

Successful control of *Elizabethkingia meningoseptica* outbreak in a neuro-surgical intensive care unit of a tertiary care center in India

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Abstract

Elizabethkingia meningoseptica has been found to be associated with a broad range of infections, most notably outbreaks of neonatal meningitis. In adults, it can also cause pneumonia, endocarditis, bacteremia, meningitis and even skin and soft tissue infections, primarily in immunocompromised individuals.

We report a cluster of 3 cases with *E. meningoseptica* infection in an adult neurology critical care unit of a 400-bedded tertiary care hospital situated in Gurugram (Delhi-National Capital Region), India.

Two patients were diagnosed with ventilator-associated-pneumonia (VAP) and one was a patient in whom the organism was isolated from a cerebrospinal fluid (CSF) sample. Clinical details were studied and outbreak investigation was carried out. We found the following common risk factors for infection: prolonged ICU stay, exposure to multiple antibiotics, presence of underlying co-morbidities and insertion of multiple invasive medical devices.

E. meningoseptica was isolated from the catheter mount connected between endotracheal tube and ventilation circuit of one patient but clonality could not be studied. Strict infection control protocols and environmental cleaning procedures terminated the outbreak.

Keywords: outbreak, *Elizabethkingia meningoseptica*, neurosurgery, India

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Introduction

Elizabethkingia meningoseptica, originally described as *Flavobacterium meningosepticum* by Elizabeth O. King in 1959, is a ubiquitous organism found widely distributed in nature.¹ It is a non-fermenting, non-motile, oxidase-positive gram-negative bacillus which is commonly found in soil and water.² *E. meningoseptica* has been found to be associated with a broad range of infections, most notably outbreaks of neonatal meningitis.³ In adults, it can also cause pneumonia, endocarditis, bacteremia, meningitis and even skin and soft tissue infections, primarily in immunocompromised individuals.^{4,5} Very few outbreaks of infection due to this organism in adult healthcare settings have been reported from developing countries like India. We report a cluster of 3 cases with *E. meningoseptica* infection in an adult neurology critical care unit of a 400-bedded tertiary care hospital situated in Gurugram (Delhi-National Capital Region), India.

Background

Environmental niches of *E. meningoseptica* include chlorine-treated municipal water supplies, including sink basins and taps and creating potential reservoirs for infections inside hospital settings. Colonization of patients occurs via contaminated medical devices involving fluids (respirators, intubation tubes, humidifiers, incubators for newborns, syringes, ventilator T-piece etc.).^{6,7} Contaminated surgically implanted devices such as intravascular catheters and prosthetic valves have also been reported.⁸ Additionally, *E. meningoseptica* has been associated with colonization of the respiratory tract in ventilated adult patients, but where some centers have attributed the pathogenicity of this organism to its role in causation of ventilator-associated pneumonia, others have found no attributable disease from colonization.^{7,9} It is known to be a highly multi-drug resistant organism, thereby limiting choice of therapeutic antibiotics especially in ICU settings.

The laboratory diagnosis of this organism is not easy due to difficulties in culture, including variable growth on MacConkey agar.² Even though *E. meningoseptica* is an emerging nosocomial pathogen, outbreaks of the same are grossly under-reported from developing countries like India where automated laboratory platforms for proper identification of the organism are not available in resource limited settings.

Materials and Methods

Setting

The outbreak occurred in a 16-bed neurosurgical intensive care unit (NICU) of a tertiary care hospital in Delhi-NCR. This hospital is Joint Commission International (JCI) and National Accreditation Board for Hospitals (NABH, India) accredited with comprehensive institutional policies for infection prevention and control and antimicrobial stewardship. Critical care staffing levels meet requisite benchmarks and a proactive infection control team provides support with antimicrobial prescription, surveillance cultures for multi-drug resistant organisms (MDROs) and outbreak investigations.

CASES: Over a period of one month (September 2016), 3 cases of *E. meningoseptica* infection were identified. Two patients were diagnosed with ventilator-associated-pneumonia (VAP) in whom *E. meningoseptica* was grown from respiratory tract samples and one was a patient in whom the organism was isolated from a cerebrospinal fluid (CSF) sample.

Microbiological Investigation

Respiratory samples from these patients were collected and sent to the microbiology laboratory for culture and identification of pathogen. Quantitative culture done on MacConkey agar and sheep blood agar showed significant growth of pathogen ($\geq 10^5$ CFU/ml). CSF sample of one patient was additionally cultured on chocolate agar also and inoculated in Brain-Heart infusion broth for sub-culture to look for fastidious organisms. The bacterial identification was done in VITEK®2 automated system (bioMérieux, Marcy l'Etoile, France) along with MIC based antibiotic sensitivity. Antibiotics like rifampicin and vancomycin were tested by the Kirby-Bauer disc diffusion method. As there is no consensus on standardized susceptibility breakpoint for this pathogen, zone sizes for *Staphylococcus aureus* (ATCC 25923) were used to interpret zone diameters for these antibiotics.

Outbreak Investigation

Chart reviews of all case-patients were done to determine age, gender, underlying co-morbidities, hospital course of treatment, time elapsed from hospital admission to the *E. meningoseptica* infection, length of intensive care unit stay (LOS ICU), use of invasive

procedures such as peripheral or central catheters, urinary catheter and mechanical ventilation, surgical procedures, antibiotic therapy following infection, time elapsed from the *E. meningoseptica* infection to death and presence of infection before, during and after isolating *E. meningoseptica* and antimicrobial exposure history.

All relevant data were entered in Healthcare-Associated Infection (HAI) surveillance forms based on the format prescribed by the CDC (Atlanta, USA).¹⁰ In order to identify the source of the organism, environmental surveillance swabs were collected from sinks, faucets, irrigation systems, airway humidifier vents and tubings, patient beds, bedside tables, cardiac monitors, flasks, dialysis machines. Samples of chlorhexidine mouthwash, normal saline, feeding bag, hand sanitizer and overhead water tank of the ICU were also tested. Hand and nasal swabs of clinicians, nurses and other health-workers were sent for culture to rule out horizontal transmission.

Environmental swabs were inoculated into 5 mL trypticase soy broth and incubated for 48 hours at 35-37°C. After 48 hours, they were subcultured on sheep blood agar and MacConkey agar and incubated for 18-24 hours at 35-37°C.

Any bacterial growth was further processed for identification in the VITEK®2 system.

All data were tabulated and analyzed.

Results

Three cases of *E. meningoseptica* infection were reported in our NICU in the month of September 2016. Two patients were admitted following haemorrhagic stroke and underwent surgery for the same, while one was admitted for a cerebral infarct and managed conservatively. The following clinical features were found to be common to all three patients:

- a. Prolonged ICU stay: Average length of stay was 54 days and average time period between admission to ICU and acquisition of infection was 15.67 days.
- b. Exposure to multiple antibiotics especially colistin prior to acquiring *E. meningoseptica* infection.

- c. Presence of underlying co-morbidities.
- d. Insertion of multiple invasive medical devices.

The organism showed similar antibiotic susceptibility pattern in all cases and was sensitive to levofloxacin, ciprofloxacin, rifampicin and minocycline. All three isolates were resistant to vancomycin.

Molecular typing to study clonality could not be done due to lack of facilities for the same.

The clinical details of concerned patients are shown in table I.

Outcome of Outbreak Investigation

E. meningoseptica was isolated from the catheter mount connected between endotracheal tube and ventilation circuit of Patient-2 (refer to Table I). The rest of the environmental swabs did not yield any growth of *Elizabethkingia* spp.

During the outbreak, potentially hazardous procedures and practices were screened and vigorous infection control measures were instituted to eliminate the risk of acquisition and further transmission of infection amongst NICU patients. Medical and nursing staff was instructed to stop the use of multiple doses from vials of medication or fluids intended for single use only. The importance of hand disinfection in between contact with different patients was re-emphasized. In addition to new suction catheters being used for each patient as was the previous practice, suction containers and tubes were changed and disinfected more regularly. The duration of use of catheter mount and bacterial filter was reduced from 72 hours to 24 hours after which it was replaced.

From October 2016 till date, no case of infection with *E. meningoseptica* has occurred in NICU.

Discussion

Ventilator associated pneumonia outbreaks caused by *E. meningoseptica* have been described in acute care facilities but there are very few reports from India detailing such outbreaks and subsequent infection control interventions. Weaver *et al.* concluded that in patients treated with prolonged mechanical ventilation or harbouring this infection, caution is important as

Table I. Clinical details of concerned patients

S. No.	Age (years) /Sex (m/f)	Underlying Co-morbidities	Primary Diagnosis	Surgical procedure	Los Icu (Days)	Time between Admission & Infection (days)	Other associated infections
1.	75/F	DM, HTN	Left sided intra-cerebral haemorrhage	Decom-Pressive Craniotomy	68	16	VAP due to MDR <i>Acinetobacter baumannii</i>
2.	66/M	HTN, CAD + CCF Carcinoma palate (post RT) + lung metastasis	Left cerebral (caudal) infarct	Nil	44	12	Previous episode of VAP & subsequent CAUTI due to MDR <i>K. pneumoniae</i>
3.	66/M	HTN, CAD, complete heart block	Right parieto-occipital intra cerebral haemorrhage	Decom-pressive Craniotomy	50	19	Previous episode of VAP due to MDR <i>Acinetobacter baumannii</i>

S. No.	Infection syndrome (due to E. M.) & Sample	Anti-microbial Exposure history	Anti-microbial therapy for E.M.	New onset chest x-ray changes	Invasive device insertion	Microbio-logical Outcome	Clinical outcome
1.	Meningitis CSF	PTZ, AK, MTZ, COL	MIN + FQ	Not applicable	EI, CVC, UC, PVC, ommaya reservoir	Follow-up CSF culture was sterile	Died
2.	Pneumonia BAL	PTZ, COL, CIP, MTZ	MIN + FQ	Yes	EI, CVC, PVC, UC	Follow up E.T. Culture showed no growth of e.M.	Died
3.	Pneumonia Endo-tracheal aspirate	PTZ, COL, TIG, CFT	MIN + FQ	Yes	EI, CVC, PVC, UC	Follow up E.T. Culture showed no growth of E.M.	Discharged in stable condition

Key: AK, amikacin; BAL, broncho-alveolar lavage; CAD, coronary artery disease; CAUTI, catheter associated urinary tract infection; CCF, congestive cardiac failure; CFT, ceftriaxone; CIP, ciprofloxacin; COL, colistin; CVC, central venous catheter; DM, diabetes mellitus; EI, endotracheal intubation, EM, *elizabethkingia meningoseptica*; FQ, fluoroquinolone; HTN, hypertension; MV, mechanical ventilation; MDR, multi-drug resistant; MIN, minocycline; MTZ, metronidazole; PVC, peripheral venous catheter; PTZ, piperacillin-tazobactam; TIG, tigecycline; UC, urinary catheter; VAP, ventilator-associated-pneumonia

such patients could serve as an important source of transmission of this multidrug resistant non-fermenting bacteria.¹¹ Colonization or infection could contaminate water sources and wet areas like taps and sinks in ICU and cause environmental contamination. This in turn would lead to a cycle of cross-contamination and infection in susceptible patients.^{9,12}

Jean *et al.* discuss risk factors for acquiring infection in their review article.¹³ They report that almost all cases of bacteraemia due to *E. meningoseptica* occur in nosocomial settings and that such patients usually have a history of multiple antibiotics exposure and/or pre-existing comorbidities. Infections with *E. meningoseptica* have also been associated with prolonged hospitalisation, prior exposure to multiple antibiotics, and immunocompromised host in other studies.^{4,5,14} We observed similar findings in our setting where all 3 patients had the aforementioned risk factors (Table I).

It is difficult to determine the most appropriate choice of antimicrobial therapy for this organism. Studies have shown susceptibility of *E. meningoseptica* to piperacillin, piperacillin-tazobactam, trimethoprim-sulfamethoxazole, ciprofloxacin, levofloxacin, vancomycin, rifampicin, tigecycline and moxifloxacin.^{4,14-16} Vancomycin was recommended to be the drug of choice in earlier studies but several groups contradicted this later since they found variable sensitivity patterns.^{3,17,18} Resistance to vancomycin was observed in all 3 isolates at our centre and patients were treated with a combination of minocycline and fluoroquinolones.

The most essential part of outbreaks management of *E. meningoseptica* infection are infection control measures which limit spread of the organism to other patients. Environmental sampling is important so as to attempt to identify a possible point source.¹⁵ Environmental sources of the bacterium are extremely important in the epidemiology of healthcare acquired outbreaks of *E. meningoseptica* infection. In this context, some investigators have reported success in controlling outbreaks using strict infection control protocols and environmental cleaning procedures.

Ceyhan *et al.*, for example, detail the control of an outbreak of a cluster of 13 paediatric cases.¹⁶ Even though an environmental source was not identified, the outbreak was terminated following introduction of hypochlorite solution and isopropanol spray for cleaning in the unit especially objects containing, or in contact with, water. Güngör *et al.* also described successful control of an outbreak following enhanced environmental decontamination.³ It was difficult to convincingly identify the source of the outbreak in this case also. The organism was isolated only from the swab taken from catheter mount. Hence, it was not clear if isolation of the organism was due to previous use on already colonized patient or whether it was the source of infection. Our outbreak terminated with these three cases and no subsequent infections with *E. meningoseptica* were identified due to timely and robust infection control measures.

Absence of typing data to study the isolate clonality is an important limitation of our study. However, reports with typing data reveal the widespread existence of multiple strains in aquatic niches within the hospital environments.^{6,9}

In conclusion *E. meningoseptica* is an important emerging opportunistic pathogen in hospital settings. There are very few case reports of outbreaks of VAP due to this organism especially from India. The prevalence of *E. meningoseptica* infections is increasing due to multiple causes like prolonged hospitalizations, immunocompromised states, rampant use of broad spectrum antibiotics in ICU settings, pre-existing comorbidities, concurrent or previous infections with MDR bacteria and exposure to invasive medical devices. Timely recognition of infections caused by this organism will assist in identifying and preventing an outbreak. Active efforts are required to investigate an outbreak and search for a possible source keeping in mind the epidemiological niche of the organism. Vigorous infection control interventions like strict hand-hygiene compliance, antibiotic stewardship, standard precautions and extensive environmental cleaning (especially wet surfaces and water sources) go a long way in controlling such outbreaks and improving outcomes in susceptible patients.

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