





## CASE REPORT

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## A Rare Infectious Agent: *Elizabethkingia anophelis*; Second Case Reported from Turkey

### ABSTRACT

*Elizabethkingia anophelis* is a Gram-negative, aerobic, nonmotile bacillus belonging to the *Flavobacteriaceae* family. In recent years, it has emerged as a cause of life-threatening infections, especially in immunocompromised patients. In this study, a 6-month-old baby patient with *E. anophelis* growth in simultaneous tracheal aspirate and urine culture samples sent to investigate the etiology of fever while being followed in the intensive care unit due to the diagnosis of optic glioma is presented. Bacteria identification was performed using the VITEK MS® system, antibiotic susceptibility tests were performed using the VITEK 2 automated system and gradient strip test. Our case is the second *E. anophelis* case reported from Turkey. This case showed that this bacterium would start to appear as a factor in our country. More studies are needed to obtain more detailed information about this bacterium, to determine its transmission routes and resistance mechanisms and to establish appropriate treatment protocols.

**Keywords:** Antibiotic Resistance, *Elizabethkingia anophelis*, Infection, Opportunistic Pathogen.

## Nadir Bir Enfeksiyon Etkeni: *Elizabethkingia anophelis*; Türkiye’den Bildirilen İkinci Olgu

### ÖZET

*Elizabethkingia anophelis*, *Flavobacteriaceae* familyasına ait Gram negatif, aerobik, hareketsiz basildir. Son yıllarda özellikle bağışıklığı baskılanmış hastalarda yaşamı tehdit eden enfeksiyonların bir nedeni olarak ortaya çıkmıştır. Hastane ortamında kolonize olabilen bakteri, dekontaminasyona dirençlidir. *E. anophelis*, antibiyotiklere karşı oldukça dirençli bir bakteridir. Bu çalışmada, optik gliom tanısı nedeniyle yoğun bakımda takip edilirken, ateş etyolojisini araştırmak için gönderilen eş zamanlı trakeal aspirat ve idrar kültürü örneklerinde *E. anophelis* üremesi olan 6 aylık bebek hasta sunulmuştur. Bakteri identifikasyonu VITEK MS® sistemi, antibiyotik duyarlılık testleri ise VITEK 2 otomatize sistemi ve gradient strip test kullanılarak yapılmıştır. Olgumuz Türkiye’den bildirilen ikinci *E. anophelis* olgusudur. Bu vaka, ülkemizde de bu bakterinin artık etken olarak karşımıza çıkmaya başlayacağını göstermiştir. Bu bakteri hakkında daha detaylı bilgi edinilebilmesi, bulaşma yolları, direnç mekanizmalarının belirlenerek uygun tedavi protokollerinin oluşturulabilmesi için daha fazla çalışmaya ihtiyaç vardır.

**Anahtar Kelimeler:** Antibiyotik Direnci, *Elizabethkingia anophelis*, Enfeksiyon, Fırsatçı Patojen.

## INTRODUCTION

The genus *Elizabethkingia* are aerobic, nonfermentative, non-motile, catalase, oxidase and indole positive Gram negative bacilli that are ubiquitous in the environment including soil, water and other animal reservoirs (1). At the end of the phylogenetic analyzes (16S rRNA gene sequence) of the bacterium known as *Chryseobacterium* genus, which was initially in the *Flavobacteriaceae* family, Kim et al. It has been reported as a new genus by (2).

The first identified strains of the bacterium were *E. meningoseptica* and *E. miricola*, while *E. anophelis*, which was isolated from the midgut of the mosquito, was lastly identified in 2011. *Elizabethkingia* are generally opportunistic nosocomial pathogens and cause meningitis, pneumonia and bacteremia with high mortality rates (3).

After the identification of *E. anophelis* from *Anopheles gambiae* mosquitoes in Africa, the first case of human infection by this species was reported in 2013, followed by several outbreaks by *E. anophelis* from Singapore, Hong Kong, Taiwan and the United States. (3-6). Today, information about the transmission routes, pathophysiology and antibiotic resistance of *Elizabethkingia* bacteria is still insufficient (5). Bacteria that can colonize in the hospital environment are resistant to decontamination. It is thought that water systems in hospitals act as reservoirs for bacteria that can contaminate and colonize various solutions and devices used in hospitals (4). Although it is known that all genera can be found in soil, water and plants, it has been reported that *E. anophelis* is especially abundant in the midgut of *Anopheles gambiae* mosquitoes (3,4). Routine phenotypic and biochemical tests often fail to distinguish *E. anophelis* from other bacteria. At the same time, this bacterium is frequently described as *E. meningoseptica* in automated systems (2). However, thanks to newly developed diagnostic methods, there is an increase in the number of cases reported worldwide (2). In infections caused by *E. anophelis*, empirical treatment options are limited due to the lack of multi-drug resistance and drug sensitivity test standards of the bacteria. It is generally seen to be sensitive to fluoroquinolones (7). However, since *E. anophelis* is a newly identified bacterium, information on antibiotic resistance spectra and resistance mechanisms is insufficient (7).

In this study, the clinical features and antibiotic susceptibility of *E. anophelis*, which was isolated for the first time in our center from the tracheal aspirate and urine cultures of a patient hospitalized in the pediatric intensive care unit, will be examined.

## CASE REPORT

A 6-month-old girl, who came to the emergency department with seizure complaints,

was intubated and taken to the intensive care unit because her general condition was poor and her breathing was tachypneic. No pathological condition was found in the patient's anamnesis taken from the mother. An intracranial mass (optic glioma?) was detected as a result of radiological imaging, and a brain tumor operation was performed on the 21st day of hospitalization. The patient's general condition was poor in the postoperative period, and his blood culture was taken because his temperature was 38.8 degrees. Fluconazole (3mg/kg) treatment was started in the patient who had *Candida albicans* growth in his blood culture. The tracheal aspirate sample, which was taken simultaneously with the blood culture from the patient and sent to the laboratory, was cultivated on sheep blood agar, eosin methylene blue agar, chocolate agar media. Simultaneously, direct smear was made from the sample and evaluated by gram staining. Gram staining revealed abundant polymorphous leukocytes and gram negative bacilli. There was growth in all plates incubated for 18-24 hours at 35±2°C. (pic 1). Gram negative bacillus growth was observed in gram staining of plaques. Oxidase, indole and catalase tests were positive. Identification of breeding colonies was performed using the VITEK MS® (Bio-Mérieux, Marcy l'Etoile, France) system. Antibiotic susceptibility studies for ciprofloxacin, levofloxacin, trimethoprim/sulfamethoxazole (TMP/SMX), piperacillin/tazobactam (PRP), ceftazidime, cefepime, imipenem, meropenem, amikacin and gentamicin were performed with the Gradient strip test (Bianalyse, Turkey).

The results of antimicrobial susceptibility tests were evaluated according to other non-*Enterobacterales* bacteria by applying CLSI (Clinical and Laboratory Standards Institute) breakpoints (8). It was observed that the bacterium was resistant to all beta-lactam antibiotics and carbapenems. Only ciprofloxacin and levofloxacin were found to be sensitive. The patient was started on vancomycin (4x80 mg) and piperacillin/tazobactam (4x 80mg/kg) combination therapy. *E. anophelis* growth with the same antibiotic susceptibility profile was detected in the urine culture sent from the patient on the same day. The same bacterial growth was observed in the tracheal aspirate culture sent again on the 10th day of the treatment. The treatment was continued by adding clarithromycin (15mg/kg) suspension. The patient in the pediatric intensive care unit died on the 15th day of treatment.

## DISCUSSION

*E. anophelis*, after being isolated from the midguts of mosquitoes and taxonomically identified in 2011, spread rapidly in many countries and caused fatal opportunistic infections in patients (1). The first reported case of *E. anophelis* in the world is a neonatal meningitis case detected in Africa in

2011. The strain, which was first thought to be *E. meningoseptica*, was found to be a new strain in 16S rRNA analysis (1-3). Later, it was reported to cause infections and epidemics in Singapore, Hong Kong and the United States (5,6,9). The largest outbreak caused by *E.anophelis* was seen in 65 patients and in a hospital in the United States (USA) in immunocompromised patients and caused high mortality rates (30.8%) (6). *E.anophelis* was first reported in our country by Mirza in 2017. Mirza et al. identified 2 of the strains as *E.anophelis* as a result of the 16S rRNA analysis they performed on 5 strains previously identified as *E. meningoseptica* in their center. They isolated the strains from peripheral blood and urine samples of infant patients (8). Our case is the second infection case caused by *E.anophelis* reported from our country.

*E. anophelis* usually causes sepsis and/or meningitis in premature, newborn or adults with underlying disease, especially in immunocompromised, malignancy, chronic renal failure, diabetes mellitus, cirrhosis. In addition, it is seen as a causative agent in pneumonia, catheter-related bloodstream infections, skin and soft tissue infections, urinary tract infections and biliary tract infections (1). Although the majority of infections are hospital-acquired, 89% of the cases in the Wisconsin outbreak were reported to be community-acquired.

It is estimated that mortality rates in infections caused by *E. anophelis* vary between 24-60% (1,6,10). Our case was also a patient with cranial malignancy. In the patient who underwent optic glioma surgery, *E. anophelis* was found to be the causative agent in the tracheal aspirate and urine samples in the postoperative period.

The modes of transmission of *E. anophelis* still remain unclear. Although the bacterium was originally isolated from *Anopheles gambiae* mosquitoes, there is no evidence to support that human infection is a mosquito-borne disease (9).

In the epidemic seen in the USA, the source of infection was investigated, and the source could not be determined despite the examinations of tap

water, food and personal hygiene products (6). In Singapore, it has been suggested that *E. anophelis*, which was detected in the tap water aerators of the hospital, was responsible for the epidemic, and that this bacterium was transmitted to the patients of healthcare workers who infect their hands during hand washing (10). Information on the susceptibility of *E. anophelis* to antimicrobials is quite limited. The fact that bacteria have high resistance rates increases the importance of early diagnosis and appropriate antibiotic treatment (9). Although high resistance rates have been reported in almost all studies on *E. anophelis*, susceptibility to ciprofloxacin, levofloxacin, piperacillin/tazobactam, and piperacillin has been reported in some studies (1,4,6,8). In our case, treatment options became very limited due to the fact that the bacterium was sensitive only to quinolones and the patient was a baby. The patient was started on vancomycin and piperacillin/tazobactam combination therapy. However, the growth of the same bacteria in the tracheal aspirate culture sent on the 10th day of the treatment showed that there was no response to the treatment.

In conclusion; As seen in our study, *E. anophelis* is a bacteria that is highly resistant to antibiotics. It has also been confirmed once again that it is generally sensitive to quinolones. Our case is the second *E.anophelis* case reported from Turkey. This case has shown that this bacterium will begin to appear as a factor in our country as well. More studies are needed to obtain more detailed information about this bacterium, to determine its transmission routes and resistance mechanisms and to establish appropriate treatment protocols.

**Ethics Committee Approval:** Since our study is a case report, ethics committee approval is not required.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author Contributions:** Concept – EÖŞ,ÖA; Supervision-OA; Data collection-EÖŞ-BE-VC; Posted by-ÖA,EÖŞ, MK

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