Case Report

Sepsis with prolonged hypotension due to *Moraxella osloensis* in a non-immunocompromised child

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We report a case of septicaemia with prolonged, refractory hypotension related to *Moraxella osloensis* isolated in a non-immunocompromised paediatric patient.

Case report

A 3-year-old boy, with a history of infantile spasms, epilepsy, cortical dysplasia, developmental delay and reactive airway disease, was taken to the University of California Los Angeles (UCLA) Emergency Department (ED) (at the UCLA Medical Center) on 3 July 2009 because of a 2 day history of emesis, diarrhoea and increased seizure activity. A chest X-ray was carried out with negative results; laboratory workup revealed a normal white blood cell count ($7.33 \times 10^3 \mu\text{l}^{-1}$), with 63 % neutrophils, 11 % lymphocytes, 25 % monocytes and a platelet count of $129\,000 \mu\text{l}^{-1}$, and a normal urinalysis. A set of standard blood cultures (aerobic and anaerobic) was drawn, the patient was given intravenous fluids and he was discharged home. The next day (day 1) the patient was lethargic, and he had developed a fever with temperature increasing to 38.9°C at home. He was taken back to the ED, where further work up included a lumbar puncture that yielded a normal cerebrospinal fluid (CSF) cell count and chemistries, Gram stain without organisms, as well as cultures that were negative. Further studies included stool being sent for bacterial culture, and direct examination of ova and parasites, *Campylobacter* culture, *Escherichia coli* O157 culture, and testing for rotavirus antigen, all with negative results. Nasal wash was sent for influenza A and B and respiratory syncytial virus antigen testing, as well as viral cultures, with negative results. The patient's white blood cell count was still within the normal range; however, an increase in the immature granulocytes and bands was noted in the differential, and the platelet count decreased to 78 000. Prior to commencing antibiotic therapy, a second set of standard blood cultures (for

aerobic and anaerobic culture) was also drawn, about 12 h after the first blood culture set. At this time, the patient remained in the ED and continued to receive hydration. Intravenous vancomycin (255 mg every 8 h) and ceftriaxone (850 mg every 24 h) were started. The patient was noted as remaining lethargic, and had multiple episodes of tonic-clonic seizures, and was eventually admitted to the Pediatric Ward on the following day (day 2). The patient was febrile to 39.5°C on day 3, and became hypotensive, with a gradual onset of poor peripheral perfusion. He was subsequently transferred to the Paediatric Intensive Care Unit and started on a $[10 \mu\text{g} (\text{kg body weight})^{-1} \text{min}^{-1}]$ dopamine drip.

Intravenous gentamicin (43 mg every 8 h) was administered when a Gram-negative coccobacillus was isolated from blood culture. A subsequent blood culture collected on day 4 was negative. On day 4, the dopamine drip had to be increased throughout the day [up to $12 \mu\text{g} (\text{kg body weight})^{-1} \text{min}^{-1}$], and the patient was persistently febrile. A head computed tomography scan was performed, which was negative for intracranial oedema or haemorrhages. Taking into consideration the patient's clinical status and the preliminary microbiology results, we aimed to expand resistant Gram-negative and anaerobic coverage by discontinuing vancomycin and ceftriaxone, and administering intravenous metronidazole (170 mg every 8 h) and ceftazidime (850 mg every 8 h). On day 5 the patient's fever persisted and he remained profoundly hypotensive, requiring an $[0.3 \mu\text{g} (\text{kg body weight})^{-1} \text{min}^{-1}]$ adrenaline (epinephrine) drip to be added to the dopamine drip in order to maintain his blood pressure. At that time, ceftazidime was discontinued and intravenous meropenem (340 mg every 8 h) was administered. On day 6, the patient became less febrile, and the rate of adrenaline was

Abbreviations: CSF, cerebrospinal fluid; ED, Emergency Department.

decreased somewhat during the day [$0.2 \mu\text{g (kg body weight)}^{-1} \text{ min}^{-1}$], and reduced [$0.1 \mu\text{g (kg body weight)}^{-1} \text{ min}^{-1}$] then eventually stopped on day 7 of admission.

On day 7, intravenous piperacillin–tazobactam ($1.6 \text{ g every } 8 \text{ h}$) was administered while all the other antimicrobial agents were discontinued, and over the next few days the dopamine was slowly reduced and eventually discontinued on day 10 [day 8, 6 then $7 \mu\text{g (kg body weight)}^{-1} \text{ min}^{-1}$ (due to recurrent hypotension); day 9, 6 then $5 \mu\text{g (kg body weight)}^{-1} \text{ min}^{-1}$]. The patient remained afebrile and was transferred out of the Paediatric Intensive Care Unit on day 12 with the last dose of piperacillin/tazobactam given on day 13. The patient was uneventfully discharged home on an anti-seizure regimen after 14 days of hospitalization.

Microbiology

At 48 h after collection, one anaerobic blood culture bottle was positive using the BacT/ALERT system (bioMérieux), yielding a Gram-negative coccobacillus on Gram stain. The Gram-negative organism was subcultured to blood agar and chocolate agar, and was identified as *Moraxella* species using the RapID NH system (Remel). The isolate was asaccharolytic, oxidase positive, catalase positive and indole negative. To obtain a definitive identification of the organism, 16S rRNA gene sequencing was performed. The 16S rRNA gene fragments were amplified by standard methods. Two subregions of 16S rRNA gene were amplified using two pairs of primers. The first part of the 16S rRNA gene was defined as an approximately 800 bp region between the sequences encoded by the primers 8UA (5'-AGAGTTTGATCCTGGCTCAG-3') and 907B (5'-CCGTCAATTCMTTGTAGTTT-3'). The second part of the 16S rRNA gene, defined as an approximately 700 bp region between the sequences encoded by the primers 774A (5'-GTAGTCCACGCTGTAAACGATG-3') and 1485B (5'-TACGGTTACCTTGTTACGAC-3'), was sequenced to obtain the complete 16S rRNA gene sequence. Sequencing data were analysed by comparison of the consensus sequences with GenBank sequences using Ribosomal Database Project (RDP-II) data and the Basic Local Alignment Search Tool software (BLAST). The percentage similarity to other sequences was determined and a top match to *Moraxella osloensis* (100%) was obtained.

Antimicrobial susceptibility testing of the isolate was carried out using a Clinical and Laboratory Standards Institute (CLSI) reference broth microdilution method. MICs were read after 24 h incubation using the CLSI interpretative criteria for non-fermentative Gram-negative bacteria. Our patient's *M. osloensis* isolate was susceptible to all the antibiotics tested: amikacin ($\leq 0.5 \mu\text{g ml}^{-1}$), ampicillin ($\leq 0.5 \mu\text{g ml}^{-1}$), ampicillin–sulbactam ($\leq 8 \mu\text{g ml}^{-1}$), cefazolin ($1 \mu\text{g ml}^{-1}$), ceftazidime ($\leq 0.5 \mu\text{g ml}^{-1}$), ceftriaxone ($\leq 0.5 \mu\text{g ml}^{-1}$), ciprofloxacin ($\leq 0.25 \mu\text{g ml}^{-1}$), gentamicin ($\leq 0.5 \mu\text{g ml}^{-1}$), imipenem ($\leq 0.25 \mu\text{g ml}^{-1}$), levofloxacin ($\leq 2 \mu\text{g ml}^{-1}$), meropenem ($\leq 0.25 \mu\text{g ml}^{-1}$), piperacillin–tazobactam

($\leq 8 \mu\text{g ml}^{-1}$), tobramycin ($\leq 0.5 \mu\text{g ml}^{-1}$) and trimethoprim–sulfamethoxazole ($\leq 1/20 \mu\text{g ml}^{-1}$). The isolate was also negative for β -lactamase according to a cefinase test.

Discussion

The genus *Moraxella* consists of pleomorphic Gram-negative bacteria that are aerobic, oxidase positive, indole negative and asaccharolytic. *Moraxella* species are inhabitants of the environment as well as part of the normal flora of skin and mucosal surfaces. *M. osloensis*, *Moraxella catarrhalis*, *Moraxella nonliquefaciens* and *Moraxella lincolnii* are part of the normal flora of the human respiratory tract. Whereas, *Moraxella canis* strains are common inhabitants of the upper respiratory tract of dogs and cats (Schreckenberger *et al.*, 2007). *M. catarrhalis* is the most common species isolated from human sources, and is responsible for such infections as otitis media, sinusitis and pneumonia (Verghese & Berk, 1991). Several other *Moraxella* species, including *Moraxella lacunata*, *Moraxella atlantae*, *M. lincolnii*, *M. nonliquefaciens* and *M. osloensis*, have also been isolated from clinical sources (Schreckenberger *et al.*, 2007).

M. osloensis is a rare causative agent of infections in humans with most cases reported in immunocompromised patients (Berger & Falsen, 1976; Schreckenberger *et al.*, 2007). *M. osloensis* was originally grouped with *M. nonliquefaciens* but was reclassified into its own distinct species in 1967 (Bövre & Henriksen, 1967). *M. osloensis* is widely distributed in nature where it has been recovered from the hospital environment (Schreckenberger *et al.*, 2007) and from waste-processing sludge (Watanabe *et al.*, 1999). In a study performed by the Centers for Disease Control and Prevention (Graham *et al.*, 1990), 933 isolates of *Moraxella* species and other closely related organisms were collected from 1953 to 1980. Of the 933 isolates, 199 isolates were identified as *M. osloensis*, making it the second most common species isolated; 44 of the *M. osloensis* strains were derived from blood cultures.

To our knowledge, there have been 28 reported cases of *M. osloensis*-related infections, including bacteraemia, central venous catheter infection, meningitis, synovitis, osteomyelitis, peritonitis and pneumonia (Table 1) (Berger & Kreissel, 1974; Berrocal *et al.*, 2002; Buchman *et al.*, 1993; Butzler *et al.*, 1974; Feigin *et al.*, 1969; Fijen *et al.*, 1994; Fritsche *et al.*, 1976; Han & Tarrand, 2004; Hansen *et al.*, 1974; Lasser & Goldman, 1978; Schonholtz & Scott, 1986; Shah *et al.*, 2000; Sifri *et al.*, 2008; Stryker *et al.*, 1982; Sugarman & Clarridge, 1982; Tiosejo *et al.*, 1988; Vuori-Holopainen *et al.*, 2001; Walls & Wald, 2005). The majority of these infections were found in patients with underlying medical conditions. Ten cases of blood and catheter infections in cancer patients undergoing chemotherapy (Han & Tarrand, 2004), and one case of bacteraemia post-solid organ transplantation (Sifri *et al.*, 2008) have been reported. Of the 28 reported *M. osloensis* cases, 9 were from the paediatric population with only 2 case reports of bacteraemia (Butzler *et al.*, 1974; Shah *et al.*, 2000). The first

Table 1. Summary of reported *M. osloensis*-related infections

Reference	Age and sex of patient	Clinical history	Clinical manifestation	Specimen source
Berger & Falsen (1976)	4 years, M	None	Meningitis	CSF
Berrocal <i>et al.</i> (2002)	89 years, F	Prior eye surgery	Endophthalmitis	Eye
Berrocal <i>et al.</i> (2002)	67 years, F	Prior eye surgery	Endophthalmitis	Eye
Buchman <i>et al.</i> (1993)	71 years, F	Chronic intestinal pseudo-obstruction syndrome, total parenteral nutrition, central venous catheter	Bacteraemia	Blood
Butzler <i>et al.</i> (1974)	2 years, M	None	Stomatitis, septicaemia, impetigo	Blood, oral lesions
Feigin <i>et al.</i> (1969)	2 years, F	None	Septic arthritis with vaginal discharge	Joint aspirate, vaginal exudate
Fijen <i>et al.</i> (1994)	15 years, M	Complement C8 β deficiency	Meningitis	CSF
Fritsche <i>et al.</i> (1976)	4 years, F	None	Meningitis	CSF
Han & Tarrand (2004)	23 years, M	Large cell lymphoma, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	57 years, F	Breast cancer, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	21 years, F	Acute lymphoblastic leukaemia, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	65 years, M	Chronic lymphocytic leukaemia, central venous catheter, sinusitis	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	48 years, F	Acute myelogenous leukaemia, central venous catheter, sinusitis	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	22 years, F	Hodgkin's disease, central venous catheter, bronchitis	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	50 years, F	Melanoma, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	31 years, M	Large cell lymphoma, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	54 years, M	Leukaemia, central venous catheter	Bacteraemia	Central venous catheter blood
Han & Tarrand (2004)	59 years, M	Lymphoma, central venous catheter blood	Bacteraemia	Blood
Hansen <i>et al.</i> (1974)	1 year, F	CSF shunt	Meningitis	CSF
Lasser & Goldman (1978)	36 years, F	None	Arthritis, bacteraemia, urethritis	Blood
Schonholtz & Scott (1986)	45 years, M	None	Septic arthritis	Synovial biopsy
Shah <i>et al.</i> (2000)	2 years, M	None	Bacteraemia	Blood
Sifri <i>et al.</i> (2008)	60 years, M	Kidney transplant	Bacteraemia	Blood
Stryker <i>et al.</i> (1982)	66 years, M	Aortic valve	Endocarditis, renal failure	Blood
Sugarman & Clarridge (1982)	34 years, M	Paraplegia	Osteomyelitis	Bone
Tiosejo <i>et al.</i> (1988)	42 years, M	Alcohol abuse with hepatic cirrhosis and oesophageal varices	Peritonitis, <i>Neisseria meningitidis</i> bacteraemia	Peritoneal fluid
Vuori-Holopainen <i>et al.</i> (2001)	6 years, F	None	Pneumonia	Lung aspirate
Walls & Wald (2005)	3 weeks old, M	None	Ophthalmia	Eye exudate

F, Female; M, male.

case of paediatric *M. osloensis* bacteraemia was reported in a child who presented with stomatitis and impetigo with necrotic skin lesions (Butzler *et al.*, 1974). Interestingly, the second case of paediatric *M. osloensis* bacteraemia reported was in a previously healthy child with no relevant medical history (Shah *et al.*, 2000). Our patient had the unique characteristic of prolonged and profound hypotension, requiring both dopamine and adrenaline drips in order to

maintain his blood pressure. The hypotension persisted for a full week, and the process of weaning the patient off the treatment was quite protracted. To the best of our knowledge, this phenomenon has not been described previously in cases of *M. osloensis* bacteraemia. Furthermore, despite the underlying illness of our patient, our patient was not immunocompromised, and had no significant history of previous infections, other than occasional upper respiratory illnesses.

Appropriate therapeutic options for the treatment of *M. osloensis*-related infections have not been fully studied. Most isolates reported have been susceptible to a variety of antimicrobial agents, including the penicillins, cephalosporins, aminoglycosides, fluoroquinolones and carbapenems (Han & Tarrand, 2004). Similar to these previous reports in the literature, our patient's isolate was found to be susceptible to all the antimicrobial agents tested. Treatment with penicillin or other cell-wall-active antibiotics has been reported to be effective in clearing such infections (Han & Tarrand, 2004). Of note, strains of *M. osloensis* that are resistant to penicillin have been reported (Hansen *et al.*, 1974).

In summary, we report a case of sepsis with prolonged, refractory hypotension related to *M. osloensis* infection in a paediatric patient. To the best of our knowledge, this is the third case of *M. osloensis* bacteraemia reported in the paediatric population, confirming that isolation of *M. osloensis* systemically is a rare clinical finding. Although infrequently isolated, *M. osloensis* does cause significant infections, particularly in the immunocompromised host. Therefore, further studies, including the accurate identification of these non-*catarrhalis* *Moraxella* species, are imperative for optimal treatment of these infections. We need to call attention to the potential of this rare pathogen to cause severe hypotension, and therefore, significant morbidity.

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