Case Report

Neonatal meningitis caused by Elizabethkingia meningoseptica in Saudi Arabia

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Abstract

Elizabethkingia meningoseptica is a multi-drug resistant organism that can cause meningitis in premature neonates. We report a case of *Elizabethkingia meningoseptica* meningitis that was detected early in an extremely premature low birth weight infant. He was successfully treated with a combination of ciprofloxacin and piperacillin-tazobactam. The spread of infection was controlled with no other reported cases.

Key words: *Elizabethkingia meningoseptica*; meningitis; premature neonates

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Introduction

Elizabethkingia meningoseptica (*E. meningoseptica*), formerly known as *Chryseobacterium meningosepticum*, is a glucose non-fermenter, non-motile, catalase and oxidase positive, aerobic Gram-negative bacilli found typically in plants, soil and water sources, including in the hospital environment [1]. This ubiquitous Gram-negative bacillus is historically associated with meningitis and sepsis in premature neonates but rarely causes infection in immunocompetent individuals [2]. In neonates, meningitis is the most common form of infection; it is fatal in more than half of the cases and may produce brain abscess and other severe post infection sequelae including hydrocephalus, deafness, and developmental delay [3,4]. The organism is sometimes responsible for epidemics of sepsis and meningitis in newborn infants in hospital nurseries [2,5]. We report one case of *E. meningoseptica* in an extremely premature low birth weight infant.

Case report

The patient was born by vaginal delivery after 27 weeks of gestation and weighed 840 grams. His mother was primigravida, with premature rupture of the membrane for 36 hours. There was no evidence of chorioamnionitis, and dexamethazone and notocolytic were administered. The infant was ventilated, and blood cultures taken at birth in the neonatal intensive care unit (NICU) showed no growth. On day 8 post-birth, the baby became lethargic and appeared ill. A septic screen was performed and empirical treatment with cloxacillin and cefotaxime was initiated; the child developed convulsions which were controlled through intravenous phenobarbitone. Additional blood culture was negative for bacterial growth, and cerebrospinal fluid (CSF) test results were inconclusive for meningitis (protein: 156 mg/dl; glucose: 84 mg/dl [blood glucose: 96 mg/dl]; white blood cell (WBC) count and red blood cell (RBC) count in CSF were 28/µl and 24,000/µl respectively). C-reactive protein was negative. One day later, C-reactive protein became positive (65 mg/l) and WBC count had increased from 11,340/µl to 49,300/µl, predominantly polymorphs. CSF culture performed on day 8 of life revealed light growth of Gram-negative bacilli on blood and chocolate agar; there was no apparent growth on MacConkey agar. Colonies on blood agar appeared pale yellow with grayish discoloration on the periphery. Preliminary microbiological identification showed that the bacterial isolates were positive for catalase, oxidase, and indole. The bacterium was identified as *E. meningoseptica* was made using VITEK 2 (bioMerieux, Marcy l'Etoile, France) with 99% confidence. Antimicrobial sensitivity testing was performed by using the microdilution method on the VITEK 2 and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) for non-

Enterobacteriaceae and Staphylococcus spp. as there is no reproducible definitive standard to interpret the antibiotic sensitivity results for *Chryseobacterium* species [6]. The organism was resistant to all beta-lactam antibiotics tested (imipenem, meropenem, aztreonam, cefepime, ceftriaxone, cefotaxime, cefoxitin, cefuroxime and cephalothin), as well as amoxicillin-clavulanic acid, aminoglycosides, doxycycline and trimethoprim-sulfamethoxazole. The isolated *E. meningoseptica* demonstrated intermediate sensitivity to vancomycin (MIC 8 μg/ml) but was sensitive to piperacillin/tazobactam (MIC 8/4 μg/ml) and ciprofloxacin (1 μg/ml).

Swabs were taken from various environmental sources, specifically, hand-washing sinks and taps; infusion pumps; oxygen humidifiers; drinking fountains; ventilator surfaces and tubes; intravenous fluid stands; hand soap dispensers; bedside shelves, cabinets and drawers; and stethoscopes. Additionally, 0.5 ml of tap water was collected after flushing the system for five minutes. All specimens were cultivated on 5 ml trypticase soy broth and incubated for 48 hours then subcultured on blood agar. Any growth suggestive of *E. meningoseptica* was further isolated and identified, but no source for the contamination could be determined.

Based on the laboratory determination of antimicrobial susceptibility, ciprofloxacin therapy was started on day 11 after birth as the treatment of choice. Cranial ultrasound on day 17 of birth showed intraventricular hemorrhage grade II with mild ventriculomegally. On day 20 post-birth, CSF testing was repeated and revealed protein: 400 mg/dl, glucose: 8 mg/dl and WBCs: 870 /μl with few RBCs; microbial culture and identification demonstrated growth of *E. meningoseptica* with the same antimicrobial susceptibility pattern. We concluded that monotherapy was ineffective and combination therapy was indicated. Subsequently piperacillin-tazobactam was added to the treatment regimen. Blood culture collected on that date showed no growth.

Combination therapy of ciprofloxacin and piperacillin-tazobactam was continued for three weeks and the patient showed marked clinical improvement. Over this time, C reactive protein became negative, blood and CSF samples were culture-negative, no subdural or abscess formations were noted, and brain imaging revealed no further increase in ventricular size.

The patient was discharged, aged three months. His weight was 1.848 kg and he was able to breathe unaided and had satisfactory suckling power. Follow-up cranial ultrasound, at time of discharge, showed no post hemorrhagic ventricular dilatation.

Discussion

E .meningeoseptica is a ubiquitous waterborne saprophytic bacillus not considered part of the normal human flora. It rarely causes infection in the post-neonatal immunocompetent host [7]. Intermittent epidemics in neonatal intensive care units (NICU) have been reported [8]; however, the exact source of these infections is often not elucidated. Environmental studies have shown that this organism can survive in chlorine-treated water, often colonizing sink basins and taps and in ventilator tubing [3,4]. Concurrent with this case, there was an outbreak of *Klebsiella pneumoniae* infection in the NICU. The *K. pneumoniae* infection was controlled through infection control practices and intensified environmental cleaning; application of these measures may explain the failure to detect the source of infection. No subsequent cases of *E. meningoseptica* were detected within the NICU or any other location within the health-care facility.

The virulence factors responsible for invasive *E. meningoseptica* disease have not yet been fully elucidated. In an immunocompetent host, this bacterium is cleared rapidly by immune defenses without antibiotic treatment. Premature birth is a primary risk factor for neonates, and half of the reported *E. meningoseptica* infections involving neonates have involved infants who weighed less than 2,500 grams at birth [4,9]. The subject of this case report was a premature infant with extremely low birth weight who developed meningitis with minimal sequelae, most probably due to early identification of the pathogen and proper management.

E. meningoseptica is resistant to most antibiotics, and the use of inappropriate drugs as empirical therapy may contribute to the poor outcome in many infections [4]. Results of susceptibility testing vary when different methods are used; disk diffusion methods appear to be especially unreliable so broth microdilution should be employed [10]. Due to the production of two beta lactamases, one ESBL and one class B carbapenem-hydrolyzing metallolactamase, many *E. meningoseptica* strains are usually resistant to extended-spectrum beta-lactam agents including carbapenems and aztreonam [10,12]. In addition, the organism is resistant to aminoglycosides, chloramphenicol and erythromycin, while in vitro, however, fluoroquinolones have been reported to be active. Controversy about the effectiveness of

vancomycin, trimethoprim-sulfamethoxazole and doxycycline has been reported [4,10-14]. The strain isolated from this patient was resistant to all beta-lactam antibiotics, amoxicillin-clavulanic acid, aminoglycosides, doxycycline and trimethoprim-sulfamethoxazole when tested by broth microdilution. The organism was sensitive to ciprofloxacin and piperacillin-tazobactam. This pattern of resistance is consistent with previous studies although a recent study showed variable susceptibilities to levofloxacin, ciprofloxacin, piperacillin-tazobactam and tigecycline [15]. While some studies have shown that the optimal regimen for serious infection by *E. meningoseptica* is ciprofloxacin plus trimethoprim-sulfamethoxazole [4,5,14], our case responded successfully to a combination therapy of ciprofloxacin and piperacillin-tazobactam for three weeks with minimal complications.

In conclusion, *E. meningoseptica* should be considered as a cause of sepsis and meningitis in premature low birth weight infants in any neonatal intensive care unit and the treatment of choice should be a combination of a quinolone/fluoroquinolone with another antimicrobial agent such as piperacillin-tazobactam, determined according to antibiotic susceptibility. Early diagnosis and proper management permits treatment of the infection with minimal sequelae. In addition, intensified environmental cleaning with proper infection control practices can successfully control the spread of infection.

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