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Elizabethkingia anophelis: An uncommon cause of hospital-acquired septic meningitis and a rare cause of community-acquired meningitis in children: A case series

Sarjana Shuchi[1], Shweta Satija[2], Manoj B Jais[3]

[1]Senior Resident, [2]Associate Professor, [3]Professor and Head, Department of Microbiology, Lady Hardinge Medical College, New Delhi, India

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ABSTRACT

Elizabethkingia is one among several new organisms which heve emerged as an important human pathogen in the past few decades. We present the first two cases of *Elizabethkingia anophelis* infection reported from our institution. The first case was of septic meningitis in a 10-day-old preterm neonate after 10 days of hospital stay and another case was of community-acquired meningitis in a 2-month-old infant. The organism was isolated from the cerebrospinal fluid of both the patients and the blood of only the neonate. *E. anophelis* is now being identified as the most prevalent species under the genus *Elizabethkingia*. Among the two cases, one was a health-care-associated infection and another was a community-acquired infection. Both cases improved after giving appropriate antibiotics. Hence, we should look for these kind of cases for early identification and to prevent mortality in patients by starting the right antibiotic.

Key words: *Elizabethkingia anophelis*; Septic meningitis; Community-acquired infection; Infant

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INTRODUCTION

Several new organisms have emerged as important human pathogens in the past few decades. *Elizabethkingia* is one of the emerging human pathogens which is a Gram-negative, non-motile, non-sporing, non-fermenter bacterium belonging to the family *Flavobacteriaceae*.[1] By far six species of the genus *Elizabethkingia* are known to cause human infection- *Elizabethkingia meningoseptica*, *Elizabethkingia miricola*, *Elizabethkingia anophelis*, *Elizabethkingia bruniana*, *Elizabethkingia ursingii*, and *Elizabethkingia occulta*. Among them, *E. meningoseptica* was the first to be identified as a human pathogen.[2]

E. anophelis was first time identified as an etiological agent of neonatal meningitis in an 8-day-old neonate from the Central African Republic in 2013.[3,4] After the identification of the first strain, another strain from 2006, which was earlier identified as *E. meningoseptica*, was sequenced retrospectively and it came out to be *E. anopheles*.[4,5] After that *E. anophelis* was reported from several places and is now reported to be more prevalent than *E. meningoseptica* which was earlier known to be more prevalent.[2,6] Because of the limited database in various laboratories for *E. anophelis*, it is often misidentified as *E. menigoseptica*.

E. anophelis is mostly a health-care-associated infection and infections caused by it can range from meningitis, and pneumonia to bloodstream infection. Mostly it is seen in immunocompromised individuals.[7,8] Here we present two case reports of infections caused by *E. anophelis*. The first

Address for Correspondence:
Dr. Sarjana Shuchi, Senior Resident, Department of Microbiology, Lady Hardinge Medical College, New Delhi - 110001, India.
Mobile: +91-8961490871. **E-mail:** sarjanashuchi21@gmail.com

case was of septic meningitis caused by *E. anophelis* in a 10-day-old preterm neonate after 10 days of hospital stay and another case of a 2-month-old infant suffering from meningitis caused by *E. anophelis*.

CASE PRESENTATION 1

Our first index case was a 10-day-old male child who was admitted to the nursery of Lady Hardinge Medical College, New Delhi, after birth. The child was a preterm (32 weeks), very low birth weight (1.55 kg) neonate who was delivered by cesarean section in the same hospital and the delivery was uneventful. The reason for preterm delivery was abruption and oligohydramnios and the mother also had gestational diabetes, gestational hypertension, and hypothyroidism. Till 10 days of life, the patient had no symptoms.

On the 10th day of life, he started developing spikes of fever, vitals became unstable, and oxygen saturation went down to 78%. The patient was suspected of having neonatal sepsis or septic meningitis. As per the hospital guidelines, a blood culture was sent and an injection of piperacillin–tazobactam (270 mg 8 hourly) and an injection of amikacin (32 mg OD) were started. Piperacillin–tazobactam has good Gram-positive and Gram-negative coverage including *Pseudomonas* but has less blood–brain barrier penetration capacity while amikacin covers most of the Gram-negative organisms and is good in penetrating the blood–brain barrier. Hence, these two were given as empirical therapy as the majority of the hospital-acquired infections are caused by Gram-negative organisms. A blood gas analysis was done and it was under normal limits. Ultrasonography of cranium was performed to check for ventricular enlargement but no such thing was noted. Lumbar puncture was also done for cerebrospinal fluid (CSF) analysis. On CSF analysis, it was found that protein level has gone up to 2.33 g/L, sugar level was 5.10 mg/L, and Cl^- level was 120 mmol. Complete blood count (CBC) revealed raised total leukocyte count (TLC) (15,000 cells/mm^3). Three days after symptom onset, vancomycin was also added, and piperacillin–tazobactam was changed to meropenem for better blood–brain barrier penetration.

Microscopic examination of the CSF revealed 5–7 pus cells per high power field on wet mount and Gram-negative, non-spore-forming, non-capsulated bacilli on Gram staining. The culture of the patient's CSF after overnight incubation revealed shiny, non-fermenter colonies on MacConkey agar which were Gram-negative bacilli on Gram staining and were oxidase and catalase positive (Figure 1a). The blood culture of the patient by automated method (BACT Alert) revealed similar colonies as CSF.

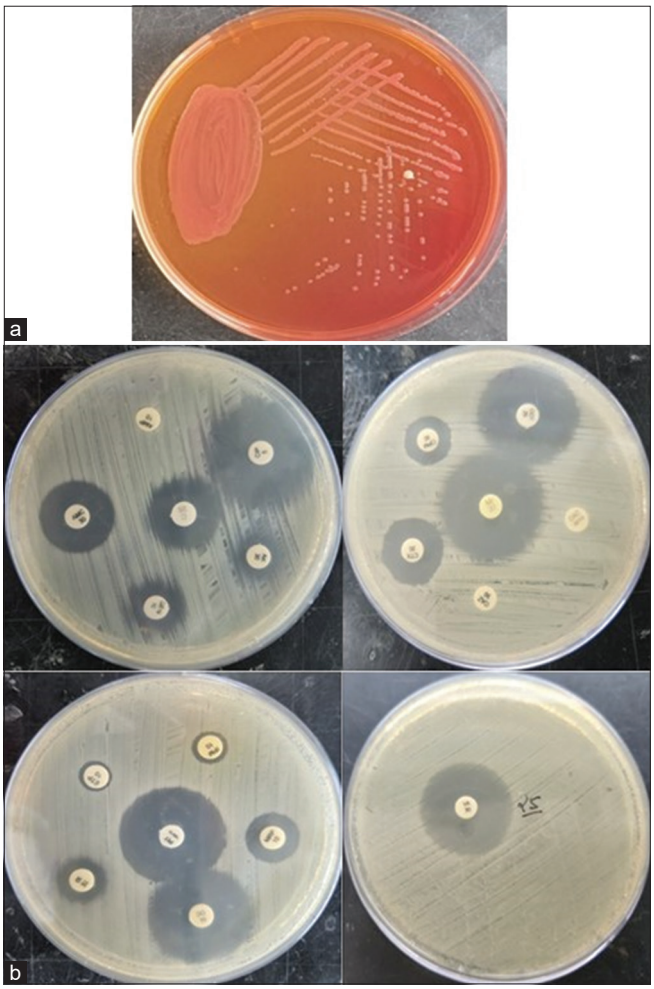

Figure 1: (a) Colony morphology of *Elizabethkingia anophelis* on MacConkey agar; (b) Antibiotic susceptibility testing of case 1 isolate by disc diffusion method

Further identification of the isolate from blood and CSF was carried out using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS) and the organism was identified as *E. anophelis* with 99.9% identity. The antimicrobial susceptibility for this strain was tested using the disc diffusion method. As per the CLSI guidelines, the strain was sensitive to piperacillin–tazobactam (zone diameter [ZD] = 28 mm), ciprofloxacin (ZD = 30 mm), chloramphenicol (ZD = 21 mm), cotrimoxazole (ZD = 31 mm) but resistant to gentamicin (ZD = 14 mm), amikacin (ZD = 14 mm), meropenem (ZD = 10 mm), imipenem (ZD = 6 mm), ceftazidime (ZD = 6 mm), cefotaxime (ZD = 20 mm), tetracycline (ZD = 16 mm), and ampicillin (ZD = 6 mm). The strain was intermediately sensitive to amoxicillin–clavulanic acid and colistin. Although no cutoff is available for vancomycin susceptibility pattern for *Elizabethkingia*, reports are there showing improvement in the patient's condition after starting vancomycin.[9] Hence, a vancomycin disc was also put and the disc diffusion ZD came out to be 25 mm (Figure 1b).

After the result of the antimicrobial susceptibility test (AST), amikacin and meropenem were stopped and the patient was started on an injection of ciprofloxacin (18 mg 12 hourly) and injection of vancomycin (48 mg 8 hourly). One to two days after starting ciprofloxacin and vancomycin, the patient showed improvement in terms of episodes of fever and oxygen saturation. Repeat CSF culture was done 6 days after starting the above-mentioned antibiotics and it came out to be sterile after 48 h of incubation.

CASE PRESENTATION 2

Our second case was a 2-month-old male child who was admitted to the Department of Pediatrics, Lady Hardinge Medical College, New Delhi, with complaints of fever of 15 days duration and cough for 12 days. The child was lethargic with a refusal to feed. There was no prior history of hospitalization or any immunocompromised condition for this child.

The patient was suspected of meningitis and its workup was done according to the standard protocol. Before starting the antibiotics, his blood and CSF were sent for culture, and meropenem (40mg/kg TDS) and amikacin (15 mg/kg OD) were started after that. Since the patient also had respiratory tract infection, meropenem was added to cover both Gram-positive and Gram-negative organisms causing respiratory tract infection. Amikacin was added because of good blood–brain barrier penetration and good Gram-negative coverage. On doing a CBC of the child, TLC came out to be 33,000/mm^3 with predominant lymphocytosis. C-reactive protein was raised to a level of 57 mg/dL. CSF analysis also revealed an increase in TLC.

On microscopic examination of CSF, 8–10 pus cells per high power field were seen on a wet mount, and Gram-negative bacilli such as in the previous case were seen on Gram staining. Overnight incubation of CSF culture showed growth of non-fermenting colonies on MacConkey agar such as the growth of the previous case. Identification of the growth was then done using the MALDI-TOF-MS (biomerux) system which identified the isolate as *E. anophelis* with 99.9% identity. Using the disc diffusion method, AST was done and results were interpreted using CLSI guidelines. The strain was sensitive to piperacillin–tazobactam (ZD = 25 mm), ciprofloxacin (ZD = 27 mm), gentamicin (ZD = 20 mm), chloramphenicol (ZD = 26 mm) and cotrimoxazole (ZD = 26 mm) but resistant to ceftazidime (ZD = 6 mm), amikacin (ZD = 6 mm), meropenem (ZD = 10 mm), imipenem (ZD = 6 mm), tetracycline (ZD = 14 mm), and ampicillin (ZD = 6 mm). Susceptibility testing for vancomycin was also done for the same reason as in the first case and ZD came out to be 20 mm. Due to the non-availability of the sensitivity cutoff of vancomycin for *Elizabethkingia*, we were not able to comment on its sensitivity. Blood culture was performed using an automated method (BACT Alert) (biomerux) system but it remained sterile even after 5 days of incubation.

Based on the AST report, the child was shifted from meropenem and amikacin to an injection of gentamicin (7.5mg/kg OD) and an injection of ciprofloxacin (10 mg/kg BD). After 3–4 days of changing the antibiotics, there was an improvement in the child's condition.

DISCUSSION

Elizabethkingia is one of the emerging human pathogens for which different routes of transmission such as tap water, contaminated hands of a health-care worker, or vertical transmission from mother to child have been speculated.[3,10,11] Health-care-associated infection is by far the most common infection (80–87.5%) caused by *E. anopheles*.[7,8] *E. anophelis* infection is usually seen in old age, newborns, and patients having comorbidities.[2]

Our first case was a 10-day-old preterm, very low birth weight neonate suffering from multiple episodes of fever, suspected of neonatal sepsis or septic meningitis. *E. anophelis* was isolated from both blood and CSF, 2 days after the onset of fever. Since our case developed symptoms 72 h after birth, we labeled the cause of infection as health-care-associated and the source might be the contaminated hands of health-care workers. *Elizabethkingia* usually causes infection in people having some predisposing risk factor. In our case, the predisposing risk factor was probably very low birth weight and preterm. Our second case was a 2-month-old infant having a fever and cough for 12 days but on admission, he was suspected of having meningitis. *E. anophelis* was isolated from CSF but unlike the previous case, his blood culture came out to be sterile. Since no history of hospitalization was there, we labeled this to be a community-acquired infection. The striking feature of this case was the absence of any immunocompromised condition which is usually seen in most of the cases.

Earlier due to the limited availability of the database in MALDI-TOF-MS, *E. anophelis* was usually misidentified as *E. meningoseptica*. However now, with an extended database, the prevalence of *E. anophelis* as a pathogen under the genus *Elizabethkingia* has gone up to 59–99% in contrast to *E. meningoseptica* whose prevalence came down to 1–21%.[6,7,12] Both of our isolates were identified by MALDI-TOF-MS. Case fatality rate due to *E. anophelis* ranges from 24% to 60%

which largely depends on inappropriate antibiotic treatment due to mis or non-identification of the pathogen.[2]

Elizabethkingia is known to be a multidrug-resistant pathogen showing resistance to the majority of β-lactams, a combination of β-lactam/β-lactam inhibitors including carbapenems, aztreonam, aminoglycosides, and chloramphenicol.[7,8,12-15] For *E. anophelis*, there is a wide range of susceptibility to various antibiotics such as 30–92% for piperacillin–tazobactam, 4–70.6% for trimethoprim–sulfamethoxazole, 16–96% for levofloxacin, 1–100% for ciprofloxacin, 0–100% for vancomycin, and 97.5–100% for minocycline.[2] Isolate from our cases also came out to be multidrug resistant showing resistance to ceftazidime, cefotaxime, amikacin, meropenem, imipenem, and tetracycline but sensitive to piperacillin–tazobactam, ciprofloxacin, trimethoprim–sulfamethoxazole, and gentamicin. Although piperacillin–tazobactam acts well against *E. anophelis* but due to its poor blood–brain barrier penetration, it was not given in our cases. No guidelines are there for susceptibility cutoff of vancomycin against *Elizabethkingia* but reports are there showing good treatment outcomes after starting vancomycin.[9] Based on the susceptibility pattern, in our first case, ciprofloxacin was started and vancomycin was added to get a better outcome as the patient was suffering from sepsis and meningitis. In the second case, the patient was started on the antibiotic ciprofloxacin but no improvement in the patient's condition even after 48 h led to the addition of gentamicin. Both cases showed good outcomes after targeted therapy.

CONCLUSION

Elizabethkingia is emerging as an important human pathogen and *E. anophelis* is now being identified as the most prevalent species under the genus *Elizabethkingia*. Here, we presented two cases of meningitis in children caused by *E. anophelis* which were identified for the first time by our institute. One case was a health-care-associated infection and another was a community-acquired infection. Both cases improved after giving appropriate antibiotics. Hence, we should look for these kinds of cases for early identification and to prevent mortality in patients by starting the right antibiotic.

REFERENCES

1. Kim KK, Kim MK, Lim JH, Park HY and 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(Pt 3):1287-1293.
   https://doi.org/10.1099/IJS.0.63541-0
2. Lin JN, Lai CH, Yang CH and Huang YH. Elizabethkingia infections in humans: From genomics to clinics. Microorganisms. 2019;7(9):295.
   https://doi.org/10.3390/MICROORGANISMS7090295
3. Kämpfer P, Matthews H, Glaeser SP, Martin K, Lodders N and Faye I. *Elizabethkingia anophelis* sp. nov., isolated from the midgut of the mosquito *Anopheles gambiae*. Int J Syst Evol Microbiol. 2011;61(Pt 11):2670-2675.
   https://doi.org/10.1099/IJS.0.026393-0
4. Frank T, Gody JC, Nguyen LBL, Berthet N, Le Fleche-Mateos A, Bata P, et al. First case of *Elizabethkingia anophelis* meningitis in the Central African Republic. Lancet. 2013;381(9890):1876.
   https://doi.org/10.1016/S0140-6736(13)60318-9
5. Bobossi-Serengbe G, Gody JC, Beyam NE and Bercion R. First documented case of *Chryseobacterium meningosepticum* meningitis in Central African Republic. Med Trop. 2006;66(2):182-184.
6. Choi MH, Kim M, Jeong SJ, Choi JY, Lee IY, Yong TS, et al. Risk factors for *Elizabethkingia* acquisition and clinical characteristics of patients, South Korea. Emerg Infect Dis. 2019;25(1):42-51.
   https://doi.org/10.3201/eid2501.171985
7. Lau SKP, Chow WN, Foo CH, Curreem SO, Lo GC, Teng JL, et al. Elizabethkingia anophelis bacteremia is associated with clinically significant infections and high mortality. Sci Rep. 2016;6:26045.
   https://doi.org/10.1038/srep26045
8. Lin JN, Lai CH, Yang CH and Huang YH. Comparison of clinical manifestations, antimicrobial susceptibility patterns, and mutations of fluoroquinolone target genes between *Elizabethkingia meningoseptica* and *Elizabethkingia anophelis* isolated in Taiwan. J Clin Med. 2018;7(12):538.
   https://doi.org/10.3390/jcm7120538
9. Shinha T and Ahuja R. Bacteremia due to *Elizabethkingia meningoseptica*. IDCases. 2015;2(1):13-15.
   https://doi.org/10.1016/j.idcr.2015.01.002
10. Lau SKP, Wu AK, Teng JL, Tse H, Curreem SO, Tsui SK, et al. Evidence for *Elizabethkingia anophelis* transmission from mother to infant, Hong Kong. Emerg Infect Dis. 2015;21(2):232-241.
    https://doi.org/10.3201/eid2102.140623
11. Yung CF, Maiwald M, Loo LH, Soong HY, Tan CB, Lim PK, et al. Elizabethkingia anophelis and association with tap water and handwashing, Singapore. Emerg Infect Dis. 2018;24(9):1730-1733.
    https://doi.org/10.3201/eid2409.171843
12. Han MS, Kim H, Lee Y, Kim M, Ku NS, Choi JY, et al. Relative prevalence and antimicrobial susceptibility of clinical isolates of *Elizabethkingia* species based on 16S rRNA gene sequencing. J Clin Microbiol. 2017;55(1):274-280.
    https://doi.org/10.1128/JCM.01637-16
13. Perrin A, Larsonneur E, Nicholson AC, Edwards DJ, Gundlach KM, Whitney AM, et al. Evolutionary dynamics and genomic features of the *Elizabethkingia anophelis* 2015 to 2016 Wisconsin outbreak strain. Nat Commun. 2017;8:15483.
    https://doi.org/10.1038/ncomms15483
14. Cheng YH, Perng CL, Jian MJ, Lee SY, Sun JR and Shang HS. Multicentre study evaluating matrix-assisted laser desorption ionization-time of flight mass spectrometry for identification of clinically isolated *Elizabethkingia* species and analysis of antimicrobial susceptibility. Clin Microbiol Infect. 2019;25(3):340-345.
    https://doi.org/10.1016/j.cmi.2018.04.015
15. Chew KL, Cheng B, Lin RT and Teo JW. *Elizabethkingia anophelis* is the dominant *Elizabethkingia* species found in blood cultures in Singapore. J Clin Microbiol. 2018;56(3):e01445-17.
    https://doi.org/10.1128/JCM.01445-17

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Work attributed to:
Lady Hardinge Medical College, New Delhi 110001, India.

Orcid ID:
Dr. Sarjana Shuchi - https://orcid.org/0009-0005-5606-557X
Dr. Shweta Satija - https://orcid.org/0000-0003-2850-6380
Dr. Manoj B Jais - https://orcid.org/0009-0003-4802-3447

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