***Fusarium* Peritonitis Successfully Managed with Posaconazole and Catheter Removal**

Peritonitis contributes to approximately 18% of infection-related mortality in peritoneal dialysis (PD) patients. Although bacterial peritonitis is more common, fungal peritonitis is severe and leads to death of the patient in approximately 25% or more of episodes (1). It typically occurs in patients who have been previously exposed to antibiotics for bacterial peritonitis (1,2). In a recent retrospective study, fungal infection was observed in 4.5% of all peritonitis episodes over a 4-year study period (2). This study showed that fungal peritonitis is linked with higher rates of hospitalization, catheter removal, transfer to hemodialysis, and mortality compared to peritonitis caused by other organisms (2). A majority of fungal peritonitis cases are caused by *Candida spp*, which are normal human skin flora that subsequently colonize the PD catheter and invade the peritoneum (1). *Fusarium spp*, on the other hand, are common soil molds, and are an emerging fungal pathogen, especially in immunocompromised patients (3). There have been a few case reports described in the literature of *Fusarium* peritonitis cured with oral antifungals; however, we describe the first published case of a patient with *Fusarium* peritonitis successfully managed with posaconazole along with dialysis catheter removal.

CASE REPORT

This was a 29-year-old female who presented with a 3-day history of abdominal pain, nausea, and vomiting. Physical examination revealed a thinly built, poorly nourished woman with a PD catheter. The insertion site was without any erythema, discharge, or tenderness. Her past medical history was significant for end-stage renal disease from systemic lupus erythematosus-induced nephritis for which she was on chronic prednisone. She had been receiving PD for 4 years since failure of a renal transplant due to severe disseminated histoplasmosis. Following treatment for the histoplasmosis, she was receiving chronic suppression with itraconazole due to immunosuppression from prednisone. Additionally, she had a history of bacterial peritonitis from *Staphylococcus epidermidis* and *Enterococcus faecalis*.

When the patient was admitted, cultures of the peritoneal dialysate, blood, and urine were obtained. The patient had been started on intraperitoneal vancomycin and tobramycin empirically for suspected bacterial peritonitis. The peritoneal fluid showed white blood cell

counts of 29,205 cells/mm³, 82% neutrophils, 10% lymphocytes and 7% monocytes. The peritoneal fluid gram stain also showed many neutrophils (> 30/high power field) as well as moderate yeast and septate hyphae (6 – 30/high power field). Therefore, the patient was started on intravenous micafungin, and the PD catheter was removed. A temporary central catheter was placed for hemodialysis. Cultures from both the peritoneal fluid and catheter tip eventually grew *Fusarium spp*. Vancomycin, tobramycin, and micafungin were discontinued, and posaconazole 200 mg by mouth 4 times daily was started in an attempt to treat *Fusarium* peritonitis and still prevent reactivation of histoplasmosis. The patient improved clinically and was discharged home on posaconazole 400 mg by mouth twice daily.

Later, the susceptibility results of the *Fusarium spp* from our patient returned from a reference laboratory and showed elevated minimum inhibitory concentrations and minimum effective concentrations of all antifungals tested (Table 1). Upon follow-up, the patient had improved and therapy was changed to a suppressive dose of posaconazole, 200mg by mouth 3 times daily, because the patient remained immunocompromised. Subsequent peritoneal fluid cultures performed 3 months after diagnosis remained negative for any bacterial or fungal pathogens.

DISCUSSION

Fusarium spp are ubiquitous molds found commonly in soil and organic debris. In culture, the characteristic feature of *Fusarium* is the production of sickle-shaped multiseptate macroconidia (4). Although disease in humans is rare, disseminated fusariosis has a high mortality rate ranging from 50 – 80%. Infection in humans is mainly through inhalation of airborne conidia or traumatic inoculation (4). The most common *Fusarium* species identified to cause human infections include *Fusarium solani*, *Fusarium oxysporum* and *Fusarium moniliforme* (4). A case report of *Fusarium dimerum* peritonitis has been reported as well (5).

The optimal treatment for *Fusarium* peritonitis has not been established. *Fusarium spp* have a high tendency to attach to foreign bodies like PD catheters (3). Once fungi have been identified by microscopy or culture, 2010 practice guidelines for treatment of peritonitis by the International Society for Peritoneal Dialysis recommend prompt removal of the dialysis catheter (1). Additional treatment with antifungals has proven effective for other molds. For example, voriconazole treatment for 5 weeks after catheter removal has been reported as successful for peritonitis caused by *Neosartorya*

TABLE 1
Susceptibility Results of *Fusarium spp*

Drug	MIC (µg/mL)	MEC (µg/mL)
Amphotericin B	4	
Anidulafungin		≥8
Caspofungin		≥8
Itraconazole	≥16	
Micafungin		≥8
Posaconazole	8	
Voriconazole	8	

MIC = minimum inhibitory concentration; MEC = minimum effective concentration.

pseudofischeri, and posaconazole has been used for *Mucor* peritonitis (1).

Fusarium spp are resistant to many antifungal agents and susceptibility is inherently different between species (6). Amphotericin B, voriconazole and posaconazole have low minimum inhibitory concentration for both *F. solani* and *F. oxysporum* (6). Previous case reports of *Fusarium* peritonitis have been successfully managed with a combination of catheter line removal, and either intravenous and intraperitoneal amphotericin B administration, or voriconazole therapy (3,5,7).

Posaconazole is a broad spectrum triazole antifungal structurally similar to itraconazole. They both have *in vitro* activity against many fungi including *Candida spp*, *Aspergillus spp*, and dimorphic fungi, but posaconazole has enhanced activity against *Zygomycetes spp*, and some *Fusarium spp* (8). Posaconazole is a lipophilic antifungal that is available as an oral suspension, delayed-release tablet and a solution for intravenous use. Posaconazole is highly protein-bound (> 98%) and has a high volume of distribution (> 5 L/kg) and peritoneal bioavailability. Additionally, posaconazole exhibits a dose ceiling effect, i.e. it has saturable absorption at doses above 800 mg/day (9). That is why our patient was started on 200 mg 4 times daily. When the patient improved clinically, she was discharged home on posaconazole 400 mg by mouth twice daily to improve patient compliance.

Our patient was immunosuppressed from chronic corticosteroids because of systemic lupus erythematosus. She also had a history of histoplasmosis for which she was on lifelong suppressive therapy with itraconazole. We discussed treating this patient with intravenous amphotericin B, but were reluctant to start it because of its common renal toxicities, electrolyte disturbances, infusion-related reactions and cardiovascular side effects. Intravenous amphotericin

B also diffuses poorly from blood into peritoneal fluid while intraperitoneal administration causes chemical peritonitis and severe abdominal pain (1). Voriconazole was also considered as a potential treatment option for this patient. However, it has unpredictable non-linear pharmacokinetics and its role in the management of histoplasmosis is limited to *in vitro* studies and case reports of using voriconazole for salvage therapy (8,10,11). Posaconazole has more potent *in vitro* activity, and has been successfully used for clinically refractory disseminated histoplasmosis (12,13). Therefore, we decided to remove the peritoneal catheter and empirically initiated oral posaconazole suspension because it was possible this new agent would have activity against both fungi.

CONCLUSION

To our knowledge, this is the first case report of *Fusarium* peritonitis successfully treated with posaconazole and catheter removal. Because of the high morbidity and mortality associated with fungal peritonitis, an aggressive approach to treatment of *Fusarium* peritonitis is warranted. Identification of the species and susceptibilities may be helpful in patients not responding to therapy, but as this case illustrates, patients may improve despite *in vitro* drug susceptibility results as long as the catheter is removed.

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Punit J. Shah^{1,2,*}
 Scott Bergman^{2,3}
 Srivalli Vegi³
 Vidya Sundareshan³

Department of Pharmacy¹,
 St. John's Hospital, Springfield, Illinois
 Department of Pharmacy Practice²,
 Southern Illinois University Edwardsville
 School of Pharmacy, Edwardsville, Illinois
 Division of Infectious Diseases³,

Southern Illinois University School of Medicine,
 Springfield, Illinois

*email: pjdshah@gmail.com

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