A Fatal *Aspergillus niger* Infection in a Peritoneal Dialysis Patient: Case Report

Periton Diyalizi Hastasında Ölümcül Seyreden *Aspergillus niger* Enfeksiyonu Olgusu

Sultan ÖZKURT, MD, Msc,[a]
Gökhan TEMİZ, MD, Msc,[a]
Garip ŞAHİN, MD, Assis. Prof.,[a]
Yasemin ÖZ, MD, Msc,[b]
Nuri KİRAZ, MD, Prof.,[c]
Ahmet Uğur YALÇIN, MD, Prof.[a]

Departments of
[a]Nephrology,
[b]Microbiology and Clinical Microbiology,
Eskişehir Osmangazi University
Faculty of Medicine, Eskişehir
[c]Department of Microbiology and
Clinical Microbiology,
İstanbul University
İstanbul Faculty of Medicine, İstanbul

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Yazışma Adresi/*Correspondence:*
Sultan ÖZKURT, MD, Msc
Eskişehir Osmangazi University
Faculty of Medicine,
Department of Nephrology, Eskişehir,
TÜRKİYE/TURKEY
dr.s.guvenir@hotmail.com

ABSTRACT Peritonitis is the most frequent and serious complication in peritoneal dialysis (PD) patients. Gram positive bacteria are isolated in 55-80% of cases. Fungal peritonitis is rare but has high mortality and morbidity rates. *Aspergillus niger* peritonitis is rare and there are only 9 reports in the literature. We tried to treat our patient according to International Society for Peritoneal Dialysis (ISPD) 2005 guideline but success was not achieved. Our case is the tenth *Aspergillus niger* peritonitis case but it is just the third mortal case in the literature. The aim of this patient report was to stress on the seriousness of fungal peritonitis.

Key Words: Peritoneal dialysis; Aspergillus; peritonitis

ÖZET Periton diyalizi (PD) hastalarında peritonit en önemli komplikasyon olup, olguların %50-80'inde Gram pozitif bakteriler izole edilmektedir. Fungal peritonitler ise nisbi olarak az görülmekle birlikte yüksek morbidite ve mortalite oranına sahiptir. *Aspergillus niger* peritoniti ise son derece nadir olup literatürde sadece 9 olgu bildirilmiştir. *Aspergillus niger* peritoniti tanısı alan hastamız, uluslararası periton diyalizi topluluğunun (ISPD) 2005 yılı rehberine göre tedavi edilmesine rağmen kurtarılamamıştır. Olgumuz literatürdeki 10. ve mortal seyreden 3. *Aspergillus niger* vakasıdır. Bu olgu raporu ile fungal peritonitlerin ciddiyetine dikkat çekmek amaçlanmıştır.

Anahtar Kelimeler: Periton diyalizi; Asperjillus; peritonit

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The most serious and widespread complication in (PD) patients is the infection of peritoneal cavity. In approximately 55-80% of the cases, the responsible agents are Gram positive bacteria.[1] Fungal microorganisms are responsible for 2-13% of cases but in recent years the frequency of fungal peritonitis has increased. The majority of fungal peritonitis is caused by Candida species.[1,2] Aspergillus peritonitis is rare but associated with a high mortality rate.[3] In this paper we described an *Aspergillus niger* peritonitis case which progressed mortal in spite of agent specific therapy and removal of peritoneal catheter.

CASE REPORT

A 53-year-old male patient who had been on PD for 6 years admitted to hospital with abdominal pain and cloudy peritoneal fluid. The patient suf-

fered two peritonitis attacks 5 and 3 years ago. Before the last peritonitis prolonged antibiotic treatment history was negative. He had no fever, nausea or vomiting. His blood pressure was measured as 110/70 mmHg. There was mild erythema in the catheter exit-site without swelling, pain and purulent drainage. Physical examinations revealed diffuse abdominal tenderness and defence without a positive rebound. His residual urine was 100 ml/day. His laboratory findings were as follows: White blood cell (WBC) count was 17.1x10³/ul, hemoglobin (Hb) was 11.1 mg/dl, platelet count was 294x10³/ul, C-reactive protein (CRP) was 10.1 mg/dl (normal range: 0-0.8), BUN: 56 mg/dl, creatinine (Cr): 8.18 mg/dl. A plain radiograph of the abdomen demonstrated no signs of bowel perforation and the PD catheter was in situ. Peritoneal fluid was sent for cell count, culture, Gram and acid-fast bacteria (AFB) staining. Fluid examination showed a cell count of 400/µl, with 80% polymorphonuclear (PMNL) leukocytes. Gram stain revealed no organisms and culture showed no growth. Blood culture and AFB were also negative. Treatment was initiated empirically with amikacin 150 mg (2 mg/kg) intra-peritoneal (IP) once a day and cefazolin 1.5 g (15 mg/kg) IP once a day (according to ISPD 2005 guide). At the 48th hour of the treatment, cell count of the peritoneal fluid increased to 2400/µl, with 50% PMNL. Because of the initial treatment failure amikacin and cefazolin were stopped and vancomycin 2 g (30 mg/kg) IP once a week and intravenous imipenem 250 mg twice a day were initiated. At the 4th day of the treatment cell count of the peritoneal fluid was 4500/µl, with 50% PMNL. A second fluid culture was performed. The Gram stain showed the absence of bacteria and the Ziehl Nielsen stain was negative for acid-fast bacilli in peritoneal fluid. At the 5th day of the treatment a non identified fungal growth was determined in the culture and we made peritoneal lavage, we pulled out the catheter, vancomycin was stopped and 1.5 mg/kg/day intravenous liposomal amphotericin B (LAB) was initiated. The patient was switched from PD to hemodialysis (HD) at the 5th day of the treatment. The material of peritoneal fluid was inoculated in sabouraud dextrose agar (SDA) in duplicate and incubated at 37°C and 25°C, respectively. After 72 hours, all cultures were seen with cottony white mycelium growth, which was soon covered with abundant black spores. No bacterial growth was detected in the culture. Microscopic characterization of the fungal isolate was carried out by preparing a lactophenol cotton blue mount from the growth. The conidiophores terminated in a vesicle covered with phialides (biseriate). The conidial head was large, black and radiate. At the 8th day of the treatment the fungal isolate was confirmed to be *Aspergillus niger* by the above-mentioned features. We also performed antifungal susceptibility testing for voriconazole and amphotericin B using the broth dilution method (M-38A, NCCLS, USA). The isolate was sensitive to both the drugs and showed inhibition of growth for amphotericin B and voriconazole at the lowest minimum inhibitory concentration (MIC). Same fungal agent was isolated from the removed peritoneal catheter and amphotericin B was stopped and intravenous voriconazole was initiated with a loading dose of 6 mg/kg every 12 hours and followed by maintenance dose of 4 mg/kg every 12 hours. However the patient failed to respond to therapy, CRP was 27.5 mg/dl at 10th day of the treatment and subsequently the patient died at the 14th day after admitted to hospital due to sepsis secondary to fungal peritonitis

DISCUSSION

Peritonitis and catheter related infections are the major complications of peritoneal dialysis. Peritonitis is the most common cause of the hospitalization in PD patients and related with a mortality rate of 1-6%.[4] Hyperosmolar peritoneal dialysis fluid with high glucose and low pH can provide a good growth medium for pathogens.[5] Bacteria are the cause of 80-90% of all peritonitis while anaerobic microorganisms, fungi or mycobacteria are rare.[6]

Fungal peritonitis is a rare but potentially fatal complication of peritoneal dialysis, associated with a mortality rate of 20-30% and in the rest of the cases, inflammatory process may lead to irre-

versible damage of the peritoneal membrane with subsequent dropout from PD. Candida, predominantly *C. albicans, C. parapsilosis and C.* glabrata are the most common causes of fungal peritonitis but much less frequently Aspergillus, Paecilomyces, Penicillium and Zygomycetes may cause to fungal peritonitis.[7]

In fungal peritonitis, the clinical findings are similar to those found in patients with bacterial peritonitis.[8] Abdominal ache and cloudy peritoneal fluid are common symptoms but sometimes there can be abdominal ache without cloudy fluid.[4] Because of that, the diagnosis can be made with the isolation of the fungus from peritoneal fluid.[9] In our patient, peritoneal fluid was cloudy and the only complaint was abdominal pain.

There are several risk factors for fungal peritonitis, such as prolonged use of immune suppressive agents and antibiotics, diabetes mellitus, age > 70 years, long duration of PD and surgical interventions.[10] Previous antibiotic therapy is probably the most important predisposing factor for fungal peritonitis. This association between fungal peritonitis occurrence and the use of antimicrobials may be due to fungal overgrowth after selective bacterial elimination and to peritoneum inflammation that would render it more prone to fungal invasion.[11] The only risk factor of our patient was the long duration of PD. In a study, including 218 patients, 11 of the patients who had fungal peritonitis had a mean PD duration of 37.45 months and 207 patients who had non-fungal peritonitis had a mean PD duration of 24.95 months and the difference between two groups was statistically significant.[11]

Major complications of the fungal peritonitis were sclerosing encapsulating peritonitis, bowel obstruction, bowel wall invasion and formation of abscess. Extra peritoneal spreading of peritonitis is not common and has a high mortality rate.[12] Although the optimal treatment for fungal peritonitis is not clear, most studies suggest the necessity of the early removal of the peritoneal catheter.[13,14] It is important to culture the removed catheter if culture negative peritonitis persists.[15] Indication of the catheter removal should consider the utility for peritoneal lavage to prevent formation of peritoneal adhesions and to maintain viability of the peritoneal membrane.[1] Ghali et al reported catheter removal was more common in fungal, mycobacterial, and anaerobic infections, with a median time to removal of 4-5 days.[16] Peritoneal catheter was removed on fifth day in our patient and exitus occured on ninth day after catheter removed.

Fungal peritonitis may have some difficulties to diagnose and in this situation a peritonitis attack which is non susceptible to the anti bacterial treatment must make us think about fungal peritonitis.[5] There is not a consensus for the treatment of fungal peritonitis. 2005 guideline of International Society for Peritoneal Dialysis (ISPD) recommended removing the catheter and switching to temporary HD. Conventional anti fungal therapy includes the use of fluconazole, amphotericin B and flucytosine either single or in combination. Caspofungin or voriconazole are more potent agents but there are not so many experiences with them and must be considered in the case of conventional therapy failure or patient's condition worsening.[7,8,11] There are also alternative treatments in the literature, such as usage of tamoxifen for sclerosing encapsulating peritoneal sclerosing following fungal peritonitis.[17] According to ISPD 2005 guideline, initial therapy may be amphotericin B until the culture results are available with susceptibilities. Caspofungin, fluconazole, or voriconazole may replace amphotericin B, based on species identification and MIC values.[18]

In conclusion, Aspergillus related fungal peritonitis is a rare complication of PD and has a high mortality rate. Signs and symptoms are similar to those of other types of peritonitis and it is sometimes very hard to isolate a fungal agent. We report a case of *Aspergillus niger* peritonitis which was described nine times previously in the literature. Despite the aggressive management according to 2005 guideline of ISPD, including catheter removal and use of both amphotericin B and voriconazole, the patient died. Our case is the 3rd fatal *Aspergillus niger* case in the literature. This case is important in that it draws attention to the probability of fungal peritonitis, especially *Aspergillus niger* etiology which might have severe clinical consequences.

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