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Case Report

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An Unusual Association of *Candida Guilliermondii* and Mycobacterium Avium Complex in a Peritoneal Dialysis Patient with Refractory Peritonitis

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Abstract

Refractory peritonitis is defined as failure of effluent clearance after five days of appropriate antibiotics in peritoneal dialysis patients. It is a reason for peritoneal dialysis failure. Although fungal and mycobacterial peritonitis are uncommon (approximately 15% of the cases), they are difficult to diagnose and treat. Herein, we report a case of peritonitis caused by two unusual pathogen, *Candida guilliermondii* and Mycobacterium avium complex, which probably reached the peritoneum via the vaginal route, in a long-term peritoneal dialysis patient with malnutrition. Rare organisms should be considered as causative agents in refractory peritonitis cases.

Keywords: Peritoneal dialysis, fungal peritonitis, mycobacterium avium peritonitis, candida guillermondii peritonitis, refractory peritonitis

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INTRODUCTION

Peritoneal dialysis (PD) related peritonitis is one of the most frequent and severe complications of PD, which contributes to morbidity and mortality. The vast majority of peritonitis cases are caused by bacteria, approximately 10-15% of cases are caused by fungi, and 3% by mycobacterial organisms (1). Approximately 70% of fungal peritonitis cases are caused by *Candida albicans* and *Candida parapsilosis*. Candida guilliermondii remains an uncommon cause of fungal peritonitis in PD patients (2). Data on peritonitis caused by nontuberculous mycobacteria are limited. Over half of the isolates are rapidly growing species such as *Mycobacterium fortuitum* and *Mycobacterium chelonae* which become detectable on routine bacteriologic cultures in up to 5 days (3). *Mycobacterium avium complex* is responsible for a small number of peritonitis cases compared with other nontuberculous mycobacterium (NTM) peritonitis cases (4).

We present a case of refractory peritonitis caused by *C. guilliermondii* and *M. avium complex* in a 22-year-old woman who had been on PD for 12 years.

CASE PRESENTATION

A 22-year-old female with end-stage renal disease due to membranous nephropathy secondary to horizontally transmitted hepatitis B infection was presented with abdominal pain, vomiting, fever, and cloudy peritoneal effluent. The patient had been on automated peritoneal dialysis (APD) since she was 10 years old. She had been diagnosed with Moyamoya syndrome after an episode of ischemic stroke seven years ago, and she had monoparesis of the left arm. The effluent had an elevated white cell count of 528/mm^3, and cultures from the effluent were sent for testing. Laboratory results were as follows: white blood cell count: 13.24 109 /L, neutrophil: 10.4 x 109 /L, C-reactive protein: 109 mg/L (reference range: 0-5 mg/L), and procalcitonin: 100 ng/mL (reference range: <0.05 ng/mL). A year ago, she was diagnosed with peritonitis caused by S. aureus and it was easily treated with intraperitoneal ceftriaxone. She was tested negative for human immunodeficiency virus (HIV), and she had no immune deficiency syndrome. Her Ig levels were within normal values. However, she was not compliant with a proper diet and was underweight (40 kg). She had no re-

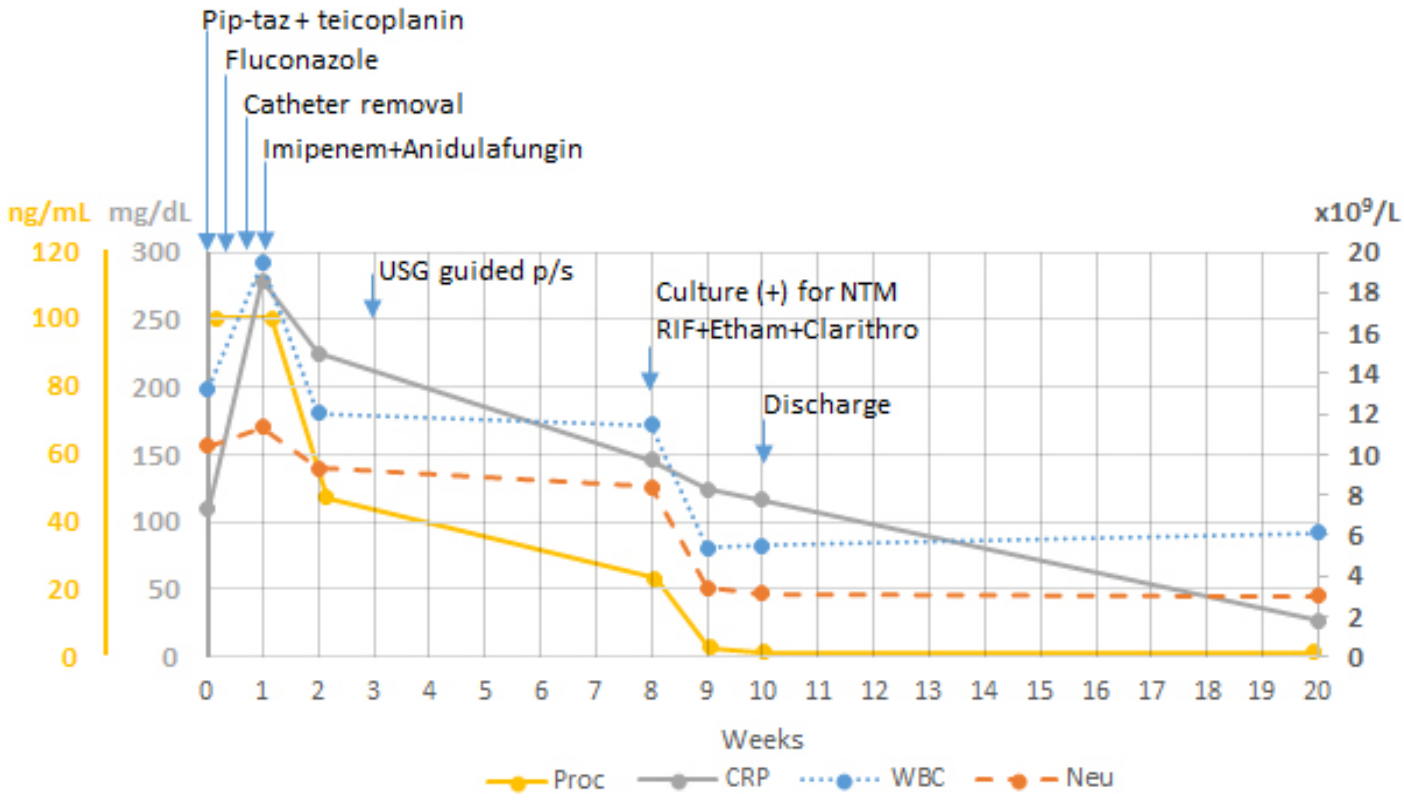

Figure 1. Clinical course

Clarithro: clarithromycin; CRP: C-reactive protein; Etham: ethambuthol; Neu: neuthrophil count; NTM: nontuberculous mycobacterium; p/s: paracentesis; Proc: procalcitonin; RIF: rifampicin; WBC: white blood cell count

cent history of antibiotic treatment. Interestingly, although she had severe oligomenorrhea for the last five years, her menstrual periods were regular for three months. In order to rule out structural reasons of abnormal uterine bleeding, gynecological examination was performed, which was normal. Her HBV DNA was 1200 IU/mL, and there were no signs, radiological, or laboratory findings for cirrhosis. Initially, she received intraperitoneal ceftriaxone; however, she got septic and intravenous piperacillin-tazobactam and teicoplanin were started. On second day, cultures resulted as positive for *Candida spp*. Therefore, fluconazole was added to the treatment. Her peritoneal catheter was removed immediately, and she was transitioned to hemodialysis via central venous catheter. Later, peritoneal catheter tip culture came back positive for *Candida guilliermondii* and *Staphylococcus pasteuri.*

Main Points

- Refractory peritonitis is defined as failure of effluent clearance after 5 days of appropriate antibiotics in peritoneal dialysis patients.
- Even though there is no obvious immunosuppression other than the longstanding chronic renal failure in dialysis patients, rare microorganisms such as fungus and mycobacterium should be considered as causative agents in refractory peritonitis cases.
- Peritonitis is most often due to contamination (touch, tunnel, and catheter site), hematogenous dissemination, and trans-visceral migration from intestines and rarely transvaginal. All possible routes must be considered.

Because of ongoing relapsing fevers and elevated acute phase reactants, antimicrobial treatment was widened with imipenem and anidulafungin. In addition, abdominal ultrasonography and echocardiography were performed. The former showed septated ascites, but there was no abscess, whereas the latter showed no signs of endocarditis. The persistent septated fluid was sampled with ultrasonography-guided paracentesis for further cultures at 3rd week of admission. Although the acid-fast bacilli (AFB) detection and nucleic acid amplification (NAA) in peritoneal fluid were negative, the cultures (with Lowenstein-Jensen medium) came back positive for NTM in the 8th week. Species identification (with Matrix-assisted laser desorption ionization time of flight mass spectrometry [MALDI-TOF]) was consistent with *M. avium complex*. Treatment with rifampicin, ethambutol, and clarithromycin was started and planned to continue for one year. After initiation of the therapy for NTM, her clinical status improved, and her acute phase reactant lev-

els began to decline (Figure 1). Her antifungal therapy was completed within six weeks. Because her right upper venous veins were found to be thrombotic, an arteriovenous fistula was created on her left upper arm despite monoparesis. Since then, she is being followed with hemodialysis with stable clinical status.

Written informed consent was obtained from the patient for this case presentation.

DISCUSSION

Refractory peritonitis and fungal peritonitis are serious complications associated with significant mortality and up to a 40% mortality rate (5). In terms of risk factors for peritonitis, immunosuppressive state such as HIV infection or diabetes are established in PD patients. In contrast, recent antibiotic therapy and recent peritonitis have been identified as risk factors for fungal peritonitis, and history of concomitant fungal or bacterial infections have been implicated as the major risk factors for NTM peritonitis (2). In addition, end-stage renal patients have relative cell-mediated immunosuppression, which may predispose to intracellular and fungal infections (6). Fungi is known to enter the peritoneal cavity intraluminally or periluminally; In rare cases, they can enter via the vaginal route (7), especially after an instrumentation of gynecological organs such as intrauterine devices.

Diagnosis of NTM peritonitis is challenging and often delayed in PD patients. There are no distinctive symptoms or physical findings regarding fungal or NTM tuberculosis between different peritonitis cases. The time interval between the initial presentation and implementation of appropriate treatment is long; the average is four weeks. Therefore, if there is a suspicion of atypical mycobacteria or fungal peritonitis, additional investigations with more rapid and certain detection capability, such as high-performance liquid chromatography, DNA sequencing, polymerase chain reaction (PCR), and special cultures should be performed (2, 4).

In our patient, there were no obvious immunosuppression other than the longstanding chronic renal failure and malnutrition. The possible relation between fungal peritonitis and the fact that our patient restarted having menstrual periods is worth discussing. In addition, our patient's clinical course is consistent with the fact that fungal peritonitis is an established risk factor for atypical mycobacterial peritonitis. Although we were considering laparoscopic peritoneal biopsy which is the gold standard for the diagnosis of tuberculosis peritonitis (8), cultures led us to final diagnosis. It was an unfortunate coincidence that there was another patient who had been diagnosed with pulmonary NTM the previous week and whose room was adjacent to the one that this patient was staying in, which raised the idea of a possible contamination. To the best of our knowledge, this is the first case report shows the association of *C. guilliermondii*, *M. avium complex* and *S. pasteuri* as peritonitis agents in a PD patient.

CONCLUSION

In conclusion, PD peritonitis caused by multiple and atypical organisms is uncommon but vital to consider because of the importance of implementation of appropriate treatment.

Informed Consent: Written informed consent was obtained from the patient.

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