunctivitis in cattle (1–5). Only one previous case report of ventriculoatrial (VA) shunt nephritis secondary to M. bovis in a pediatric patient has previously been described (6). Here, we describe the first case of bacteremia and polyarticular septic arthritis secondary to M. bovis in an adult patient.

#### **CASE PRESENTATION**

A 37-year-old woman in her third trimester of pregnancy presented to the emergency department with a 1-day history of pain in her left knee, right third metacarpophalangeal (MCP) joint, and lower back. Her medical history included active injection drug use, hypothyroidism, HIV, hepatitis C, and mitral valve infective endocarditis diagnosed 14 years earlier. She denied vision loss or other ocular complaints. Her active medications included tenofovir–emtricitabine, dolutegravir, methadone, and prenatal vitamins. She reported excellent adherence with her anti-retroviral therapy. She denied any exposure to cattle or other animal exposure.

#### **DIAGNOSIS**

On examination, she was afebrile, and her vital signs were normal, with no signs of fetal distress. Her right third MCP joint was erythematous, swollen, and warm on palpation. Her left knee was also warm and tender and displayed decreased range of motion, and a palpable effusion was present. No stigmata of infective endocarditis and no meningeal signs were present on examination. Multiple sets of blood cultures were obtained upon hospital admission, and she was empirically prescribed ceftriaxone and vancomycin.

Investigations revealed a normal leukocyte count with lymphopenia and elevated C-reactive protein (CRP) of 109.3 mg/L (normal 0–7 mg/L). Her CD4 count was 119 cells/ $\mu$ L, and her HIV viral load was 21 copies/mL. A synovial fluid aspirate from her left knee was obtained with aspiration of 5 cc of thick, purulent, yellow fluid. A cell count could not be performed as a result of insufficient volume but was predominantly neutrophils and negative for crystals. Her nasopharyngeal swab was negative for severe acute respiratory syndrome coronavirus 2 by polymerase chain reaction, and nucleic acid amplification testing from a urine sample was negative for both *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.

Although the Gram stain and culture of her synovial fluid aspirate was negative, two sets of blood cultures obtained 5 hours apart were positive for gram-negative bacilli in multiple bottles. She was taken to the operating room and found to have evidence of septic arthritis of her left knee and right third MCP joints, with irrigation and debridement performed for both joints. Abundant polymorphonuclear white blood cells were noted, but the Gram stain and culture of both samples were negative.

On the second day of her hospital admission, her vancomycin was discontinued, and her ceftriaxone was switched to ceftazidime. The gram-negative bacilli isolated from her blood cultures were initially identified as *Moraxella lacunata/ovis* by matrix-assisted laser desorption/ionization time of flight mass spectrometry (Knowledge Base Version 3.2, BioMérieux MS, Kirkland, Quebec). Organism identification was subsequently confirmed as *Moraxella bovis* using Nanopore MinION Mk1C ligation sequencing with sequence analysis using the EPI2ME software from Oxford Nanopore Technologies (Oxford, United Kingdom). The average sequencing length was 4,970 base pairs, with a total yield of 38.3 Mbases and 7,714 reads analyzed. The quality score was 10.49 (a score of <7 is considered poor).

Repeat blood cultures obtained on the third day of her hospital admission were negative for bacterial growth. A transthoracic echocardiogram showed thickening of her mitral valve with severe mitral regurgitation but was unchanged from her imaging 14 years earlier. A trans-esophageal echocardiogram was not performed. An MRI of the lumbar spine showed no evidence of vertebral osteomyelitis or epidural abscess.

On the fourth day of her admission, she developed a generalized erythematous maculopapular rash suspected to be a drug reaction, and her ceftazidime was switched to moxifloxacin. Intra-operative tissue cultures from her right third MCP were positive for bacterial DNA using 16S primers, and sequencing of both her blood culture and synovial tissue isolates identified *Moraxella bovis*. Antimicrobial susceptibility testing performed on her blood culture isolate revealed minimum inhibitory concentrations (MICs) as follows: cefuroxime, MIC = 0.19  $\mu$ g/mL; ceftazidime, MIC = 0.25  $\mu$ g/mL; moxifloxacin, MIC = 0.19  $\mu$ g/mL; and trimethoprim–sulfamethoxazole, MIC = 0.50  $\mu$ g/mL.

Her rash resolved with the cessation of ceftazidime, and her joint pain continued to improve with ongoing moxifloxacin therapy during her hospital admission with her CRP levels trending down. An elective cesarean delivery was performed on the 10th day of her hospital admission because there was evidence of oligohydramnios and fetal growth restriction; there was no evidence of neonatal infection. Unfortunately, hours after her cesarean delivery, she became hypotensive,

developed multi-organ system failure, and disseminated intravascular coagulation, which was most likely due to a non-traumatic fat embolism; and died.

#### **DISCUSSION**

*M. bovis* is a gram-negative bacillus that is commonly found in the conjunctivae and nasal secretions of cattle, which are the only known reservoir for the bacteria (5). It is widely reported in the literature as an opportunistic pathogen causing infective bovine keratoconjunctivitis in cattle, with primary modes of transmission being direct animal-to-animal contact or through animal handlers (5).

Moraxella species apart from M. catarrhalis are extremely uncommon pathogens in human hosts, but case reports have described Moraxella species as unusual causes of invasive infections in humans, including septic arthritis, endocarditis, bacteremia, and meningitis (1–4, 6–14). Risk factors for invasive disease secondary to Moraxella species may relate to comorbidities, immunocompromising conditions, injection drug use, and inherited and acquired complement deficiencies (1,4,8,15). Antimicrobial susceptibility testing should be performed on Moraxella isolates recovered from normally sterile sites; Moraxella isolates are generally susceptible to penicillins, cephalosporins, and fluoroquinolones (16).

Here, we describe the first case of bacteremia and polyarticular septic arthritis secondary to *M. bovis* in an adult patient and the second case in the literature of an invasive human infection secondary to M. bovis. We identified a prior case of invasive infection of secondary M. bovis in an 11-year-old girl with congenital hydrocephalus who had bilateral VA shunts placed in the first year of life (6). The patient's cerebrospinal fluid (CSF) cultures persistently grew *M. bovis*, and over the same time period she developed a mesangial proliferative glomerulonephritis (MPGN) that was confirmed by renal biopsy. The patient received multiple courses of antibiotics, including rifampin, trimethoprim-sulfamethoxazole, ceftriaxone, and intraventricular gentamicin, with recurrence of the infection and MPGN despite initial CSF clearance. Eventually, total VA shunt replacement was required to achieve clinical cure. The pathogenesis of her invasive VA shunt infection secondary to M. bovis is unclear. Although we were similarly unable to identify the precise etiology of *M. bovis* infection in the patient described here, she may have been predisposed given concurrent infection with HIV, and injection drug use with contaminated paraphernalia may have created a portal of entry for her bacteremia and polyarticular septic arthritis.

#### **CONCLUSION**

We describe the first case of *M. bovis* septic arthritis and the second case of human infection caused by *M. bovis*. Apart

from *M. catarrhalis*, other *Moraxella* species are unusual causes of invasive infections in humans. Although *M. bovis* is classically associated with infective bovine keratoconjunctivitis in cattle, it is exceedingly rare in human hosts. Further research is needed to identify risk factors associated with invasive infections secondary to *Moraxella* species.

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#### **REFERENCES**

- 1. Woodbury A, Jorgensen J, Owens A, Henao-Martinez A. Moraxella lacunata septic arthritis in a patient with lupus nephritis. J Clin Microbiol. 2009;47(11):3787–8. https://doi.org/10.1128/JCM.01403-09. Medline:19794049
- 2. Juvin P, Boulot-Tolle M, Triller R, Juvin E. Moraxella lacunata infectious arthritis. J R Soc Med. 1991; 84(10):629–630
- 3. Kuo S-H, Rodriguez-Barradas M, Lu L. Symmetric polyarticular septic arthritis caused by Moraxella lacunata. Infect Dis Clin Pract. 2008;16(4):249–51. https://doi.org/10.1097/IPC.0b013e31814b1b5a.
- 4. Khalife M, Merashli M, Kanj SS. Moraxella nonliquefaciens septic arthritis in a hematopoietic stem cell transplant patient a case report and review of the literature. J Infect Public Health. 2019;12(3):309–12.

- https://doi.org/10.1016/j.jiph.2019.01.059. Medline:30711347
- 5. Postma GC, Carfagnini JC, Minatel L. Moraxella bovis pathogenicity: an update. Comp Immunol Microbiol Infect Dis. 2008;31(6):449–58. https://doi.org/10.1016/j.cimid.2008.04.001. Medline:18514312
- 6. Bogdanović R, Marjanović B, Nikolić B, et al. Shunt nephritis associated with Moraxella bovis. Acta Paediatr. 1996;85(7):882–3. https://doi.org/10.1111/j.1651-2227.1996.tb14174.x. Medline: 8819561
- 7. Duployez C, Loïez C, Ledoux G, Armand S, Jaillette E, Wallet F. A fatal endocarditis case due to an emerging bacterium: Moraxella nonliquefaciens. IDCases. 2017;8:12–13. https://doi.org/10.1016/j.idcr.2017.02.006. Medline:28271043
- 8. Nakayama A, Yamanaka K, Hayashi H, Ohkusu K. Moraxella lacunata infection associated with septicemia, endocarditis, and bilateral septic arthritis in a patient undergoing hemodialysis: a case report and review of the literature. J Infect Chemother. 2014;20(1):61–4. https://doi.org/10.1016/j.jiac.2013.06.002. Medline:24462428
- 9. Noman F, Khan SG, Khursheed M, Noor SA, Abubaker J. Moraxella lacunata endocarditis treated with penicillin. J Pak Med Assoc. 2008;58(6):336–7.
- Dasari S, Shetty R, Devasia T. A rare case of Moraxella lacunata producing combined native mitral and aortic valve endocarditis. Australas Med J. 2011;4(7):386–8. https://doi.org/10.4066/AMJ.2011.718. Medline:23393524

- 11. Kao C, Szymczak W, Munjal I. Meningitis due to Moraxella nonliquefaciens in a paediatric patient: a case report and review of the literature. JMM Case Rep. 2017;4(2):e005086. https://doi.org/10.1099/jmmcr.0.005086. Medline:28348808
- Fox-Lewis A, Coltart G, Rice S, et al. Extensive subclinical sinusitis leading to Moraxella osloensis meningitis. IDCases. 2016 Sep 21;6:39–42. https://doi.org/10.1016/j.idcr.2016.08.007. Medline:27695673
- 13. Roh KH, Kim CK, Koh E, et al. Three cases of Moraxella osloensis meningitis: a difficult experience in species identification and determination of clinical significance. J Korean Med Sci. 2010;25(3):501–4. https://doi.org/10.3346/jkms.2010.25.3.501. Medline:20191057
- Veerabathini BC, Manthani K, Gandhi S. An unusual case of Moraxella osleonsis bacteremia in an immunocompetent patient with SARS-CoV-2 Infection. Cureus. 2020;12(8):e10154. https://doi.org/10.7759/ cureus.10154.
- Thønnings S, Jansåker F, Sundqvist C, Thudium RF, Nielsen SD, Knudsen JD. Prevalence and recurrence of bacteraemia in hospitalised people who inject drugs—a single centre retrospective cohort study in Denmark. BMC Infect Dis. 2020;20(1):634. https://doi. org/10.1186/s12879-020-05357-0. Medline:32847528
- 16. Webber JJ, Fales WH, Selby LA. Antimicrobial susceptibility of Moraxella bovis determined by agar disk diffusion and broth microdilution. Antimicrob Agents Chemother. 1982;21(4):554–7. https://doi.org/10.1128/AAC.21.4.554. Medline:7081977