



## Case Report

# Successfully treated case of meningitis caused by *Elizabethkingia anophelis* in an adult with fluoroquinolone-based treatment: A case report and literature review

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## ABSTRACT

*Elizabethkingia anophelis*, a Gram-negative bacillus, is a rare cause of adult meningitis with high mortality. Due to its resistance to most  $\beta$ -lactams including carbapenems and aminoglycosides, the standard treatment for meningitis remains undetermined. Herein, we report the first case of adult meningitis caused by *E. anophelis* after nasal endoscopic transnasal surgery. In our patient, *E. anophelis* colonized the respiratory tract without clinical evidence of pneumonia. Although an apparent cerebrospinal fluid leak was not identified, we believe that a minor leak following brain surgery was the entry site for *E. anophelis*. Levofloxacin resulted in rapid resolution of fever and headache. All previously reported cases of meningitis in adults treated with fluoroquinolones survived. We highlighted the importance of prompt identification of the strain and considering changing antimicrobial agents as necessary. Although regional susceptibility rates must be carefully considered, fluoroquinolones can be a viable treatment option for adult meningitis caused by fluoroquinolone-susceptible *E. anophelis*.

## Introduction

The genus *Elizabethkingia* comprises aerobic, non-motile, oxidase-positive, and indole-positive Gram-negative bacilli that inhabit natural environments, including soil, water, and hospital settings [1,2]. Three major species of this genus cause human infections: *Elizabethkingia meningoseptica*, *E. anophelis*, and *E. miricola* [1,2]. Among them, *E. anophelis* has recently emerged as a clinically important pathogen.

The first case of human infection with *E. anophelis* was reported in Central Africa in 2013 [3]. Since then, reported cases and outbreaks have been increasing worldwide [4]. Although the clinical significance of *E. anophelis* is not fully understood, 16S rRNA sequencing has revealed that many strains previously identified as *E. meningoseptica* are *E. anophelis* [1].

*E. anophelis* can cause hospital-associated infections, such as pneumonia and catheter-related bloodstream infections, mainly in immunocompromised patients, with bacteremia mortality rates reaching 24–60% [5]. Furthermore, *E. anophelis* causes neonatal meningitis; however, only a few cases of meningitis in adults have been reported. As *E. anophelis* is resistant to most  $\beta$ -lactam antibiotics, including carbapen-

ems [2], treatment options for meningitis caused by *E. anophelis* are limited.

Herein, we report a case of adult meningitis caused by *E. anophelis* following nasal endoscopic surgery that was successfully treated with fluoroquinolone-based therapy.

## Case presentation

A 63-year-old Japanese woman who had undergone six transnasal skull base surgeries and five sessions of stereotactic radiosurgery for recurrent skull base chordoma underwent endoscopic transnasal resection of an intradural recurrent tumor with dural reconstruction. No postoperative cerebrospinal fluid leakage was observed. The patient received intravenous meropenem and vancomycin as perioperative antibiotics until postoperative day 6. On day 12, she developed a fever and complained of a headache.

On examination, the patient was alert and oriented. She was febrile and her other vital signs were normal. The patient exhibited nuchal rigidity. Cranial nerve deficits, such as visual impairment, eye movement disorder, hearing impairment, and motor and sensory impairment

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**Table 1**Clinical details and outcomes of reported cases of meningitis caused by *Elizabethkingia anophelis* in adults.

Case	Country	Age	Sex	Background and complications	Initial therapy	Effective targeted therapy	Fluoroquinolone	Outcome	References
1	Denmark	76	Male	Primary macroglobulinemia	Penicillin G, cefotaxime	Moxifloxacin, rifampicin,	+	Survived	[7]
2	France	72	Female	Splenectomy, diabetes mellitus	Cefotaxime	Levofloxacin, doxycycline, piperacillin/tazobactam	+	Survived	[9]
3	India	75	Male	Hypertension	Unknown	Minocycline, piperacillin/tazobactam	-	Survived	[8]
4	India	41	Female	Acute lymphoblastic leukemia	Unknown	Minocycline, piperacillin/tazobactam, vancomycin	-	Survived	[8]
5	India	79	Male	Hypertension	Unknown	Minocycline, piperacillin/tazobactam, vancomycin	-	Died	[8]
6	Singapore	53	Male	None	Ceftriaxone	Levofloxacin, TMP-SMX	+	Survived	[6]
7	Japan	52	Male	SLE, diabetes mellitus	Meropenem	Minocycline, piperacillin/tazobactam	-	Died	[4]
8	Japan	63	Female	Basilar chordoma	Meropenem, vancomycin	Levofloxacin, TMP-SMX	+	Survived	This case

Abbreviations: TMP-SMX, trimethoprim-sulfamethoxazole. SLE, systemic lupus erythematosus.

of the face were present; however, they did not change before surgery. The following blood test results were remarkable: an elevated white blood cell count of 18,100/ $\mu$ l and C-reactive protein of 1.43 mg/dl (reference range: 0–0.3 mg/dl). The cerebrospinal fluid (CSF) opening pressure was 5 cm H<sub>2</sub>O, with an elevated cell count (866 cells/ $\mu$ l, 90% polymorphonuclear leukocytes), elevated protein levels of 143 mg/dl, and lowered glucose levels of 35 mg/dl. Intravenous meropenem (2 g every 8 hours) and vancomycin (1 g every 12 hours) were initiated following the diagnosis of postoperative bacterial meningitis. Spinal fluid culture identified *E. anophelis* using a Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Biotyper (version 11; Bruker Daltonics, Bremen, Germany), which was later confirmed by 16S rRNA sequencing using the Sanger method. The sequence was 100% identical to that of *E. anophelis* in the V1–V4 region (GenBank accession number AP022313). Blood culture results were negative. Furthermore, *E. anophelis* was cultured from the sputum; however, pneumonia was not clinically considered. Considering the CSF penetration of antibiotics and previously reported antibiotic susceptibility of *E. anophelis*, we added intravenous levofloxacin (750 mg every 24 hours), and the patient became afebrile with an improved headache the following day. The antibiotic susceptibility test, determined by the Clinical and Laboratory Standards Institute M100, Ed 30, showed susceptibility to levofloxacin (minimum inhibitory concentration [MIC]  $\leq$ 0.5  $\mu$ g/ml) and trimethoprim-sulfamethoxazole (TMP-SMX) (MIC  $\leq$ 2.0  $\mu$ g/mL), resistance to meropenem (MIC >8.0  $\mu$ g/ml), and a high MIC for vancomycin (>16  $\mu$ g/ml). Antibiotics were replaced with intravenous levofloxacin and TMP-SMX (240 mg TMP daily). The patient completed therapy for 14 days and remained recurrence-free at a 7-month follow-up.

## Discussion

Notably, *E. anophelis* causes neonatal meningitis, suggesting its potential affinity for the central nervous system. However, meningitis is rare in adults. We reviewed PubMed/MEDLINE and found seven adult cases of *E. anophelis* [4,6–8], and this was the first case of meningitis caused by *E. anophelis* following nasal endoscopic brain surgery (Table 1). Interestingly, in our patient, *E. anophelis* colonized the respiratory tract. Although an apparent CSF leak was not identified, we believe that a minor leak following brain surgery was the entry site for the colonized *E. anophelis*.

The appropriate treatment for meningitis caused by *E. anophelis* is unclear and has not been previously reviewed in the literature. Astonishingly, due to high resistance to antibiotics, none of the patients received effective initial antibiotics at the diagnosis of meningitis (Table 1) [4,6–9]. Although predicting *E. anophelis* meningitis in advance is difficult, initiating appropriate antimicrobial therapy as soon as the bacteria are

identified is crucial because a delay in effective initial treatment can greatly deteriorate the meningitis prognosis [10].

Notably, *E. anophelis* is resistant to the most commonly used  $\beta$ -lactams, including carbapenems [2]. Piperacillin-tazobactam is a reliable option for *E. anophelis* bacteremia and pneumonia; however, it poorly penetrates the CSF. Although *E. anophelis* is a Gram-negative bacillus, vancomycin is effective against it in vitro [11]. However, the clinical efficacy of vancomycin remains controversial, and the MIC cut-off has not been determined [11]. Minocycline is also a treatment option for *E. anophelis* with a relatively high sensitivity rate. Although minocycline is the most lipophilic among tetracyclines, and the CSF concentration reaches 11–56% of the plasma concentration [12], it is a biostatic antibiotic, and evidence for the treatment of bacterial meningitis is lacking [10]. Four patients were treated with minocycline, piperacillin/tazobactam, and/or vancomycin (cases 3,4,5, and 7); however, two died.

Among the potentially effective antibiotics against *E. anophelis*, fluoroquinolones, and TMP-SMX sufficiently penetrate the CSF [10]. Of the eight previously reported cases, fluoroquinolone was used in four (cases 1,2,6, and 8), all of whom survived. The susceptibility of *E. anophelis* to levofloxacin varies among countries: 71.4–96% in the United States [2,13], 78.5% in Singapore [14], 16–58.3% in Taiwan [2,15], 29% in South Korea [2], and 0% in India [8]. The susceptibility rate of *E. anophelis* to ciprofloxacin is significantly lower than that to levofloxacin [2,8,13–15], and susceptibility data for moxifloxacin is lacking. Therefore, we believe that levofloxacin is the most reliable treatment option for *E. anophelis* among the fluoroquinolones; however, regional susceptibility rates must be carefully considered.

Notably, *E. anophelis* was susceptible to TMP-SMX in 85.7% (12/14) of the studies in the United States [2]; however, the susceptibility rate ranged widely from 4–97% in Asian countries [14,15]. TMP-SMX was used in combination with levofloxacin in two surviving cases of adult meningitis [6], including our case. Despite its many side effects, TMP-SMX is generally acceptable as an empiric therapy until susceptibility is determined. In the present case, the fever and headache resolved quickly after initiating levofloxacin therapy, suggesting that levofloxacin might be effective as monotherapy. However, considering the possibility of levofloxacin resistance, the addition of TMP-SMX and/or minocycline may be preferable.

## Conclusion

Herein, we report the first case of adult meningitis caused by *E. anophelis* after nasal endoscopic transnasal surgery. In this case, levofloxacin resulted in rapid resolution of fever and headache. Notably, *E. anophelis* is resistant to most commonly used  $\beta$ -lactams, including

carbapenems, and aminoglycosides; therefore, promptly identifying the strain and considering changing antimicrobial agents is necessary.

In adult cases of meningitis caused by *E. anophelis*, such as in the present case, levofloxacin and TMP-SMX are considerable treatment options in terms of sensitivity and CSF concentration.

## Declarations of competing interest

The authors have no competing interests to declare.

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## Ethical approval statement

We obtained informed consent for the publication from the patient.

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## Author contributions

M.N. and H.H. performed the surgical procedures for the patient. Antimicrobial therapy was selected by a team consisting of C.K., M.A.-K., K.I., S.Y., S.O., and T.T. T.H. and Y.H. conducted the genetic analysis of the microorganism.

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