ANAESTHESIA, PAIN & INTENSIVE CARE
www.apicareonline.com

CASE REPORT

An uncommon Elizabethkingia meningoseptica septicemia in hemorrhagic stroke with septic shock patient during prolonged neuro-intensive care management

Wan Mohammad Nazaruddin Wan Hassan, MD, MMed (Anesth)[1], Ramissh Paramasivam, MD[2], Regunath Kandasamy, MBBS, MMed (Neurosurg)[1], Mohamad Hasyizan Hassan, MBBS, MMed (Anesth)[3], Rhendra Hardy Mohammad Zaini, MBBS, MMed (Anesth)[4]

[1]Senior Lecturer, [4]Lecturer, Dept of Anesthesiology and Intensive Care & P3 Neuro Clinical & Research Centre, [2]Resident, Dept of Neurosciences, [3]Senior Lecturer, Dept of Neurosciences & P3 Neuro Clinical & Research Centre, [5]Senior Lecturer, Dept of Anesthesiology and Intensive Care, School of Medical Sciences, University Sains Malaysia, Kota Bharu, Kelantan, (Malaysia)

Correspondence:
Dr. Wan Mohd Nazaruddin Wan Hassan, School of Medical Sciences, University Sains Malaysia, 16150 Kota Bharu, Kelantan, (Malaysia);
Tel: +60199630385;
E-mail: drnaza_anaest@yahoo.co.uk m

Received: 2 May 2017
Reviewed: 3 May 2017
Corrected: 7 May 2017
Accepted: 28 May 2017

ABSTRACT

Elizabethkingia meningoseptica septicemia is an uncommon nosocomial infection but has gradually emerged as the potential threat in intensive care setting. This organism is a multi-drug resistant, non-fermentative gram negative bacillus that is equipped with the ability to adapt to a spectrum of different environmental conditions. We report our first experience of managing *E. meningoseptica* septicemia in our ventilated hemorrhagic stroke patient with septic shock during prolonged neuro-intensive care management. The aim of this report is to highlight the update of this uncommon infection on incidence, risk factors, strategy of management and mortality related to it.

Key words: Elizabethkingia meningoseptica; Septicemia; Septic shock; Intensive care; Intensive Care Unit; Multi-drug resistance

Citation: Hassan WMNW, Paramasivam R, Kandasamy R, Hassan MH, Zaini RHM. An uncommon Elizabethkingia meningoseptica septicemia in hemorrhagic stroke with septic shock patient during prolonged neuro-intensive care management. Anaesth Pain & Intensive Care 2017;21(2):268-271

INTRODUCTION

Elizabeth meningoseptica, previously known as *Chryseobacterium meningosepticum*, is an important member of genus *Chryseobacterium*, a non-motile, non-fastidious, catalase negative and oxidase positive, aerobic glucose-non-fermentative gram-negative bacillus.[1]

It is frequently isolated from water sources within the soil, salt water, fresh water and even in adequately chlorinated municipal water supplies. The latter source has greatly contributed to extensive contamination by this organism within healthcare settings.[2] *E. meningoseptica* infection is uncommon but the awareness about its potential threat to life and the challenges in the management is still lacking. We report a case of *E. meningoseptica* septicemia in hemorrhagic stroke with septic shock patient during prolonged neuro-intensive care management.

Box 1: Patient's Laboratory Parameters	
Hemoglobin:	15.9 g/dL
White cell count:	10,100 cell/mm^3
Platelet count:	356,000 cell/mm^3
Sodium:	137 mmol/L
Potassium:	3.1 mmol/L
Blood urea:	4.4 mmol/L
Creatinine:	88 μmol/L and
Blood glucose:	14.5 mmol/L

CASE REPORT

A 58-year-old gentleman with history of hypertension, dyslipidemia and gouty arthritis, was brought to the hospital after being found unconscious at home. On admission, he was able to open his eyes spontaneously, localized to pain stimuli but without any verbal response (Glasgow coma score 10/15). On examination, his blood pressure was 153/90 mmHg, pulse rate was 92 beats per minute and temperature was 36.2 °C.

There were presence of facial asymmetry and right sided hemiparesis on neurological examination. His baseline full blood counts, renal function test and coagulation profile were within normal limits (Box 1).

A computerised tomography (CT) scan of his brain revealed an average volume of 20 cm^3 intraparenchymal hemorrhage in the left putaminal region. There was no significant midline shift, basal cistern effacement or intraventricular extension.Patient was subsequently planned to be managed conservatively by the neurosurgical team and he was admitted to the acute ward where close monitoring of his vital signs as well as stroke rehabilitation could be initiated.

After 72 hours of hospitalization, patient developed spikes of temperature (39 °C) associated with tachypnea and productive cough. Air entry in his lungs was equal with no adventitious sounds. However, a chest x-ray (CXR) showed presence of pneumonic changes. His total white cell count (TLC) at that time was 25,300 cells/cm^3 and C-reactive protein (CRP) was > 200 mg/L. Patient was empirically started on cefepime1g intravenous (IV) 8 hourly for hospital acquired pneumonia. Inj cloxacillin 1 g IV 6 hourly was added on the subsequent day for the treatment of thrombophlebitis which was newly identified on his right antecubital fossa.

On the 8th day of his hospitalization, patient developed worsening tachypnea due to an episode of aspiration during the attempt of oral feeding by his next of kin. After the next 48 hours, his condition was further deteriorated and required an intubation as well as neuro- intensive care unit management. He was treated as respiratory failure secondary to aspiration pneumonitis with underlying septic shock secondary to ongoing nosocomial pneumonia. He required fluid therapy as well as inotropic support and his antibiotic therapy was decided to be changed to inj piperacillin-tazobactam 2.25 g IV 8 hourly and inj metronidazole 500 mg IV 8 hourly based on his worsening condition. His hemodynamic status was improving with the therapy but he subsequently developed acute kidney injury with oliguria. His renal function showed blood urea level of 28.1 mmol/L, creatinine 574 μmol/L, sodium 160 mmol/L and potassium 5.1 mmol/L. He was then referred to nephrology team and planned for renal replacement therapy on alternate days with sustained low-efficiency daily dialysis (SLEDD).

On the 16th day of hospitalization, endotracheal tube (ETT) specimens that previously yielded no growth, isolated extended-spectrum β-lactamase (ESBL) *Klebsiella pneumoniae*. Based on this positive culture as well as worsening septic parameters (e.g. TLC 37.1 x 10^9/L and CRP > 200 mg/L) patient was subsequently put on meropenam 500 mg IV 12 hourly after renal adjustment dose. The patient initially responded to the antibiotic but after few days, there was another new onset of fever with new changes of pulmonary infiltration on CXR. After a week, repeat ETT culture came back with positive culture of multi-drug resistant (MDR) *Acinetobacter baumanii*. Therefore, polymyxin B 600,000 U 12 hourly was added to ongoing inj meropenem. At the same time, the blood culture and sensitivity result isolated *E. meningoseptica*, which was only sensitive to ciprofloxacin and trimethoprim-sulfamethoxazole. In view of his still unresolved septic shock, ciprofloxacin 400 mg IV 12 hourly was also started in addition to the two ongoing antibiotics.

In view of his prolonged ventilation and ventilator-associated pneumonia, tracheostomy was performed. After tracheostomy and commencement of ciprofloxacin, his spiking temperature improved and subsequent serial of TLC and CRP levels were gradually normalized. CXR image also improved and

he was managed to be weaned off from inotropic and ventilatory support. Repeat ETT culture and sensitivity on the 36th day of admission revealed a mixed growth of organisms suggesting of contamination but the blood sample showed a negative culture. Renal function and biochemical parameters also improved after serial dialyses with recent urea level of 9.5 mmol/L and creatinine level 147 µmol/L. Repeat CT brain showed resolving blood clot with no mass effect to adjacent structures in the brain. However, patient developed an acute coronary syndrome on 38th day of admission and expired because of his cardiac complication.

DISCUSSION

This was the first case of septicemia related to MDR *E. Meningoseptica* in our neuro ICU involving neurosurgical patient. Even though *E. meningoseptica* related infection is infrequent but its involvement as causative organism for hospital acquired infections is increasingly recognized. A study on 118 patients with *E. meningoseptica* bacteremia at a medical centre in Taiwan from 1999 to 2006 showed a significant increase of the incidence (per 100,000 admissions) from 7.5 in 1996 to 35.6 in 2006. Among them, 86% had nosocomial infections, and 60% had acquired the infection in ICU[3]. In our case, the *E. meningoseptica* septicaemia is actually acquired while the patient was on treatment in neuro ICU.

The potential risk factors that have been previously identified for developing *E. meningoseptica* bacteremia include preterm children, malignancies, steroid use, diabetes mellitus, neutropenia, organ transplantation, chronic hemodialysis therapy, immunocompromised patients and those exposed to antibiotics in critical care units.[2,4] The data from Taiwan showed that the most common underlying diseases in *E. meningoseptica* septicaemia cases were malignancy (36%) and diabetes mellitus (25%). If based on the site of infection, 78% of them had primary bacteremia, followed by pneumonia (9%), soft tissue infection, and catheter-related bacteremia (6%). 38% of them actually had polymicrobial bacteremia.[3] In our case, the patient was noted to have elevated blood glucose level on admission which might indicate the possibility of undiagnosed diabetes mellitus. In spite of without HbA1c level, serial measurement of elevated blood glucose levels might indicate us that our patient might have the possibility of diabetes mellitus as one of the risk factor. The other potential risk factors for our patient were other ongoing MDR infections with ongoing multiple antibiotics, renal replacement therapy for septic shock related acute kidney injury and prolonged mechanical ventilation.

The source of organism is most likely from contaminated water supply, hospital equipment and environment. A study on *E. meningoseptica* in a Beijing hospital showed that 26 *E. meningoseptica* isolates were obtained from 487 collected samples from medical devices, hospital surfaces and medical staff hands. More than half of it were from the sinks, faucets, and drains.[5] Saline, lipid and chlorhexidine gluconate solutions as well as contaminated sinks have also been implicated as sources of infection following outbreak investigations.[2] The isolation of this organism in handwash sink and water is a significant finding as they have been reported to survive in chlorinated water.[6] Arvanitidou M *et al.*, reported that *E. meningoseptica* is the second highest gram-negative bacteria isolated from tap water (6 isolates), treated water (8 isolates) and dialysate (8 isolates) of multicentre renal units.[7]

Over a seven-year period of observation on the clinical and microbiological profiles of infections due to *E. meningoseptica*in one of trauma centre in India, 16 out of 21 observed cases (76.2%) exhibited multidrug resistance.[8] It has been described that *E. meningoseptica* are inherently resistant to most of the antibiotics which are prescribed to treat gram negative bacteria, like aminoglycosides, β-lactam agents, chloramphenicol and carbapenems, but susceptible to the agents which are used to treat gram positive bacteria (rifampicin, ciprofloxacin, vancomycin and trimethoprim–sulfamethoxazole).[3,9] Other study showed that more than 80% of the *E. meningoseptica* bacteremia isolates were susceptible to trimethoprim-sulfamethoxazole, moxifloxacin, and levofloxacin.[3] However, the data from Beijing was slightly contradictory, which revealed that 56.7% of isolated *E. meningoseptica* was actually resistant to trimethoprim-sulfamethoxazole but all were sensitive to vancomycin and piperacillin/tazobactam.[5] According to in-vitro susceptibility data, another report mentioned that vancomycin, rifampicin, newer fluoroquinolones, piperacillin-tazobactam, minocycline and possibly tigecycline are preferred empirical choices for *E. meningoseptica* infection. Combination therapy has also been used for infections that are not responding to single agents.[2] In our patient, *E. meningoseptica* was resistant to most antibiotics, except for ciprofloxacin and trimethoprim-sulfamethoxazole. Concomitant infections by ESBL *K. Pneumoniae* and *A. baumanii* MDR which were isolated from tracheal aspirates, made our decision on the antibiotic treatment as slightly complicated. We decided to start

ciprofloxacin and the significant clinical improvement was subsequently seen in our patient. The resistance of *E. meningoseptica* to most of beta-lactam antibiotics can be due to the presence of three bla genes which have been identified in *E. meningoseptica*, coding for the extended-spectrum serine-beta-lactamase CME (class D) and two unrelated wide-spectrum metallo-beta-lactamases, BlaB (subclass B1) and GOB (subclass B3). E. meningoseptica is singular in being the only reported microorganism possessing two chromosomally encoded MBL genes.[10]

In addition to reinforcement of standard infection control measures, actions that have successfully terminated *E. meningoseptica* outbreaks include pre-emptive contact isolation, systematic investigations to identify the source of the bacterium and thorough cleaning of equipment and environmental surfaces.[2] Disinfecting the sinks and using filtered water for hand washing in critical areas may alsohelp in preventing infections with this organism.

The reported morbidity and mortality are varies with *E. meningoseptica* infection. A report in UK during the outbreak found that monomicrobial *E. meningoseptica* infection had an attributable morbidity rate of 54%.[11] Rastogi, *et al*, reported the observed in-hospital mortality rate of 47.6% and another study reported 41% of 28 days mortality rate. Based on multivariate[8,12] analysis, shock and the use of inappropriate antibiotics were independent risk factors for mortality.[12]

CONCLUSION

In conclusion, management of *E. meningoseptica* septicemia is a great challenge due to its being multi-drug resistant in nature. Ongoing other resistant polymicrobial infections with other ongoing antibiotics treatment, prolonged mechanical ventilation and renal replacement therapy as in our patient, might be the risk factors for this septicemia. Early and appropriate antibiotic treatment is important for the better outcome of this septicemia.

Conflict of interest: Nil declared by the authors

Authors' Contribution: WMNWH & RP: Concept, conduction of the study work, manuscript preparation and manuscript editing

RK: Conduction of the study work, manuscript preparation and manuscript editing

MHH& RHMZ: Manuscript preparation and manuscript editing

REFERENCES

1. Kim KK, Kim MK, Lim JH, Park HY, Lee ST. Transfer of Chryseobacterium meningosepticum and Chryseobacterium miricola to Elizabethkingia gen. nov. as Elizabethkingia meningoseptica comb. nov. and Elizabethkingia miricola comb. nov. Int J Syst Evol Microbiol 2005;55:1287-1293. [PubMed] [Free full text]
2. Jean SS, Lee WS, Chen FL, Ou TY, Hsueh PR. Elizabethkingia meningoseptica: an important emerging pathogen causing healthcare-associated infections. J Hosp Infect 2014;86:244-249. doi: 10.1016/j.jhin.2014.01.009 [PubMed]
3. Hsu MS, Liao CH, Huang YT, et al. Clinical features, antimicrobial susceptibilities, and outcomes of Elizabethkingia meningoseptica (Chryseobacterium meningosepticum) bacteremia at a medical center in Taiwan, 1999-2006. Eur J Clin Microbiol Infect Dis 2011;30:1271-1278. [PubMed]
4. Shinha T, Ahuja R. Bacteremia due to Elizabethkingia meningoseptica. IDCases 2015;2:13-15. doi: 10.1016/j.idcr.2015.01.002. [PubMed] [Free full text]
5. Jiang X, Wang D, Wang Y, Yan H, Shi L, Zhou L. Occurrence of antimicrobial resistance genes sul and dfrA12 in hospital environmental isolates of Elizabethkingia meningoseptica. World J Microbiol Biotechnol 2012;28:3097-3102. [PubMed] [Free full text]
6. Ratnamani MS, Rao R. Elizabethkingia meningoseptica: Emerging nosocomial pathogen in bedside hemodialysis patients. Indian J Crit Care Med 2013;17:304-307. doi: 10.4103/0972-5229.120323. [PubMed] [Free full text]
7. Arvanitidou M. Occurrence and antimicrobial resistance of Gram-negative bacteria isolated in haemodialysis water and dialysate of renal units: results of a Greek multicentre study. Journal of Applied Microbiology 2003;95:180-185. [Free full text]
8. Rastogi N, Mathur P, Bindra A, Goyal K, Sokhal N, Kumar S, et al. Infections due to Elizabethkingia meningoseptica in critically injured trauma patients: a seven-year study. J Hosp Infect 2016;92:30-32. doi: 10.1016/j.jhin.2015.07.008. [PubMed]
9. Dias M. Case Series: Elizabethkingia Meningosepticum. Journal of Clinical & Diagnosis Research 2012;6:1550-1551. doi: 10.7860/JCDR/2012/4076.2557. [PubMed] [Free full text]
10. Gonzalez LJ, Vila AJ. Carbapenem resistance in Elizabethkingia meningoseptica is mediated by metallo-beta-lactamase BlaB. Antimicrob Agents Chemother 2012;56:1686-1692. doi: 10.1128/AAC.05835-11. [PubMed] [Free full text]