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Case Report

Elizabethkingia meningoseptica bacteremia in a patient with B cell ALL with severe neutropenia- A Case Report

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ABSTRACT:

Patients with malignancies, severe neutropenia, diabetes mellitus, organ transplantation, long term systemic corticosteroids therapy are predisposed to develop infection with unusual organisms. *Elizabethkingia meningoseptica* is a non-motile, oxidase and indole positive Gram negative non-fermenter associated with various nosocomial outbreaks including bacteremia, endocarditis, neonatal meningitis and pneumonia. The sources of infection are soil and water, saline and infusion pumps, solutions used for reconstitution of chemotherapeutic drugs and antimicrobials. The organism possess an unusual high drug resistance pattern to commonly used multiple antibiotics for Gram negative rods. We report an unusual isolation of *E. meningoseptica* bacteremia in a patient with pre B cell ALL with severe neutropenia successfully treated intravenous vancomycin.

Keywords: neutropenia, nosocomial outbreaks, bacteremia, B cell ALL, vancomycin.

INTRODUCTION

A Gram negative non-motile, non-fermentative, non-sporing bacillus belonging to order Flavobacteriales and family Flavobactriaceace previously known as *Chryseobacterium meningosepticum*, now reclassified as *Elizabethkingia meningoseptica* is widely distributed in nature[1]. The organism is abundantly found in soil and water and considered to be an important agent responsible for nosocomial outbreaks in hospitals. The organism has been implicated in various infectious etiologies. In literature, outbreaks in neonatal intensive care unit especially neonatal meningitis and oncology setup have been reported[2]. Three important species of *Elizabethkingia* which are of clinical significance

are *E.anopelis, E. meningoseptica, E.miricola* of which *E. meningoseptica* is common clinical isolate. *E. meningosepticum* was first successfully isolated by an American bacteriologist Elizabeth O. King in the year 1959 while establishing an etiological agent of outbreak of neonatal meningitis[3]. Immunocompromised adult patients are commonly predisposed presenting with bacteremia, pneumonia and endocarditis[4]. Malignancies, organ transplantation, diabetes mellitus and long-term administration of systemic corticosteroids are the common underlying conditions responsible for infections with these clinical isolates. Malignancies (36%) and diabetes mellitus (25%) are found to be most common predisposing conditions for bacteremia associated with *E. meningoseptica*[5]. Identification and performing antimicrobial susceptibility preferably with micro-broth dilution technique (although standard MIC breakpoints are not available) is of utmost importance as these rare isolates are highly drug resistant and if not treated adequately in time may have poor clinical outcomes. Here we report an unusual case of bacteremia with *E. meningoseptica* in a patient with pre B cell ALL with ventricular septal defect.

CASE

A 3 year old girl known case of premembranous ventricular septal defect and left to right shunt was evaluated 4 months back in Oman for fever and was diagnosed as acute leukemia. The patient was admitted for induction chemotherapy and supportive care in a tertiary care cancer center. During the chemotherapy the patient was in her usual status until five days prior to presentation when she developed high grade fever not responding to broad spectrum antimicrobials over 48 hours. On physical examination, child was febrile with temperature 101^0F,vitals were stable, conscious, oriented and irritable. Per abdominal examination showed soft, non-tender abdomen, spleen and liver were not palpable. Laboratory investigations showed haemoglobin -7.4 gm%, platelet count of 2, 15000 cells/mm^3, and total leucocyte count was 20400 cells/mm^3. Absolute neutrophil count (ANC) was 200 cells/mm^3. The child was icteric with de-arranged liver function tests, aspartate transaminase (AST) level of 220 IU/L, alanine transaminase (ALT) of 205 IU/L, alkaline phosphatase (ALP) of 462 IU/L with total bilirubin of 3.6 mg% and prothrombin time- 18 sec, INR- 1.4. Serum creatinine was 0.4 mg/ml, serum sodium -136 Mmol/L, serum potassium- 4.8 Mmol/L. Viral markers including, HbsAg, HCV and HIV were non-reactive. Patient was diagnosed as pre B cell acute lymphoid leukemia and received chemotherapy after liver function tests became normal. The child had persistent fever spike from day 5 of admission. Non contrast computed tomographic scan of thorax did not show any abnormality. Two sets of blood cultures were collected (Both Central and peripheral). After 14 hours of collection, automated blood culture system (BD BACTEC™ FX 40 Instrument, Becton Dickinson, USA) were shown positive signals. The differential time to positivity (DTP) between central and peripheral blood was 4 hours 12 minutes. The Gram stain from blood bottles showed thin slender, slightly curved Gram negative bacilli. After 24 hours of incubation, nutrient agar grew smooth, circular translucent colonies with slight white to yellow pigmentation. MacConkeys agar (containing crystal violet) showed no growth. Blood agar grew smooth, translucent, mucoid, non-hemolytic colonies. Colonies on blood agar were oxidase positive non-motile presumptively reported as Gram negative non-fermenter. On further biochemical reactions, the strain was indole positive, urease negative and lysine decarboxylase and

esculine hydrolysis positive subsequently identified as *E. meningoseptica* on MALDI-TOF (Matrix assisted laser desorption ionization-time of flight mass spectrometry). To rule out contamination and confirm the true pathogenicity of this isolate, repeat paired blood cultures were taken 24 hours after first blood culture. Repeat blood specimens grew the same organism with similar antimicrobial resistance pattern. On day of onset of fever, patient was on meropenem and amikacin. In view of multidrug resistance pattern of this isolate, patient was put on IV vancomycin for 7 days. As there are no standard guidelines to establish minimum inhibitory concentration, extrapolated breakpoints for pseudomonas has been taken.

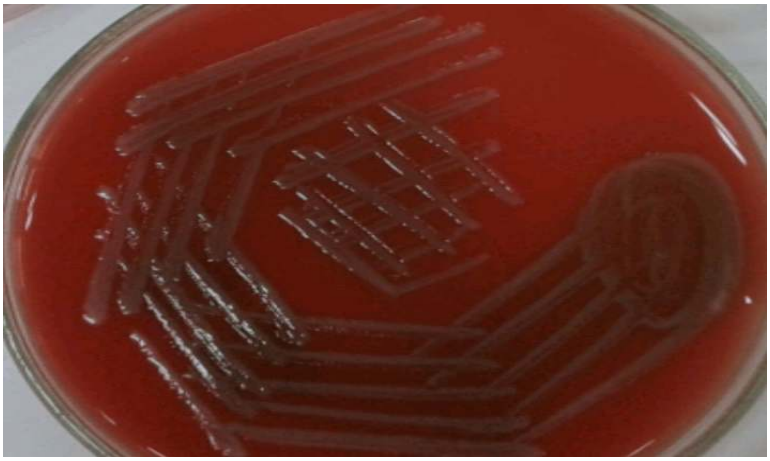

Fig. 1: Blood agar showing smooth, mucoid, non-hemolytic colonies with slight white to yellow pigmentation

Table 1. Biochemical differences between oxidase positive, indole positive Gram-negative Nonfermenting bacilli

Characteristics	*E. meningoseptica*	*E. miricola*	*C. indologenes*
Yellow pigment	N	N	P
Gelatin hydrolysis	P	P	P
Esculin hydrolysis	P	P	P
Urea hydrolysis	N	P	N

Adapted From- What's in a Name? The Taxonomic Overview of the Genus Elizabethkingiaby *Peter C. Iwen, PhD, D (ABMM), Associate Director, NPHL*

DISCUSSION

The common sources of *E. meningoseptica* are plants, soil, food, fresh water, marine water. The exact virulence factors and pathogenesis is not known however *E. meningosepticum* associated with human infections, can be encapsulated or produce proteases and gelatinases that destroy host cells and tissues. Saline and infusion sets, solutions used for reconstitution of antimicrobials and chemotherapeutic drugs, intravascular devices, sinks and hospital tanks are the sources of outbreaks in hospitals.

The organism produces various carbapenemases and metalo-betalactamases, which imparts resistance to commonly, used antimicrobial agents. The bacteria has been implicated in nosocomial outbreaks like neonatal meningitis, bacteraemia, septicaemia, pneumonia and endocarditis[6]. Diabetes mellitus, use of corticosteroids, bone marrow transplantation and malignancies are established risk factors of which prolonged and profound neutropenia plays a significant role in the acquisition of infection. Our patient presented with pre B cell ALL with long standing history of profound neutropenia. Local physician has treated the similar episodes of fever in the past. Other situations where *E. meningoseptica* bacteremia has been described by various authors are diabetic nephropathy with prolonged renal dialysis and pleural effusion in a patient with diabetes[7, 8].Bayrak B in 2014 has presented an unusual case of *E. meningoseptica* bacteremia in a patient with Bardet-Biedl syndrome and chronic renal failure where dialysis fluid has been implicated as a source of infection[9].Our patient has developed catheter related blood stream infection with differential time to positivity of more two hours between central and peripheral blood cultures on two successive occasions with more than 15 colonies by Makis semi quantitative roll plate method. We could not establish the exact source of organism although cultures of all intravenous fluids and chemotherapeutic drugs infused for patient were sterile. Our isolate was resistant to most of the commonly used antimicrobial agents like carbapenems, penicllins and cephalosporins, polymyxin B and colistin, all aminoglycosides, for treatment of Gram-negative infections. Surprisingly the strain was sensitive to Vancomycin, rifampicin, cotrimoxazole and levofloxacin with lower MIC values. Vancomycin, a Gram-positive antimicrobial agent is used as a drug of choice for these pathogens, which can be combined, with rifampicin for successful outcome. Combination therapy is preferred over monotherapy to prevent relapse. It is essential to establish standard minimal inhibitory concentrations for these rare isolates for successful clinical outcome, as they are potentially drug resistant[10, 11, 12]. Micro-broth dilution method is preferred over disk diffusion method although susceptibility results may vary when different methods are used.

CONCLUSIONS

A non-lactose fermenting, non-motile, oxidase and indole positive organism isolated from any clinical specimens in an immunocompromised patient should raise the suspicion of *E. meningoseptica* infection. The organism is associated with nosocomial outbreaks in hospitals especially bacteraemia, neonatal meningitis, pneumonia and endocarditis as it is ubiquitously found in soil and water. Malignancies with prolonged and profound neutropenia is an independent risk factor for bacteraemia with *E. meningoseptica.* It is of utmost importance to perform antimicrobial susceptibility due to its unusual resistance pattern to multiple antimicrobial agents. Multicentre studies to establish the MIC values to determine clinical breakpoints for such resistant isolates is warranted to have better prognosis.

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