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URINARY SYSTEM INFECTIONS CAUSED BY CANDIDA KEFYR AND TREATED WITH FLUCONAZOLE (Case Report)

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ÖZ

Approximately 25% to 50% of nasocomial candida infections are seen in the medical, medico-surgical, surgical, and intensive care units (ICU) and out of these 35% to 65% are the non-albicans Candida (NAC) types. C. kefyr is responsible less than 1% of the candidemias among the NAC types. Other candidas might also be pathogenic in the event of increasing use of drugs, surgical interventions, organ transplantations, and AIDS, which damage the immunity system of individuals. It has been observed that the most sticky type is C. albicans and that this characteristic is not found in C. kefyr. This difference indicates a relationship between adherence and pathogenity.

Although amphotericine B treatment has been suggested for patients who have C. kefyr multiplication in their urine, in our patient we applied fluconazole and the patient responded. Therefore, in the treatment of patients who are elderly and who have a history of surgical interventions and diabetes mellitus, instead of amphotericine B, which has many nephrotoxic and systemic side effects, we selected fluconazole as an anti-fungal as a drug in our treatement and got a response from our patient and we wished to present our case.

Anahtar Kelimeler: Candida Kefyr, Flukonozal, Yoğun Bakım Ünitesi

FLUKONAZOLLE TEDAVİ EDİLEN CANDİDA KEFYR'E BAĞLI BİR ÜRİNER SİSTEM ENFEKSİYONU (Olgu Sunumu)

ABSTRACT

Nazokomiyal Candida enfeksiyonlarının yaklasık % 25-50'si medikal, medikal-cerrahi, cerrahi Yoğun bakım ünitelerinde (YBÜ) görülüp, bunların da % 35-65'inden Non-albicans Candida (NAC) türleri

sorumludur. C. kefyr NAC türleri içerisindeki kandidemilerin % 1'inden daha azından sorumludur.

Artan ilaç kullanımı, cerrahi girisimler, organ nakilleri ve AIDS gibi bireyin bağısıklığını bozan durumlarda, diğer candidalar da patojen olabilir. En fazla yapısma yeteneği bulunan türün C. albicans olduğu, ancak bu özelliğin C. kefyr'de bulunmadığı gözlemlenmistir. Bu farklılık adherens ile patojenliğin iliskisine isaret etmektedir. Ðdrarda C. kefyr üreyen hastalarda genelde tedavide amfoterisin B önerilmesine rağmen, bizim hastamızda uyguladığımız gibi Flukonazol verilerek tedaviye yanıt alınması nedeniyle bu sekilde ileri yasta olan, cerrahi girisim ve Diabetes Mellitus öyküsü olan hastalarda tedavide amfoterisin B gibi nefrotoksik ve sistemik yan etkileri çok olan bir ilaç yerine antifungal olarak Flukonazol tedavisine cevap veren bir olgumuzu sunmayı amaçladık.

Key words: Candida Kefyr, Fluconazole, İntensive Care Unit

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INTRODUCTION

In the past, amongst the Candida types, only C. albicans was taken to be pathogenic. After the 1960s, depending on clinical experience and the results of various experimental models, it has been accepted that there are 17 pathogenic Candida types [1-3]. In intensive care units, nosocomial Candida infections are seen at the rate of 25% to 50%. Out of all candidemias 35% to 65% are caused by non-albicans Candida (NAC) types. C. kefyr is one of the pathogenic types that is less than 1% responsible for the candidemias amongst the NAC types. Other Candida types might also be pathogenic in the event of the increasing use of drugs, surgical interventions, organ transplantations, and AIDS, which damage the immunity system of individuals [4,5]. It has been observed that C. albicans is the most sticky type amongst the Candida types but this characteristic does not exist in C. kefyr. This difference amongst the Candida types indicates a relationship between adherence and pathogenicity [1,2,5]. Herein, we present a patient in our intensive care unit in whom C. kefyr was produced in the urine and who was diagnosed with urinary system infection and who was generally treated with amphotericine B, but who responded to fluconazole treatment.

CASE REPORT

A woman patient aged 86 was admitted to our emergency service with complaints of dizziness, being generally unwell, loss of power in the left half of her body, disorder in speech, tendency for sleep, respiratory problems, vomiting and aspiration, and a damaged condition of consciousness. As a result of the information obtained from her family, we learnt that she had no systemic problems other than hypertension. In the cranial computer tomography that was processed urgently, the patient, who was diagnosed with right parietal lobar haemorrhage, was examined in our intensive care unit. Her blood pressure was 220/160 mmHg, pulse was 150 beats per minute, respiration rate was 35 per minute, and in the first arterial blood gas analysis, 4 L/min 02 while was given by mask, pH 7.16, p02 53 mmHg, pCO2 53 mmHg, SO2 79.3%, HCO3 16.8 mmol, Bex–8.1 mol results were observed. The general condition was medium, the pupils were isochoric, the reflexes of light and cornea existed, the consciousness was blurred, and the co-operation and orientation of the patient were nil. When asidos, hypocsemia, and hypercapni were detected in the arterial blood gasses of the patient, endo-tracheal intubation was applied and mechanical ventilation was started. In the cardio-vascular system examination, the heart was rhythmic and ejection blowing existed in the tachycardiac, aortic focus. No other pathology was detected in the other systemic examinations. In the total blood test, leukocyte number was 7000/uL, hemoglobin 13.2 g/dL, and hemotocrit 40.4%, and, in the

blood biochemistry, glucose was 123 mg/dL, lactate 47 mg/dL, Na+ 141 mmol, Ca++ 9.6 mmol, K+ 3.7 mmol, BUN 14 mg/dL, creatin 1.0 mg/dL, PT 14.0 s, and PTT 25 s. The liver function tests, the total urine test, and pheripherical multiplication, sedimentation, and infection parameters such as c reactive protein (CRP) were normal. The posterior-anterior chest scans and EKG were normal and no signs of ischemia were observed in the heart. The patient underwent surgery immediately in the department of neurosurgery and the haemorrhage was stopped. Interior brain anti-oedema treatment was started. The post-operation fever was 38.4 °C and so cultures were taken. Due to the reproduction of Klepsiella pneumoniae in the endotracheal aspirate the patient was given sulbactam + ampicillin 4 x 1 g IV + ciprofloxacin 2 x 200 mg IV. When the lungs were examined, bilateral rough rales were observed and in the PA lungs graphic infiltrative signs of pneumonia were observed. During the time she was in the intensive care unit, the daily energy and protein requirements were met with NG catheter enteral nutrition. She was thought to require mechanical ventilation for a long time, and on the 14th day percutaneous tracheostomy was performed. It was thought that the patient would stay in the intensive care unit for a long time. On the 21st day percutaneous gastrostomy was performed. In order to avoid bed sores, the patient's position was changed and dressings to the wounds were applied in a routine manner, and for the purposes of avoiding contracture development, passive joint exercises were performed in the company of a physical therapist. After 23 days the patient's fever was 38.5 °C, upon which cultures were taken and Pseudomonas aerogonosa was diagnosed in the endotracheal aspirate. Therefore, the patient was given netilmicin 1 x 400 mg and ceftazidime 2 x 500 mg IV. The treatment lasted 15 days. Meanwhile a urine culture was taken from the patient who had a Foley catheter it was found that 100,000 colony U/mL C. kefyr had reproduced. Therefore, fluconazole 2 x 100 mg IV was started since it is the most appropriate agent with minimum inhibitor concentration (MIC). The MIC of C. kefyr is given in Table 1. The treatment continued for 10 days and a response was achieved. There was no reproduction in the cultures taken both after 48 h of the treatment and at the end of the treatment. Then we passed on to the thrombophlebitis and pulmonary emboly proflaxy. When her lung scans had normalised, the ventilator application was stopped and the patient was followed up with a T piece. After this the patient was observed with the spontaneous respiration of air in the room. Her general condition improved and the viral findings stabilised and she was discharged from the hospital 45 days after her admittance with tracheostomy and percutaneous gastrostomy.

Table 1: The sensitivity of Candida kefyr towards antifungal agents.

Antifungal drug	**Antifungal agent reference gap**				**Result**
Fluconazole	< = 8	16 - 32	-	> = 64	0.125 sensiti
Amphotericine ve B	< = 1	-	-	-	0.064 sensitive
Ketoconazole	-	-	-	-	0.016 sensitive

DISCUSSION

More than 150 Candida types have been defined, but only nine cause disease in human beings. C. albicans is the type that causes the most frequent number of diseases in human beings. The Candida type does exist in the human flora normally but when the defence mechanism of the host changes it might lead to the development of disease [1,2,4]. Intervention with a tool into the urinary system, the use of antibiotics, and old age are among the risk factors for a fungus infection and most frequently the cause is Candidas, but most of the separating causes are about harmless colonisations. With the change of Foley catheter, it has been reported that candiduria (<20%) have been removed. However, in some patient groups, after the candiduria, candidiasis might develop with the acute hematogen spread or sometimes candiduria could be the only symptom of disseminated candidiasis. Candida infections have a wide range from urinary tract infections to infections spreading by hematogenous ways, is very frequently encountered amongst intensive care patients. NAC types of infections are even more frequent and the fact that they have resistance against isolation is worrisome. Pathogenic fungal C. kefyr infections are not very frequent [5-8]. Accordingly, for the purposes of eliminating the symptoms and findings of the infection in the parenchyma from the urine collecting system, fluconazole (200 mg/day, for a period of 7-14 days) oral or IV or amphotericin B (0.3-1.0 mg/kg/day, for a period of 1-7 days) IV options that are foreseen to be applied to the selected patients under the disseminated candidiasis development risk [9-11].

Although it has not been documented widely in the literature, it has been reported that C. kefyr causes clinical disease in human beings. Eight clinical studies and 2 case reports have been published in which C. kefyr has been isolated from fungal pathogens. The C. kefyr case that has developed as a secondary complication of a disease has been reported in a patient with cystitis. This patient was treated with antibiotics for a long time after the surgical procedure. In the other case, it was reported that C. kefyr had caused fungemia and the patient's immune system had been suppressed. In a scanning of 10 years, fungemia was observed in 168 patients and in only one patient C. kefyr was isolated as a pathogen [3,4].

Corpus et al. (12), in a patient who developed liver dysfunction secondary to polycythemia vera disease with Budd Chi-

ari, at the age of 43, applied antibiotics treatment, where the pathogens were not detected in the patient, but assumed to have spontaneous bacterial peritonitis, of ceftriaxone 1 g IV and in the culture samples taken later, in accordance with the reproduction of different microorganisms. In addition, in the urine culture taken (from Foley catheter) 100,000 colonies U/mL C. kefyr were isolated. In the treatment, the Foley catheter was changed and amphotericin was applied for 5 days, which is the agent with the most appropriate minimum inhibitor concentration (MIC).

Corpus et al. [12] isolated C. kefyr in a culture sample taken from the pleural serum of a patient who was treated with combined antibiotics with septic shock and ARDS, who was diagnosed with colon cancer and to whom chemotherapy was given and who had neuropathic entube with nosocomial pneumonia. In the treatment for 14 days amphotericin B (MIC 0.125) 420 mg per day IV was applied, which is the most appropriate agent with the minimum inhibitor concentration (MIC). However, they did not get a response from the treatment and after 6 days in a culture taken they again isolated C. kefyr. They stopped amphotericin treatment, and they reported that they continued with voriconazole 312 mg IV 2 x 1 for 2.5 months.

In the urine culture sample taken from our patient, after C. kefyr had been isolated, for treatment we changed the Foley catheter and we started fluconazole (200 mg per day, for 14 days) IV, which is the most appropriate agent with the MIC and the patient responded to the treatment. In the urine culture checked after 48 hours, no microorganisms had reproduced. In such cases the treatment should not immediately be started with amphotericin B. Both of the patients reported by Corpus et al. [12] had both received various drug treatments and their immune systems were suppressed. Our patient also had lots of antibiotics treatments and had hemiplegy in the intensive care unit and tracheostomy.

In in vitro studies, it has been reported that antifungal agents have an effect on C. kefyr and the pathogens that appear. It has been shown that C. kefyr should be 1 mg/mL for MIC 50 and 4 mg/mL for MIC 90. In 8 cases out of 10, the C. kefyr infections of the patients resolved and fluconazole treatment as a start was successful, and the treatment was ineffective for the remaining 2 patients. One out of the 2 remaining patients was treated with high doses of IV fluconazole (400 mg per day), and the other patient was treated with amphotericin B. In the literature, it is stated that the 2 patients whose fluconazole treatments were insufficient at the beginning should receive fluconazole treatment within 2 months [9-12]. In our patient, after the C. kefyr had been isolated, we continued the treatment by changing the Foley catheter, and we started fluconazole (200 mg per day, for 14 days) IV, which is the most appropriate agent with the MIC and the patient responded to the treatment. In the urine culture checked after 48 hours, no microorganisms had reproduced. Amphotericin B treatment was not necessary for our patient.

The data show that although C. kefyr is rarely seen it is a potential pathogen. In patients with the risk of development of disseminated candidiasis, it has been advised to use fluconazole or amphotericin B for treatment [1-3]. Fluconazole (400 mg per day) was given to 2 out of 10 patients in whom C. kefyr had been detected, and amphotericin B IV was given to the rest of the patients. Although in the literature most of the time amphotericin B is recommended for patients with reproducing C. kefyr [9-12], for the reason described in our patient, namely a response was seen after the application of fluconazole, for patients who are old, and who have a history of surgical intervention and DM, we think that it is more appropriate to use fluconazole instead of amphotericin B, which has many systemic and nephrotoxic side effects.

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REFERENCES

1- Krcmery V, Barnes AJ. Non-albicans Candida spp. causing fungaemia: pathogenicity and antifungal resistance. J Hosp Infect 2002;50:243-60.

2- Gudlaugsson O, Gillespie S, Lee K, Vande Berg J, Hu J, Messer S, et al. Attributable mortality of nosocomial candidemia revisited. Clin Infect Dis 2003;37:1172-1177.

3- Farina C, Vailati F, Manisco A, Goglio A. Fungaemia survey: a 10-year experience in Bergamo, Italy. Mycoses 1999;42:543-548.

4- Arendrup M, Horn T, Frimodt-Moller N. In vivo pathogenicity of eight medically relevant Candida species in an animal model. Infection 2002;30:286-291.

5- Passos XS, Sales WS, Maciel PJ, Costa CR, Miranda KC, Lemos jde A, et al. Candida colonization in intensive care unit patients' urine. Mem Inst Oswaldo Cruz 2005 ;100:925-928.

6- Mlinaric-Missoni E, Lipozencic J, Marinovic-Kulisic S, Mlinaric-Dzepina A. Fungal infections of urogenital system. Acta Dermatovenerol Croat 2004;12:77-83.

7- Zer Y, Balci I, Meric G. Identification and antifu ceptibility of Candida isolated from intensive care unit patients. New Microbiol. 2002 ;25:489-494.

8- Munson EL, Troy DR, Weber JK, Messer SA, Pfaller MA. Presumptive identification of Candida kefyr on levine formulation of eosin methylene blue agar. J Clin Microbiol 2002;40:4281-4284.

9- Prasad KN, Agarwal J, Dixit AK, Tiwari DP, Dhole TN, Ayyagari A. Role of yeasts as nosocomial pathogens & their susceptibility to fluconazole & amphotericin B. Indian J Med Res 1999;110:11-17.

10- Morera Y, Torres-Rodriguez JM, Catalan I, Granadero A, Josic Z, Alvarez-Lerma F. Candiduria in patients with urethral catheter admitted in Intensive Care Unit. Etiology and in vitro susceptibility to fluconazole. Med Clin (Barc). 2002;18:580-582.

11- Thompson L, Pino M, Castrillion MA, Schenone D, del Canto E. Fluconazole in treatment of urinary candidiasis. Experience with 24 patients. Rev Med Chil 1995;123:1505-1509.

12- Corpus K, Hegeman-Dingle R, Bajjoka I. Candida kefyr, an uncommon but emerging fungal pathogen: report of two cases. Pharmacotherapy 2004;24:1084-1088.