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Candida guilliermondii Peritonitis During Peritoneal Dialysis. Case Report and Literature Review

Case Report

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Abstract

Peritonitis is the most frequent complication of peritoneal dialysis (PD) and 3–6% of episodes have fungal origin. Candida guilliermondii is an uncommon species of Candida with invasive behavior in patients affected by severe underlying disorders or using indwelling vascular devices. Here we report the case of an 84-year-old woman undergoing outpatient PD for 4 years who had fever, chills, and diffuse increasing abdominal pain. After empiric antimicrobial therapy, based on teicoplanin in the dialytic circuit plus oral ciprofloxacin plus fluconazole, the patient was hospitalized. Afterwards, the culture from the peritoneal fluid showed the presence of C. guilliermondii.

PD-related fungal peritonitis is an infrequent event, but the morbidity and mortality rates are significant. In this scenario, appropriate prevention strategies including antifungal prophylaxis during antibiotic treated bacterial peritonitis should be evaluated.

Keywords: Candida guilliermondii; Nephrology; Peritoneal Dialysis; Peritonitis
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INTRODUCTION

Initially named *Endomyces guilliermondi* by A. Castellani [1], *C. guilliermondii* complex is a genetically heterogenous group of yeasts including four species, i.e., *C. guilliermondii*, *C. fermentati*, *C. carpophila*, and *C. xestobii*. *C. guilliermondii* has a broad environmental diffusion, as is also part of the normal human skin-mucous flora.

The *C. guilliermondii* complex is sometimes misidentified as *C. famata* and vice versa, because these species share several biochemical characteristics. In the literature, studies reporting epidemiological and clinical information on candidemia and deep-seated infections caused by *C. guilliermondii* complex are limited. Patients with candidemia caused by the *C. guilliermondii* complex had severe and debilitating underlying conditions. The main conditions predisposing to *C. guillermondii* infection include malignancy, immunosuppressive therapy, and neutropenia. As an emerging, opportunistic agent, it has an invasive behavior in patients with severe underlying disorders or with indwelling vascular devices. This non-*albicans Candida* species determinates 1–3% of all episodes of candidemia according to geographical regions, with a greater frequency in Latin America [2].

Why Do we Describe This Case

Even though peritonitis is a well-known complication of peritoneal dialysis, fungal etiology is rare. As it is burdened by high morbidity and mortality rate, it is mandatory to raise awareness among physicians, who should put in place an effective permanent monitoring of infections

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Nosocomial transmission has been documented, although outpatient transmission has also been reported in nearly 30% of cases [3], the majority being healthcare-related, with central venous catheters (CVCs) involved in a high percentage of patients [3]. Catheter removal plays an important role in the management of patients with *Candida* carrying a CVC.

Overall, the isolates exhibit decreased *in vitro* susceptibility to fluconazole and echinocandins, whose activity may result dose-dependent [4], although poor biofilm formation and the low virulence have been associated with a favorable outcome [3]. The rate of true fluconazole resistance remains unknown [3] and the MICs of micafungin and anidulafungin have been detected 16- and 60-fold higher, respectively, than the MICs against *C. albicans* [3]. However, the clinical significance of less susceptibility of *C. guilliermondii* to triazoles and echinocandins remains to be elucidated.

CASE REPORT

An 84-year-old woman undergoing outpatient peritoneal dialysis (PD) for 4 years because of chronic kidney disease secondary to an adult polycystic renal disease developed fever, chills, and diffuse, increasing abdominal pain. The efflux peritoneal fluid proved cloudy, with increased leukocyte-neutrophil count, but there was no microscopical and culture evidence of microorganisms. Moderate peripheral leukocytosis accompanied a marked increase of serum C-reactive protein (180 mg/mL).

An empiric antimicrobial therapy based on teicoplanin in the dialytic circuit plus oral ciprofloxacin plus fluconazole was started, but patient conditions worsened, leading to hospital admission. While waiting for microbiological assessment, intravenous (i.v.) meropenem, metronidazole and voriconazole were added to intraperitoneal teicoplanin. After three days, from the peritoneal fluid *Candida guillliermondii* grew. The yeast strain tested fully sensitive to voriconazole and all available echinocandins, with a lower fluconazole susceptibility. Considering the diagnosis of fungal peritonitis, the antifungal therapy was continued, removing the Tenckhoff catheter and activating the hemodialysis treatment. All antibacterial treatments were suspended. A progressive improvement of clinical conditions associated with repeatedly negative weekly cultures from peritoneal fluid allowed the switch from i.v. to oral formulation of voriconazole after two weeks, and its discontinuation after three weeks.

DISCUSSION

Peritonitis is the most frequent complication of PD. It is burdened by an elevated frequency of failure of this ultrafiltration technique and a significant morbidity and mortality rate (up to 18% and 16% of subjects, respectively), in accordance with the eligibility criteria for PD and patient comorbidities, although it frequently remains under/misdiagnosed. Recently, thanks to the improved prevention measures and the advancements of both biomaterials and techniques, a decreased infection rate was noticed. Among the potential causative factors of PD, we underline the contamination of catheters exit sites subcutaneous tunnels, chronic gut disorders, catheter-related bacteremia, gynecologic infections and local invasive procedures, as well as prior antibiotic treatment administered for a peritonitis or a catheter-associated infection. Yeast infections are more frequent when intestinal and/or gynecological diseases or procedures are of concern.

Fungal etiology accounts for 3–6% of episodes of PD-associated peritonitis [2]. It leads to longer hospitalization, higher morbidity and mortality rates, as well as shift to hemodialysis, compared with bacterial ones, because FP is associated with a significant risk of temporary or permanent membrane failure requiring hemodialysis. However, peritonitis caused by fungi carries a higher morbidity and mortality than bacterial infections.

In addition, 40% of patients develop a peritoneal fibrosis which does not allow catheter repositioning, whereas the fatality rate may reach 20–30% [2,5]. The major predisposing factor of fungal PD is a previous antibiotic course, especially given for a bacterial peritonitis (34–80% of cases) [2]. As expected, antibiotics modify the normal gut microbiota, favoring the migration of fungi in the peritoneal cavity, which is often already altered in frail, comorbid subjects [2,5]. Furthermore, advanced renal diseases lead to a suppression of non-specific defense mechanisms against many infections [5-9].

The largest study of fungal peritonitis in the setting of PD was authored by R. Miles

and coworkers: 162 cases were reported, with a prevalence of non-*albicans Candida* spp. over *C. albicans* and other fungi. A two-week antifungal treatment was carried out with fluconazole in the large majority of episodes, but the mortality risk was more frequently related to antimycotic therapy alone (18%), as opposed to catheter removal strategies (13% overall) [10].

C. guillermondii peritonitis during PD was observed again by M. Kim et al. in the year 2016 [11].

In conclusion, PD-related fungal peritonitis, although being a proportionally infrequent event, is burdened by a significant morbidity and mortality in subjects undergoing PD. An elevated clinical suspicion should address a prompt diagnosis and a timely treatment in a multidisciplinary setting (including nephrologists, microbiologists, and infectious diseases specialists). In this scenario, appropriate prevention strategies should be evaluated, including antifungal prophylaxis during bacterial peritonites treated with antibiotics that are still controversial, although it is recommended in International Society for Peritoneal Dialysis guidelines, with a strength of recommendation indicated as Level 1 (we recommend), and the quality of the supporting evidence as B (moderate quality) [12]. It has been observed that non-albicans *Candida* species, including *C. guilliermondii*, *C. tropicalis*, and *C. parapsilosis* may exhibit higher adhesion abilities, while their biofilm-forming capabilities varied across species [13]. Biofilm-forming *Candida* species are more resistant to antimicrobial agents, but little information is available on non-albicans *Candida* biofilms [13].

A permanent monitoring of infections with special attention devoted to emerging bacterial and fungal species, together with the resort to novel treatment strategies, will help in containing these significant nosocomial disorders.

Key points

- *Peritonitis is the most frequent complication of peritoneal dialysis, although it frequently remains under/misdiagnosed.*
- *Fungal etiology accounts for a small percentage of episodes of peritoneal dialysis-associated peritonitis, but, compared to bacterial ones, it leads to higher morbidity-mortality rate, longer hospitalization, and a shift to hemodialysis.*
- *The major predisposing factor of fungal peritoneal dialysis is a previous antibiotic course, that favors the migration of fungi in the peritoneal cavity.*

Consent to publication

We confirm that informed consent was obtained from the patient, who has given full permission to publish this case.

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Conflicts of interests

The authors declare they have no competing financial interests concerning the topics of this article.

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