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INFECTION DUE TO DRUG RESISTANT ELIZABETHKINGIA MENINGOSEPTICA IN A TERTIARY CARE HOSPITAL IN INDIA

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ABSTRACT Elizabethkingia meningoseptica is a Gram-negative nonfermentative bacilli found ubiquitous in soil, plants, water etc.. It is colonized in different medical devices like intravascular catheters, implanted devices etc. causing life-threatening infections like bacteremia, pneumonia, neonatal meningitis, sepsis, endophthalmitis, soft-tissue infections etc. primarily in the patients of intensive care units (ICUs). This study highlights the emergence of E.meningoseptica infection in the healthcare setting and its unusual drug resistance pattern making it more challenging for the therapeutic management. The maximum susceptibility (80%) was observed against cefoperazone-sulbactum, piperacillin-tazobactum and levofloxacin followed by meropenem (60%). Susceptibility against imipenem, ciprofloxacin, cotrimoxazole was observed approximately 40%.

KEYWORDS : Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS), Elizabethkingia meningoseptica, Intensive care units (ICUs)

INTRODUCTION

Elizabethkingia meningoseptica (previously called as Flavobacterium meningosepticum) is the most common species belongs to genus Elizabethkingia. [1] It is a Gram-negative nonfermentative bacilli found in nature, and in places of water supplies of healthcare settings such as water taps and sink basins.[2,3,4]It commonly colonizes in different medical devices like intravascular catheters, implanted devices etc.and act as a source of healthcare associated infections. [4] E. meningoseptica is an uncommon pathogen causing bacteraemia, pneumonia, neonatal meningitis, sepsis, endophthalmitis, soft-tissue infections etc. and primarily reported in immunocompromised patients. [5-10] Since last one decade it has been increasingly reported causing various healthcare associated infections especially among the patients in intensive care units (ICUs) and responsible for high mortality.[4] E. meningoseptica has been emerged as a multidrug resistant pathogen raising concern in antimicrobial steward program in current scenarios due to its intrinsic resistance to many antibiotics and no existing guidelines for treatment.

MATERIALS AND METHODS

This study was conducted in the Department of Microbiology of a tertiary care hospital in North India. This was a prospective study conducted for duration of 3 years i.e. from January, 2017 to December, 2020. Ethical clearance for this study had been obtained from the institute ethical committee. In this study we aimed to find out the recent trends, antimicrobial resistance pattern, and clinical correlation of E. meningoseptica species in different clinical specimens.

Isolates from consecutive clinical samples {blood, CSF, urine, pus, respiratory samples, stool , pleural, peritoneal, pericardial fluids, bone marrow aspirates, catheter tips etc.} had been processed for aerobic culture in bacteriology laboratory during the above defined period using standard operative procedures. The final identification of the pure growth on culture was carried out using Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS). As limited data was available, antimicrobial susceptibility testing in the current study was done using Kirby-Bauer disc diffusion method and interpretation was made as per the break points available for Pseudomonas aeruginosa, Staphylococcus aureus (for cotrimoxazole, nitrofurantoin and rifampicin) and Enterococcus spp. (for interpretation of vancomycin) using Clinical and Laboratory Standards Institute (CLSI) 2017 guidelines.[17] All the cases prospectively were followed up for any change in the treatment/discharge/death and data was recorded.

RESULTS

All the culture positive isolates identified as E. meningoseptica by MALDI-TOF MS during the above specified period were assessed and followed up for the clinical history. E. meningoseptica was isolated from five patients of which 3 were from blood samples and 2 were from BAL samples. [Table 1] All the five patients were having one or more underlying illness. Four out of five patients had one or more indwelling devices like central line catheter or endotracheal tube and only one patient with a diagnosis of Acute myeloid leukemia (AML) was without device. Four out of five patients had history of prolonged hospital stay and antibiotic intake due to one or more major surgical interventions. Two out of five patients developed septic shock during treatment. Empirical treatment was continued in all the five cases; of which three succumbed to death within a month of primary isolation of E. meningoseptica and two were discharged with clinical improvement. The maximum susceptibility (80%) was observed against cefoperazone-sulbactum, piperacillin-tazobactum and levofloxacin followed by meropenem (60%). Susceptibility against imipenem, ciprofloxacin, cotrimoxazole was observed approximately 40%. Vancomycin and rifampicin were tested in only two isolates and both of them were susceptible. All the 5 isolates of E. meningoseptica were found resistant to aminoglycoside and 3rd generation cephalosporins. [Chart 1]

DISCUSSION

E. meningosepticais an uncommon pathogen observed to cause outbreaks in neonatal ICUs. [12,13] This species is frequently cultured from soil, water including chlorinated municipal supplies, sinks, taps, intravenous solutions used for flushing the medical devices like catheters, respirators etc.[2-4] It is also isolated from incubators of peadiatric ICUs, intubations tubes, humidifiers and other medical devices.There were reports of neonatal meningitis, bacteraemia, pneumonia, sepsis, endophthalmitis, soft-tissue infections and other infections, primarily in immunocompromised patients caused due to E. meningoseptica. [5-10] One of the study had shown small proportion (3%) of patients with airway colonization had new onset pulmonary infiltrates. [18] The major risk factors associated with this species were prematurity and immunocompromised condition, prolonged hospital stay particularly in ICUs and debilitating co-

morbid conditions.[4]Very few studies established bio film formation as one of the important virulence factors for causation of pathogenesis. Few other literatures also documented the association of genes encoding for DNA-binding proteins and transcription factor proteins with virulence of the bacteria. [21]

But now a days this pathogen has emerged as a multidrug resistant organism causing healthcare associated infections with a very high case fatality rate ranging from 30%-54%.[14]In our study also out of 5 patients 3 were succumbed showing 60% case fatality rate.

Earlier studies suggested a strong correlation between E. meningoseptica and indwelling medical devices. [4] In the current study, 80% (4/5) of the cases were associated with one or more indwelling catheter or medical devices and one patient was suffering from AML without any medical device emphasizes the pathogen ability to cause infection. There are no clear guidelines on the therapeutic management of the patients suffering from E. meningoseptica infections available till now. Many studies had observed vancomycin alone or in combination with other agents as an effective therapeutic agent against this pathogen. [15,16]. However, study by Kirby et al. was the only study showed intermediate MIC against vancomycin against majority of E. meningoseptica isolates and maximum susceptibility to Rifampicin (85.7%) followed by trimethoprim-sulfamethoxazole (79.2%) and piperacillin-tazobactum(71%).[17]

In our study susceptibility to cefoperazone-sulbactum, piperacillin-tazobactum and levofloxain was observed maximum followed by meropenem, imipenem, ciprofloxacin and cotrimoxazole. More studies are needed to establish these facts. The role of hospital infection control is of primary requisite to control the outbreaks associated with this organism. Hand hygiene practice among the healthcare professionals is key factor in this regard. [19] Proper use of disinfection with hypochlorite can reduce the chance of outbreak by this organism. [20] So proper screening of environmental sources and hospital infection control measures can have a checkpoint on the outbreaks caused by E. meningoseptica.

CONCLUSION

Over the past few decades, E. meningoseptica has emerged as a superbug causing serious infection not only in extremes of ages, immunocompromised individuals and patients in ICUs one or more devices, but also in immunocompetent adults. Correct identification and appropriate therapeutic regimen are the need of the hour for the infections caused due to this multidrug resistant E. meningoseptica. Further studies are required to establish the correct empirical antimicrobial therapy.

Table 1: Clinical details of the patients with positive culture ofElizabethkingiameningosepticadetected by MALDI-TOF MS

Organism Identified By Maldi-tof Ms In Patients	Clinical specimen	Age/ sex	Underlying disease	Indwelling devices	Repeat isolation of the rare/uncommon organism	Previous antibiotic therapy (1 week before culture)	Change in therapy	Outcome of the patient
Case 1	Blood	59 Y/ M	Fungal brain abscess, pneumonia, septic shock	Central venous line, endotracheal tube, urinary catheter	Yes	Imipenem, colistin, teicoplanin, caspofungin, oseltamivir	None	Death
Case 2	BAL	26 Y/ F	Intra-abdominal sepsis, Post ileostomy	Endotracheal tube, central venous line, urinary catheter	Yes	Meropenem, colistin, teicoplanin, metronidazole	None	Death
Case 3	Blood	6 Y/ F	AML	None	None	P/T, Colistin	Levofloxac-in	Discharged
Case 4	Blood	52 days/F	ASD + PDA, ASD + ASD closure done	Endotracheal tube, central venous line	None	Colistin, C/S	None	Discharged
Case 5	BAL	34 Y/ F	Stroke syndrome	Endotracheal tube, central venous line	None	Meropenem, teicoplanin	None	Death

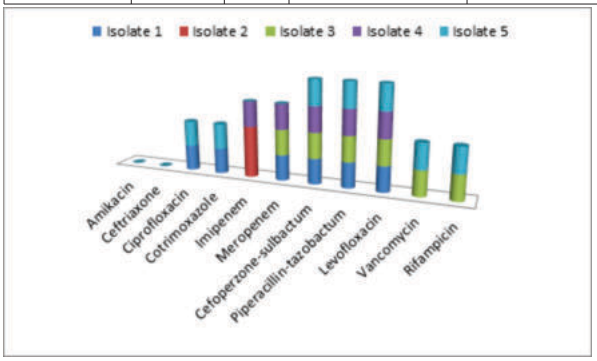

Chart: 1 Antimicrobial susceptibility patterns of 5 isolates of Elizabethkingia meningoseptica

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