

# Catheter-Related Bacteremia in a Hemodialysis Unit: Cronobacter Sakazakii

## *Hemodiyaliz Ünitesinde Kateter Kaynaklı Bakteriyemi Etkeni: Cronobacter Sakazakii*

### ABSTRACT

In this study, a case of catheter-related bacteremia caused by *Cronobacter sakazakii*, which was successfully treated with antibiotic therapy, was presented. Since 1989, cases of contamination of powder infant formula caused by *C. sakazakii* have been reported. However, adult infections related to *C. sakazakii* are exceedingly rare.

A 61-year-old male patient was in dialysis treatment with chronic renal failure and blood cultures were taken from peripheral veins and catheter because of fever. At the same time, moxifloxacin (400 mg/day iv) and ampicillin-sulbactam (1 g/day iv) were started as empirical therapy. One bacterium was detected on blood cultures obtained from peripheral veins and catheters and this bacterium was identified as *C. sakazakii* by the VITEK 2 Compact automated system. The species identification of the isolated strain was confirmed by 16S rRNA sequence analysis. The treatment of the patient, who was thought to represent a case of catheter-related bacteremia, was continued and the catheter was not removed since subsequent cultures did not reveal any bacterial growth. To our knowledge, the presented case is the first bacteremia related to *C. sakazakii* from Turkey. As a result, *C. sakazakii* is an infection agent that we have recently encountered and may pose a threat to public health.

**KEY WORDS:** *Cronobacter sakazakii*, Bacteremia, Catheter-related infections

### ÖZ

Çalışmada, antibiyotik tedavisi ile başarılı bir şekilde tedavi edilmiş *Cronobacter sakazakii*'nin etken olduğu kateter kaynaklı bakteriyemi olgusu sunulmuştur. 1989 yılından bu yana *C. sakazakii*'nin neden olduğu toz bebek maması kontaminasyon olguları bildirilmiştir. Bunun haricinde *C. sakazakii*'ye bağlı yetişkin enfeksiyonları çok nadir görülmektedir.

Altmış bir yaşında erkek hasta kronik böbrek yetmezliği tanısı ile diyaliz tedavisinde iken ateş yüksekliği nedeniyle periferik venden ve kateterden kan kültürü alınmıştır. Aynı zamanda hastaya ampirikmoksifloksasin (400 mg/gün) ve ampisilin-sulbaktam (1 gr/gün) tedavisi başlanmıştır. Hastanın hem periferik veninden hem de kateterinden alınan kan kültürlerinden bir adet bakteri üremiştir ve bu üreyen bakteri VITEK 2 otomatize sistemi ile *C. sakazakii* olarak tanımlanmıştır. İzole edilen suşun tür tayini 16S rRNA sekans analizi ile doğrulanmıştır. Kateter kaynaklı bakteriyemi olgusu olarak değerlendirilen hastanın tedavisi sürdürülmüştür ve daha sonra alınan kan ve kateter kanı kültürlerinde üreme saptanmadığı için kateteri çekilmemiştir. Sunduğumuz olgu, bildiğimiz kadarıyla, ülkemizden bildirilen *C. sakazakii*'ye bağlı ilk bakteriyemidir. Sonuç olarak, *C. sakazakii* yeni karşılaştığımız bir enfeksiyon etkeni olup halk sağlığına tehdit oluşturabileceği düşünülebilir.

**ANAHTAR SÖZCÜKLER:** *Cronobacter sakazakii*, Bakteriyemi, Kateter kaynaklı enfeksiyon

### INTRODUCTION

*Cronobacter sakazakii*, a member of the family Enterobacteriaceae, is a mobile, oxidase-negative, facultative anaerobe bacil-

lus that is occasionally found in microbiology laboratories. Yellow-pigmented colonies are an important characteristic of the species. Although it was previously named

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as *Enterobacter sakazakii*, it was reclassified later and defined as a species of *Cronobacter* genus comprising seven species. These species are *C. malonaticus*, *C. turicensis*, *C. dublinensis*, *C. muytjensii*, *C. condimerti*, *C. universalis* and *C. sakazakii*. Clinically, the most frequently isolated species among them is known to be *C. sakazakii* (1,2).

*C. sakazakii* can be isolated from a wide variety of environmental samples such as hospitals, houses, water resources and food and has been identified as an opportunistic pathogen. Its capacity to form biofilms may confer it resistance to antimicrobials and lead to serious long-term problems on surfaces such as plastic, silicon and rubber in hospital environments. It has caused epidemic outbreaks, especially in the neonatal units due to contamination incidences in powdered infant formulas. In premature newborns, it may cause sepsis, meningitis and necrotizing enterocolitis infections. The risk factors for *C. sakazakii* infections are preterm babies, low birth weight and suppression of the immune system. It has also been identified as the infectious factor in a wide variety of clinical conditions such as bacteremia, pneumonia, cholecystitis and urinary system infections in adult patients. Patients aged older than 55 years with a suppressed immune system and patients with underlying diseases such as malignancy are especially at risk. The mortality rate in *C. sakazakii* infections ranges from 10 to 80% (3-5).

### CASE REPORT

In this study case, a 61-year-old male patient who had chronic renal failure due to hypertension for 7 years was presented. This patient has been undergoing dialysis at the Ahi Evran University Educational and Research Hospital twice a week for three years. There was a history of surgery for bypass and an aortic aneurysm.

The following laboratory tests were performed in January 2016 on admission to hemodialysis. The peripheral blood count results were as follows: white blood cells  $6.4 \times 10^3$  cells/ $\mu$ L, red blood cells  $4.49 \times 10^6$ / $\mu$ L, hemoglobin 12.7 g/dL, mean corpuscular volume 86.9 fL and hematocrit 39%. The white blood cell count was within the reference ranges but with a left shift where 73.4% of the cells were neutrophils. The C-reactive protein (CRP) level was 3.8 mg/dL. Because the patient had a fever (38.8 °C), two sets of blood cultures, one from the peripheral veins and the other from the catheter were taken. The blood culture taken from the catheter yielded a positive signal after incubation for 12 h. The blood culture obtained from the vein yielded a positive signal after incubation for 16 h in BACTEC 9120 (Beckton Dickinson, USA). Gram staining was performed directly from the vial and gram-negative bacilli were observed. Blood agar and eosin methylene blue (EMB) agar were inoculated from the vial and incubated at 37°C for 24 h. Yellow-pigmented colonies were observed in EMB agar within 1 day after the incubation. It was determined that the strain was oxidase negative. Finally, the strain was identified as *C. sakazakii* by the VITEK-2 Compact automated system (bioMerieux).

The species identification of the strain was also confirmed by 16S rRNA gene sequencing. The 16S rRNA sequence data was edited by BioEdit (6) and the obtained sequence was analyzed by BLAST searches using the NCBI GenBank database (7). The 16S rRNA gene sequence for *C. sakazakii* FM1 has been deposited in the GenBank database under the accession number of KY119380.

Antimicrobial susceptibilities of the strain were evaluated by the VITEK-2 Compact automated system. Among the studied antimicrobial agents, the strain had an overall high antimicrobial susceptibility pattern with resistance only to cefazolin, cefuroxime and cefuroxime axetil. Antimicrobial susceptibility rates and minimum inhibitory concentration values of the antimicrobials are given in Table I.

Empirical therapy with moxifloxacin (400 mg iv) and ampicillin-sulbactam (1 g i.v.) was initiated for the patient. The treatment was not changed later because the isolate was susceptible to the applied antibiotics. The CRP level decreased to 0.8 mg/dL in the laboratory test performed within 5 days after the treatment and the patient's body temperature was measured as 36.7 °C. His blood pressure was 130/80 mm Hg. There was no evidence of bacterial growth in the repeated blood cultures.

**Table I:** Antimicrobial susceptibility of *Cronobacter sakazakii* FM1.

Antimicrobials	MIC ( $\mu$ g/ml) by VITEK	CLSI interpretation VITEK
Amoxicillin/Clavulanic acid	$\leq 2$	S
Piperacillin/Tazobactam	$\leq 4$	S
Cefazolin	4	R
Cefuroxime	4	R
Cefuroxime Axetil	4	R
Ceftazidime	$\leq 0.12$	S
Ceftriaxone	$\leq 0.25$	S
Cefepim	$\leq 0.12$	S
Ertapenem	$\leq 0.12$	S
Meropenem	$\leq 0.25$	S
Amikacin	$\leq 2$	S
Gentamicin	$\leq 1$	S
Ciprofloxacin	0.5	S
Tigecycline	$\leq 0.5$	S
Colistin	$\leq 0.5$	S
Trimetoprim/Sulfametoxazol	$\leq 20$	S

**MIC:** Minimal inhibitory concentration, **R:** Resistance, **S:** Susceptible.

## DISCUSSION

Various bacterial and fungal species, and especially the microbial flora of the skin, lead to catheter-related infections. Infectious agents may vary depending on various factors such as the catheter type, location of the catheter, and the conditions of the host and hospital unit. Coagulase-negative staphylococci, *Staphylococcus aureus*, aerobic gram-negative bacilli and *Candida albicans* are the most common infectious agents observed in catheter-related infections (8).

Our case indicates a catheter-related blood stream infection caused by a gram-negative rod. *Cronobacter* spp. are primarily found in water, soil, food and the intestines of humans and animals. Passive carriage on the hands of medical personnel is the most important cause of the infection. The bacterium *C. sakazakii* can contaminate, survive and reproduce in hospital equipment such as hemodialysis and respiratory instruments (3).

Up to now, *C. sakazakii* has been reported in more than 100 newborns as a causative agent of invasive infections such as meningitis and necrotizing enterocolitis (9). This bacterium, which can cause serious infections in the elderly and immunocompetent patients, is actually rare in adults (10). A few cases of clinical infections have been reported in elderly. Tamigniau et al. reported a case of *C. sakazakii* bacteremia secondary to a suspected cyst infection in a heart-and-kidney transplanted patient with polycystic kidney disease. They also reviewed 17 adult infection cases (10 males and 7 females) reported in the literature, with an average age of 63 years, and found that *C. sakazakii* was the most frequently isolated bacterium in the blood (53%). The other samples from which this bacterium was isolated were sputum (17%), bile (6%), urine (6%), biopsy (6%), bone (6%) and mouth (6%). The clinical manifestations of these cases were reported as bacteremia, pneumonia, acute cholecystitis, urinary tract infection and osteomyelitis, whereas the underlying diseases were mainly carcinomas, diabetes mellitus and chronic renal failure. It was stated that clinical success was not achieved in 6 out of 17 patients and these patients died (4). Kang et al. reported a bacteremia related to *C. sakazakii* as the causative agent in a 76-year-old female patient who suffered from various chronic diseases such as uterine carcinoma, urinary tract infection, type II diabetes, hypertension and chronic renal disorder (10).

In the literature, *C. sakazakii* isolates have been reported to be highly susceptible to antibiotics (4). Among the studied antimicrobials, the isolate in the present case was found to be resistant only to cefazolin and cefuroxime. A positive clinical response was achieved in this case that was empirically treated with moxifloxacin and ampicillin-sulbactam. Therefore, the catheter was not removed.

In conclusion, although *C. sakazakii* is mainly known to cause epidemic outbreaks in newborns via infant formulas, it can be also isolated from a wide variety of environmental samples. In addition, this bacterium emerges as an infectious agent in hospitals by attaching to various hospital surfaces due to its capacity to form biofilms. Finally, we would like to emphasize that this species should be investigated and considered so that it does not become a threat to public health in the future.

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