

CASE REPORT

Rare *Elizabethkingia meningosepticum* meningitis case in an immunocompetent adult

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Though *Elizabethkingia meningosepticum* typically causes meningitis in neonates, its occurrence in adult is rare, with sixteen cases described worldwide. We report a case of *E. meningosepticum* meningitis in an immunocompetent adult. Bacterial identification was made a day earlier than conventional method by using matrix assisted laser desorption ionization time-of-flight (MALDI-TOF) Vitek mass spectrometry RUO (VMS), which resulted in successful treatment with rifampin, trimethoprim-sulfamethoxazole, levofloxacin and minocycline.

Emerging Microbes and Infections (2013) 2, e17; doi:10.1038/emi.2013.16; published online 10 April 2013

Keywords: *chryseobacterium*; *Elizabethkingia meningosepticum*; *flavobacterium*; meningitis; MALDI-TOF mass spectrometry; Vitek

CASE REPORT

A 68-year-old woman with known hypertension and osteoarthritis was found down in her residential complex and brought to the emergency department on 15 July 2011. On physical examination she was afebrile (36.1 °C), normotensive (107/43) and tachycardic (95 beats/min), with an oxygen saturation of 98% on room air. Swollen, erythematous lower extremities with areas of induration and scattered bullae were noted. Although initially alert and oriented, within 4 h she became difficult to arouse and was not following commands. Her neurological exam was non-focal, with pupils equally round and reactive to light, normal muscle tone and dull deep tendon reflexes. Initial laboratory findings were consistent with an anion-gap metabolic acidosis, acute renal failure, elevated liver enzymes and creatine phosphate kinase (Table 1). Head computed tomography imaging was unremarkable at the time of presentation. The patient was emergently intubated, and surgical exploration of her lower extremities was performed. No signs of necrotizing fasciitis were noted.

On post-operative reevaluation, the patient exhibited left horizontal gaze palsy, a left dilated non-reactive pupil, extensor Babinski response bilaterally and decerebrate posturing. Repeat head computed tomography imaging 20 h after the initial scan showed interval development of hydrocephalus requiring placement of an external ventricular drain. Interestingly, the initial cerebrospinal fluid (CSF) sample analysis on external ventricular drain placement yielded zero white blood cells, mildly elevated protein levels and normal glucose levels. However, Gram-negative rods were noted on microscopy (data not shown). Although she had already received doses of vancomycin, piperacillin-tazobactam, ceftriaxone and ampicillin by the end of day 1, the patient developed septic shock.

Within 24 h of admission, initial blood culture collected in emergency department, tissue and CSF cultures collected later were processed turned positive for the Gram-negative rod. Instead of waiting for another day for bacterial identification by using conventional culture method, the Gram-negative rod was identified as *Elizabethkingia meningosepticum* on the same day of positive culture by using matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) Vitek mass spectrometry (VMS). The spectrum of VMS is shown in Figure 1. The patient's antimicrobial regimen was subsequently changed on the evening of hospital day 2, to levofloxacin 750 mg daily, trimethoprim-sulfamethoxazole 400 mg intravenous every 8 h, minocycline 100 mg every 12 h and rifampin 600 mg every 24 h. The regimen was derived from a review of the literature, 24 h prior to obtaining the conventional microbiological identification and sensitivities. The pathogen was susceptible to fluoroquinolones (minimal inhibitory concentration (MIC) \leq 1 μ g/mL for ciprofloxacin and $<$ 2 μ g/mL for levofloxacin) and trimethoprim-sulfamethoxazole (MIC \leq 2–38 μ g/mL), but was resistant to aminoglycosides, imipenem and piperacillin-tazobactam by using MicroScan WalkAway (Siemens, West Sacramento, CA, USA) with LabPro software and Clinical and Laboratory Standards Institute guidelines.¹ The patient's clinical status progressively improved, and within 72 h starting a tailored antibiotic regimen, her vital signs normalized.

Although this patient's initial neurological findings portended a poor prognosis, she exhibited early signs of neurological recovery with spontaneous movement of her extremities and head, eye tracking, as well as facial grimacing with withdrawal to pain. Magnetic resonance imaging of the brain performed on hospital day 6 revealed leptomeningeal enhancement compatible with a diagnosis of meningitis, but no other findings that could explain here neurological status. After a

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Received 21 December 2012; revised 18 February 2013; accepted 26 February 2013

Table 1 Laboratory evaluation

Test	Result	Reference range
Chemistry		
Sodium	131	132–144 mEq/L
Potassium	3.7	3.4–5.1 mEq/L
Chloride	98	101–111 mEq/L
Bicarbonate	17	22–32 mEq/L
Urea nitrogen	62	8–22 mEq/L
Creatinine	3.8	0.4–1.0 mg/dL
AST	180	10–42 U/L
ALT	70	14–54 U/L
Alkaline phosphatase	73	38–141 U/L
Total bilirubin	1.1	0.3–1.6 mg/dL
Creatine phosphate kinase	4367	38–234 U/L
Hematology		
WBC	9.2	4.0×10^3 – 8.5×10^3 / μ L
%Neutrophils	81	25%–62%
%Bands	18	<13%
RBC	4.1	3.9×10^6 – 5.2×10^6 / μ L
Hemoglobin	11.7	11.5–15.5 g/dL
Hematocrit	35.1	35.0%–45.0%
Platelet count	172	140×10^3 – 440×10^3 / μ L
Cerebrospinal fluid		
WBC	0	<11/ μ L
RBC	28	0 μ L
Protein	67	15–45 mg/dL
Glucose	53	40–70 mg/dL

Abbreviations: AST, aspartate aminotransferase test; ALT, alanine aminotransferase; WBC, white blood cell; RBC, red blood cell.

hospital course of 2 weeks, she was discharged to a long-term acute care hospital where she received 6 weeks of levofloxacin, minocycline and trimethoprim-sulfamethoxazole. By 8 weeks post-discharge, the patient had become alert and oriented and was actively participating in physical and occupational therapy, albeit with residual receptive aphasia.

DISCUSSION

E. meningosepticum, previously known as *Flavobacterium* and reclassified as *Chryseobacterium*,² was initially identified by Dr Elizabeth

King as a causative agent of meningitis in neonates.³ *E. meningosepticum* infections, whether in infants or adults, are mostly nosocomial, with less than 15% acquired in the community.^{4,5} Case reports have described patients with endocarditis, cellulitis, necrotizing fasciitis, hepatitis, osteomyelitis and eye infections, in addition to the more common *E. meningosepticum* bacteremia and pneumonia.⁴ The majority of infections in neonates present as meningitis. However, *E. meningosepticum* meningitis in adults is rare. Only 16 cases have been described worldwide; 15 of these cases described patients who had underlying comorbidities or who had undergone surgical procedures (Table 2).

E. meningosepticum is found ubiquitously in freshwater, saltwater and soil.⁶ However, the majority of *E. meningosepticum* infections are nosocomial in origin.^{4,5} As a biofilm-forming organism, it commonly colonizes sink drains and medical equipment such as ventilators, intravascular catheters and surgical tools, as well as solutions such as chlorhexidine.⁷ Hospital isolates are thought to be the underlying cause of sporadic nosocomial outbreaks. Positive screening cultures should, however, be interpreted cautiously, as only 60% have shown clinical correlation with an infectious process.⁵ Risk factors for *E. meningosepticum* infections relate to underlying immune dysfunction. In neonates, the main risk factor for *E. meningosepticum* infection is prematurity.⁵ Most adults with *E. meningosepticum* meningitis suffer from comorbidities such as hematologic malignancies, diabetes or have recently undergone surgical procedures (Table 2). In two retrospective case studies of *E. meningosepticum* bacteremia, the most common comorbidities were cancer and diabetes mellitus.⁴ Mortality rates in these patients are as high as 53%.^{4,5} Although one case involved a 46-year-old man with no known underlying systemic disorder who succumbed to meningitis,⁸ no immunologic evaluation was performed prior to his death. Our patient had regular follow-up visits with her primary care physician. Screening colonoscopy and mammogram were completed the year prior to presentation and were unremarkable. She had never been on corticosteroids. HIV antibody and a viral hepatitis panel were negative. Her hemoglobin A1C was 6.0%. Serum immunoglobulin and complement levels were within normal limits and anti-nuclear antibody screen was non-reactive.

Table 2 : Characteristics of *E. meningosepticum meningitis* reported cases in adults

References	Age, Sex	Underlying condition	Treatment	Outcome	Source
15	17, Male	Thalassemia major, splenectomy	Vancomycin for 21 days	Cured	NR*
16	88, Female	Diabetes mellitus, cellulitis	NR	Died	Community
11	21, Female	Diabetes mellitus	Cefepime for 21 days	Cured	Community
17	27, Female	Acute myelogenous leukemia	Rifampicin, piperacillin, ciprofloxacin for 23 days	Cured	Nosocomial
18	–	–	–	–	–
19	NR	Myelography	NR	NR	Nosocomial
8	43, Male	NR	Piperacillin, cefoperazone, minocycline erythromycin	Died	Community
20	56, Female	Pituitary tumor s/p transphenoidal hypophysectomy	Rifampin, cefoperazone, chloramphenicol	Cured	Nosocomial
21	60, Male	Squamous cell cancer s/p resection	Amikacin, erythromycin for 25d	Cured	Nosocomial
22	26, Female	CKD, renal transplant, tuberculosis	Erythromycin	Died	Nosocomial
23	66, Female	Acute myelogenous leukemia	Erythromycin	Died	Nosocomial
24	43, Male	Squamous cell cancer s/p irradiation/ resection	Ampicillin	Cured	Community
25	19, Male	Aplastic anemia	Neomycin IV/intrathecal	Died	Nosocomial
26	33, Male	Pulmonary tuberculosis, malnutrition	Chloramphenicol, erythromycin	Died	NR
27	NR	Postpartum	NR	NR	NR
3	NR	Polycythemia	NR	Cured	NR

Abbreviations: CKD, chronic kidney disease; NR, not reported; – unavailable

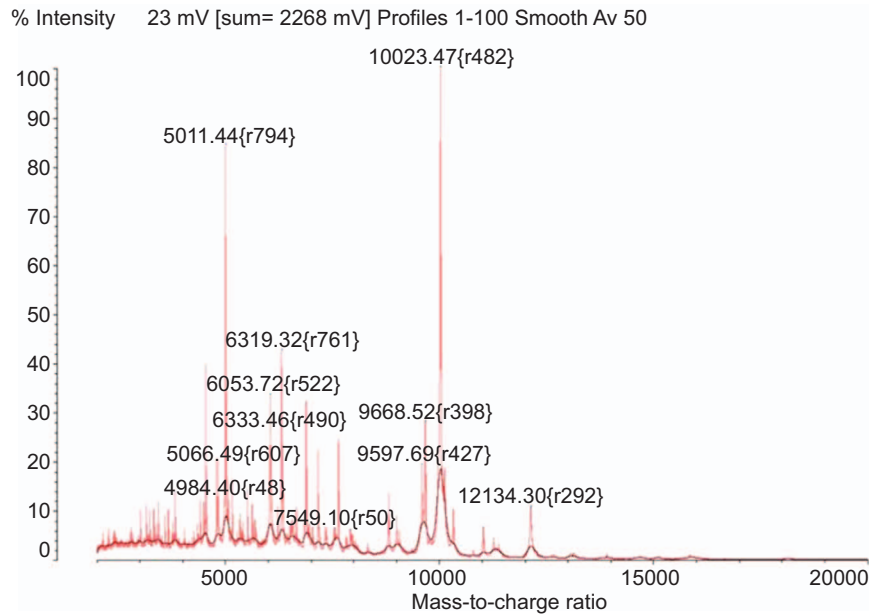


Figure 1 *E. meningosepticum* spectral signature from Vitek MS with SARAMIS RUO software.

Thus, *E. meningosepticum* meningitis can occur in an immunocompetent host.

E. meningosepticum's unusual antimicrobial sensitivity is due to its production of two different metallo- β -lactamases, conferring the ability to degrade all β -lactam antibiotics.⁹ Antibiotic susceptibility profiles vary across the reported literature^{4,5} and thus, there is no consensus on appropriate therapy. The largest study examining 99 isolates and their susceptibilities to 19 antimicrobial agents suggested that *E. meningosepticum* is most sensitive to trimethoprim-sulfamethoxazole (91%), followed levofloxacin and moxifloxacin (81%–87%), doxycycline and piperacillin-tazopactam (78%).⁴ The SENTRY report examining 24 isolates noted 87% susceptibility to rifampin.¹⁰ Aminoglycosides and vancomycin have shown poor activity against *E. meningosepticum*.⁴

The CSF findings in this case illustrate potential diagnostic challenges. Three out of 10 cases reporting CSF findings of adult patients with *E. meningosepticum* meningitis showed a paucity of CSF inflammation as low as 6 white blood cells (WBCs)/ μ L.¹¹ In this patient's case, there were 0 WBCs/ μ L in the initial CSF obtained during extraventricular drain insertion, despite positive Gram stain and culture. These findings show that meningitis caused by this organism cannot be ruled out with a very low or even normal CSF WBC count.

Rapid bacteriologic identification is essential as *E. meningosepticum* is typically resistant to the common antimicrobials used to empirically treat Gram-negative rod infections. MALDI-TOF Mass Spectrometry (MS) technology provided the diagnosis within 24 h of admission. Its utility in protein profiling has emerged as a powerful tool for the rapid

identification of bacteria and yeast isolates.¹² MALDI-TOF MS can be performed very quickly, requiring a mean of a few minutes per sample to identify an isolate, and with high accuracy.¹³ In this case, MALDI-TOF VMS aided management by providing an early identification of an unusual and inherently resistant organism, allowing adjustment of the antibiotic regimen (Table 3). The Vitek MS RUO System with SARAMIS database by bioMérieux (Durham, NC, USA) is a research use only MALDI-TOF MS system for rapid detection of bacterial and yeast isolates. The MALDI-TOF VMS analysis was performed by using the Shimadzu instrument and the SARAMIS database originally developed by AnagnosTec GmbH and later acquired by bioMérieux.¹⁴ With this technique, colonies from the bacterial culture plate were placed on disposable VMS target plates (cat. no. 220-99999-FM1; Shimadzu Biotech, Columbia, MD, USA) by using disposable loop, overlaid with 1 μ L α -cyano-4-hydroxycinnamic acid matrix (bioMérieux cat. no. 411071), and then air dried before being processed by the spectrometer. The result is a spectral fingerprint which is unique to each species, as the mass peaks reflect ribosomal and other constitutive proteins (Figure 1). The spectral signature is cross-referenced in a database to identify the organism according to its genus or species. The percent of confidence identification ranged from 76% to 89.9%. Within 24 h, the result was confirmed by conventional method using MicroScan (Siemens, West Sacramento, CA, USA) Gram-negative identification panel with 99.9% probability of *E. meningosepticum* and later by Vitek2 Gram-negative card (bioMérieux). In general, SARAMIS confidence level of $\geq 75\%$ is acceptable for identification. For confirmation of bacterial identification by conventional method

Table 3 Timeline of bacterial identification

Day 0	Day 1	Day 2	Day 3	Day 4
Blood was collected	Blood culture was positive, and subculture to plate	Positive growth, identified by MALDI-TOF MS	Identification by conventional method	Antimicrobial susceptibility testing by conventional method
	CSF was collected	Positive growth, identified by MALDI-TOF MS	Identification by conventional method	Antimicrobial susceptibility testing by conventional method

Abbreviations: CSF, cerebrospinal fluid.

such as MicroScan, the isolate was sent to another laboratory (Dr Xiang-Yang Han of MD Anderson in Houston, TX, USA) for 16S ribosomal RNA sequencing. It was identified as *Elizabethkingia meningoseptica* with a score of 1056 bits (1170) and identities 587/588 (99%). MALDI-TOF MS was performed for all isolates; blood, CSF, tissue, as well as sputum samples, identifying the same bacterium with identical spectrum, as well as antimicrobial susceptibility profile.

CONCLUSION

E. meningosepticum is a virulent pathogen, not only in the immunocompromised host, but also in immunocompetent patients. Clinical and laboratory manifestations of *E. meningosepticum* infections are not pathognomonic; thus, early microbiological diagnosis using emerging automated technology such as MALDI-TOF MS is essential in selecting appropriate therapy. As the available data suggest 81% to 91% of isolates are sensitive to trimethoprim-sulfamethoxazole, levofloxacin and rifampin, early identification could predict the antimicrobial susceptibility pattern and help clinicians to choose the right antibiotics.

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