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First Case of Intravenous Drug Use-Related Candidemia in Türkiye

Türkiye'de İntravenöz İlaç Kullanımına Bağlı İlk Kandidemi Vakası

Abdurrahman KAYA[1](İD), Hasan ZERDALİ[3](İD), Buse KOÇ[1](İD), Ümit TOZALGAN[1](İD), Can ÇİFTÇİ[3](İD), Ali MERT[2](İD)

[1] Clinic of Infectious Diseases and Clinical Microbiology, İstanbul Training and Research Hospital, İstanbul, Türkiye
[2] Department of Infectious Diseases and Clinical Microbiology, Medipol University Faculty of Medicine, İstanbul, Türkiye
[3] Clinic of Internal Diseases, İstanbul Training and Research Hospital, İstanbul, Türkiye

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ABSTRACT

Although Candida species are normal flora elements of the body, they can cause various diseases from mucocutaneous infections to candidemia. The presence of a central venous catheter, use of broad-spectrum antibiotics, parenteral nutrition, dialysis, neutropenia, malignancy, and immunosuppressive treatments are the most reported risk factors for candidemia. Complications that develop during follow-up increase both morbidity and mortality. The incidence of fungal infections has been increasing in recent years. This increase is also seen in intravenous drug users. In these patients, candidemia can cause serious life-threatening complications including septicemia and end-organ failure. To date, no cases of intravenous drug use-related candidemia have been reported in our country. This patient represents the first documented case. In this case, we aim to draw attention to the relationship between intravenous drug use and candidemia.

Key Words: *Candidemia; Intravenous drug use; Hemoculture*

ÖZ

Türkiye'de İntravenöz İlaç Kullanımına Bağlı İlk Kandidemi Vakası

Abdurrahman KAYA[1], Hasan ZERDALİ[3], Buse KOÇ[1], Ümit TOZALGAN[1], Can ÇİFTÇİ[3], Ali MERT[2]

[1] İstanbul Eğitim ve Araştırma Hastanesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, İstanbul, Türkiye
[3] Medipol Üniversitesi Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, İstanbul, Türkiye
[4] İstanbul Eğitim ve Araştırma Hastanesi, İç Hastalıkları Kliniği, İstanbul, Türkiye

Kandida türleri, vücudun normal flora elemanları olmalarına rağmen mukokutanöz infeksiyonlardan kandidemiye kadar birçok değişken hastalığa neden olabilmektedir. Santral venöz kateter varlığı, geniş spektrumlu antibiyotik kullanımı, parenteral beslenme, diyaliz,

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nötropeni, malignite ve immünsupresif tedaviler kandidemi için en çok bildirilen risk faktörleridir. Kandidemi sırasında gelişen komplikasyonlar ise hem morbiditeyi hem de mortaliteyi arttırmaktadır. Mantar infeksiyonlarının insidansı son yıllarda artış göstermektedir. Bu artıştan intravenöz ilaç bağımlısı olan bireylerde nasibini almaktadır. Bu hastalarda kandidemi, sepsis ve organ yetmezliği gibi hayatı tehdit eden ciddi komplikasyona neden olabilmektedir. Şu ana kadar ülkemizden bildirilmiş intravenöz ilaç kullanımına bağlı kandidemi olgusu yoktur. Bu yönüyle bu hasta ilk vaka olma özelliği göstermektedir. Bu vakada amacımız, intravenöz ilaç kullanımı ile kandidemi arasındaki ilişkiye dikkat çekmektir.

Anahtar Kelimeler: *Kandidemi; Damar içi ilaç kullanımı; Kan kültürü*

INTRODUCTION

Candidemia is a bloodstream infection caused by *Candida* spp. Among healthcare-related bloodstream infections, it ranks as one of the leading causes of mortality and morbidity[1]. The infection usually becomes evident in a few days or weeks after hospitalization, and the typical risk factors include recent abdominal surgery, prolonged hospital stay or intensive care unit stay, hemodialysis, organ transplantation, malignancy, broad-spectrum antibiotic use, total parenteral nutrition (TPN) and central venous catheter use[2-5]. Intravenous drug use (IVDU) is not an established risk factor for candidemia. However, there has been a marked increase recently in invasive *Candida* infections in patients with IVDU[6]. In a multi-regional report from the USA in 2017 on candidemia surveillance, one in eight cases was associated with recent IVDU. This suggests that IVDU may be a specific risk factor for candidemia[7]. In this case report, we present a patient who, after 10 years of intravenous drug use, developed candidemia.

CASE REPORT

A 32-year-old male with no comorbidities and a 10-year history of intravenous drug use presented to the emergency department with complaints of fever, chest pain, cough, and muscle aches for the past three days. Physical examination revealed a fever of 39.3°C, tachycardia (120/min), and SpO_2 of 97% in room air. On auscultation, rales were detected on the left lung at the end of inspiration. Blood analysis revealed white blood cells= 28.000/mm^3, C-reactive protein (CRP)= 326 mg/L. Computed tomography of the thorax revealed a 20 mm pleural effusion and focal ground-glass opacities in the right upper lobe and the left lingular segment. COVID-19 PCR test was negative, the patient was initially diagnosed with pneumonia, and empirical treatment with ceftriaxone 2 x 1 gram and moxifloxacin 1 x 400 mg was initiated. When methicillin-sensitive *Staphylococcus aureus* (MSSA) was detected in two sets of hemoculture, ceftriaxone treatment was switched to piperacillin-tazobactam 3 x 4.5 gr. On the fifth day of antimicrobial therapy, as the fever persisted, drainage of the pleural effusion was performed. The biochemical analysis of pleural fluid indicated an exudate, adenosine deaminase level was within normal limits, and polymorphonuclear leukocyte predominance was observed on Giemsa staining. The material was also sent out for tuberculosis PCR and culture. The aerobic culture was negative. No vegetation was detected with transthoracic and transesophageal echocardiography. On serological tests, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) were negative but anti-hepatitis C virus (HCV) was positive, and HCV RNA was 950.000 IU/mL. Due to the persistent fever and a lack of marked improvement in the general clinical condition, the treatment was switched to meropenem (3 x 1 gram) and vancomycin (2 x 1 gram). On the eighth day of hospitalization, candida was observed on blood culture smears; consequently, fluconazole was given empirically. The blood culture results revealed the presence of *Candida tropicalis*. There were no lesions on the skin. On ophthalmic examination, two lesions compatible with fungal endophthalmitis were detected. Due to the demonstration of yeast on gram stain, fluconazole therapy was switched to liposomal amphotericin B. On the 11^{th} day of the hospital stay, *Candida glabrata* was identified in the blood culture. A detailed history was obtained due to multiple positive *Candida* blood cultures. A meticulous medical history revealed that the patient used IV drugs intermittently during the hospital stay. On the fourth day of

antifungal therapy, the patient's fever subsided, and during follow-up, there was an improvement in clinical condition. The CRP decreased to 48 mg/L, and the serum procalcitonin level became negative. However, the patient opted to leave the medical service and, upon his request, was discharged from the hospital on the 10th day of liposomal amphoterisin B treatment.

DISCUSSION

Candida spp. normally can colonize on the mucosal surfaces including the mouth, throat, guts and vagina, and also skin, without causing disease[8]. It can lead to invasive *Candida* infections by invading internal organs or the bloodstream in some patients with risk factors. Candidemia is one of the common causes of bloodstream infections among hospitalized patients in the United States (US) and causes longer hospital stays and higher mortality rates[9,10]. Therefore, it is responsible for high medical costs. In our case, despite broad-spectrum antibiotic therapies for pneumonia, the fever did not subside and elevated acute-phase reactants persisted. On follow-up, antifungal therapy was initiated due to *Candida* seen on the gram staining of the blood smear.

Opioid addiction is becoming an increasingly important public health problem worldwide. In 2015, over 50.000 people died from opioid overdose in the US. The mortality rate secondary to opioid use has increased five-fold since 1990[11]. These individuals frequently develop acute infections including injection site abscesses and endocarditis, and chronic viral infections caused by HBV, HCV, and HIV. In addition, complications of these infections are common in individuals with such conditions. In our case, MSSA was isolated in blood cultures taken upon hospitalization, and anti-HCV and HCV RNA positivity were detected in the sera. The cause of candidemia and MSSA bacteremia was IVDU, and pneumonia and pleurisy developed as a result of the bacteremia.

In the literature, studies from the 1970s to the 1990s on *Candida albicans* infections in intravenous drug users emphasize that these infections often result from nonsterile injection practices[12]. They concluded that candidemia resulted from inadequate skin disinfection and saliva contact with syringes. In addition, the use of lemon juice to dissolve impure brown heroin suggests that the source of *Candida* is these contaminated fruit juices. In affected patients, clinical symptoms manifest as nodular and pustular cutaneous lesions, chorioretinitis, and osteoarticular infections[13]. After the 1990s, the increase in pure heroin resources eliminated the need for acidic solvents such as lemon. Therefore, the IVDU-related candidiasis problem has substantially disappeared. However, there has been an increase in opioid addiction and corresponding intravenous drug use recently.

Although intravenous drug use is not traditionally considered a risk factor for candidemia, there is an observed increase in *Candida* infections among intravenous drug users in the literature. Poowanawittayakom et al. investigated 198 candidemia cases and found that 24 of them were intravenous drug users[6]. When evaluating all candidemia cases, non-albicans *Candida* frequency, chronic hepatitis C co-infection, and complications such as endocarditis and osteomyelitis were more commonly observed in intravenous drug users. Additionally, intravenous drug users had additional risk factors such as cancer, surgical operations, dialysis, or the presence of a central venous catheter. In another study from the US between 2014-2018, a total of 637 candidemia cases were diagnosed in 599 patients, with intravenous drug use observed in 82 of them[14]. 180 patients (77 IVDU) were evaluated, IVDU patients were younger, majority of them were white and female. There were accompanying risk factors such as central venous catheter in more than half of patients, recent antibiotic use in 73%, surgical operation in 16%, cancer in 9%, and total parenteral nutrition in four patients with IVDU. Complications of candidemia including endocarditis, septic embolism, and organ failure were seen more frequently in IV drug users compared to the non-candidemia patients. In both studies, patients without risk factors were not reported. Barter et al. reported 203 candidemia cases; 23 (11%) occurred in 22 patients with a history of IVDU and 10 (43%) were considered community-onset infections, while six cases were considered hospital-acquired candidemia[15]. The

authors concluded that IVDU can be a risk factor in the hospital setting as well as in the community. Many patients had some additional risk factors including admission to an intensive care unit, presence of a central venous catheter, and use of broad-spectrum antibiotics. As in our patient, three patients left against medical advice, and four died in hospital. During follow-up, our patient developed fungal endophthalmitis, and he had no additional risk factors.

In our country, intravenous drug use was not identified as a risk factor in any studies of *Candida* bloodstream infections. Additionally, no cases related to IVDU have been reported. Mete et al. examined 210 candidemia cases and found that the most common risk factors were the presence of a central venous catheter and recent surgery[16]. Although non-albicans species were common in total, *Candida albicans* was isolated in 32% of the patients. Koçak et al. identified candidemia in 38 of 22.507 adult patients with bloodstream infections; 36 (95%) were hospital-acquired, and one (2.5%) was healthcare-related[17]. *Candida albicans* was isolated in more than half of the blood cultures, and the presence of a central catheter was noted in the majority of the cases (68.4%).

In conclusion, IV drug users are at risk for various viral and bacterial infections. Persistent intravenous drug use introduces the risk of rare diseases, such as fungal infections, into the clinical scenario. It is crucial to prevent intravenous drug use within the hospital setting, and healthcare providers should remain vigilant for the potential occurrence of candidemia in these patients.

CONFLICT of INTEREST

No conflict of interest declared.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: AK, AM

Analysis/Interpretation: AK, CÇ

Data Collection or Processing: BK,ÜT

Writing: AK, HZ, CÇ

Review and Correction: ÜT, BK

Final Approval: AK, AM

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Address for Correspondence/Yazışma Adresi

Dr. Abdurrahman KAYA

Clinic of Infectious Diseases and Clinical Microbiology, İstanbul Training and Research Hospital,
İstanbul, Türkiye

E-mail: dr.abdkaya@hotmail.com