

Case Report:***Aspergillus niger* peritonitis in a patient on continuous ambulatory peritoneal dialysis**Usha Kalawat,¹ C. Krishna Kishore,² Abhijit Chaudhury,¹ V. Siva Kumar²Departments of ¹Microbiology, ²Nephrology
Sri Venkateswara Institute of Medical Sciences, Tirupati

ABSTRACT

Fungal peritonitis is an uncommon condition which is associated with high morbidity and mortality in patients on continuous ambulatory peritoneal dialysis (CAPD). It is associated with several complications and many of the patients who develop this condition are unable to resume CAPD treatment and have to shift to haemodialysis. Here we report the rare occurrence of fungal peritonitis due to *Aspergillus niger* in a patient on CAPD.

Key words: Peritonitis, Fungal, Continuous ambulatory peritoneal dialysis, *Aspergillus niger*.

Kalawat U, Krishna Kishore C, Chaudhury A, Siva Kumar V. *Aspergillus niger* peritonitis in a patient on continuous ambulatory peritoneal dialysis. J Clin Sci Res 2013;2:169-73.

INTRODUCTION

Peritonitis is the most frequent complication among patients receiving continuous ambulatory peritoneal dialysis (CAPD) and accounts for 40% - 47% technique failures and 7% - 10% of deaths.¹ Peritonitis is caused by bacteria in 80% - 85%, fungi in 4%-8% of patients.¹ Fungal peritonitis though rare, is a disease with a high morbidity and mortality ranging from 15%-50%. Fungal peritonitis can lead to complications like technique failure, sclerosing peritonitis, adhesions with resulting bowel obstruction or stricture, invasion of the bowel wall, and abscess formation resulting in inability to resume CAPD and reversal to haemodialysis.^{1,2}

Fungal peritonitis is most often caused by yeasts, with *Candida* species as the leading cause, responsible for 70%-90% of cases in adults and 80%-100% cases in paediatric population. Though filamentous fungi (moulds) are less common (10%), several of them have been reported in association with peritonitis. Commonly reported filamentous fungi include *Aspergillus* sp., *Penicillium* sp., and *Curvularia* sp. The other yeasts are much less common, and together represent about 10% of cases. In some of the reports *Candida* sp. such as *C. parapsilosis* have taken the lead over *C.*

albicans which is the most common among yeast like fungi causing fungal peritonitis.^{3,4} *Aspergillus* sp., are rarely identified as causative agents of CAPD peritonitis with only 32 cases reported in the literature so far with *Aspergillus fumigatus*, *A. niger*, *A. nidulans*, *A. terreus*, *A. oryzae*, *A. sydowii*, *A. thermomutatus*, being documented as the common causes.⁵

All these patients had non specific symptoms resembling bacterial peritonitis like pain abdomen with or without fever, cloudy dialysate and sometime rebound tenderness.

Even though a vast array of antifungal agents are available, still the outcome of fungal peritonitis is not encouraging due to delay in the diagnosis. There is a need for surrogate markers which can help in establishing the diagnosis and predict the outcome accurately. Detection of galactomannan and β -D-glucan by a colourimetric assay⁶ which was successfully used for establishing the diagnosis has been encouraging. Peritoneal fluid eosinophilia in the absence of peripheral blood eosinophilia has also been found to be useful in the diagnosis.⁷ Polymerase chain reaction (PCR) has been reported to be a sensitive assay for early diagnosis of fungal peritonitis.⁸

Received: 23 January, 2013.

Corresponding author: Dr Usha Kalawat, Associate Professor, Department of Microbiology, Sri Venkateswara Institute of Medical Sciences, Tirupati, India. **e-mail:** ukalawat@yahoo.com

CASE REPORT

A 70-year-old woman, with hypertension, type 2 diabetes mellitus, end-stage renal disease and hypothyroidism was started on CAPD in February 2005. She had a urine output of 800 mL/day. After two years of problem-free course on CAPD she developed a left-sided hydronephrosis due to calculus ureteric obstruction and Staphylococcal urinary tract infection. She was treated with left ureterorenoscopic lithotripsy (URSL) for stone removal and was maintained on a ureteric stent for six weeks.

After 10 months of asymptomatic period, she developed abdominal discomfort not associated with fever with decreased ultrafiltration for one day followed by clouding of peritoneal drain fluid which revealed neutrophilic leukocytosis (150 cells with 80% neutrophils and 20% lymphocytes). Peritoneal dialysis fluid culture grew *Pseudomonas aeruginosa*. Patient was treated as per International Society for Peritoneal Dialysis (ISPD) guidelines¹ for treatment of peritonitis with change of transfer set. Despite appropriate antibiotic therapy for 10 days and usage of heparin with peritoneal dialysis fluid, the drainage remained cloudy with fibrin clots.

The patient was admitted and highly Suspecting fungal peritonitis, the patient was admitted for in-hospital diagnostic work-up. Everyday, the dialysate was sent for microscopic examination for fungi. Initially, the dialysate fluid examination was negative for fungi; but, on the fifth day of admission, microscopic examination of the fibrin clot revealed the presence of septate hyaline hyphae suggestive of filamentous fungi. The dialysate was inoculated on Sabouraud's dextrose agar (SDA).

The peritoneal dialysis catheter was removed and patient was started on i.v. voriconazole with loading dose of 6 mg/kg every 12 hours the first day, followed by maintenance dose of 4 mg/kg as a maintenance dose intravenously every 12 hours. The patient was initiated on haemodialysis support. The next day, SDA showed growth of a filamentous fungus which was confirmed as *Aspergil-*

lus niger on lactophenol cotton blue mount of the culture isolate. The colony on SDA was cottony, grayish initially which later turned black.

Microscopically the conidiophores were long, hyaline, darker at the apex and terminated in a globose vesicle. Metulae and phialides covered the entire vesicle. Conidia were brown to black and globose (Figures 1 and 2).

As the patient was old and had other co-morbid illnesses like type 2 diabetes mellitus, could not tolerate post-operative stress, and developed difficulty in breathing. On third post-operative day she required assisted mechanical ventilation. Subsequently, she developed hospital acquired bacterial infection leading to sepsis syndrome, multiple organ dysfunction syndrome.

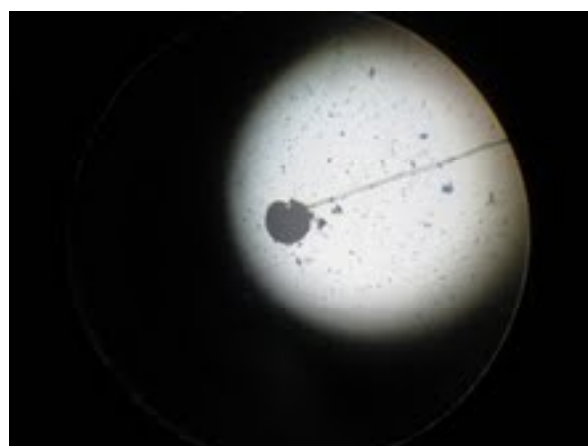


Figure 1: Lactophenol cotton blue mount of the growth on SDA (× 100)
SDA = sabouraud's dextrose agar



Figure 2: Lactophenol cotton blue mount of the growth on SDA (× 400)
SDA = Sabouraud's dextrose agar

DISCUSSION

Several factors have been postulated to favour the occurrence of fungal peritonitis in patients on CAPD. These include, rupture of the cutaneous barrier, decreased cellular immunity, a recent episode of bacterial peritonitis requiring antibiotic therapy, and hospitalization.^{5,9} Presence of diabetes mellitus has not been recognized to be an important contributory factor for the development of fungal peritonitis.^{9,10}

It has been suggested that fungi enter the peritoneal cavity through touch contamination of dialysis tubing or by direct extension of the infection from the catheter exit site. Prolonged antibiotic therapy alters the microbial flora of the intestine which may transmigrate into the peritoneal cavity. The fungus colonizes the peritoneal catheter and is embedded in the amorphous matrix on the surface of the catheter leading to fungal peritonitis.^{11,12} Our patient had received antibiotic therapy for an episode of peritonitis due to *Pseudomonas aeruginosa*. However, it is not clear as to whether fungal infection followed bacterial peritonitis or was concurrently present along with fungal peritonitis as the symptoms did not resolve despite of antibiotic therapy. The possibility of *Pseudomonas* being a contaminant also cannot be ruled out as subsequent cultures did not grow *Pseudomonas aeruginosa*.

Diagnosis of fungal peritonitis is difficult due to the non-specific signs and symptoms which mimic bacterial peritonitis. Clinical presentation includes abdominal pain, cloudy dialysate with 100 white blood cells per cubic millimeter and more than 50% polymorphonuclear cells with or without fever and rebound tenderness.¹ Our patient had mild abdominal pain without any fever.

Gram stain is useful in case of fungal peritonitis due to yeast infections and direct microscopy of the dialysate may be useful in detecting filamentous fungi. If fungal peritonitis is strongly suspected, microscopy of dialysate fluid can be repeated sev-

eral times as this can be rewarding. In our case, the initial microscopy results for filamentous fungi were negative, and it was on the fifth day that we could observe the filamentous septate, hyaline hyphae suggesting a filamentous fungal infection. Though fungal culture takes long time to be positive some of the filamentous fungi such as *Aspergillus sp.* are fast growers and can be identified early. In our case, the growth was apparent on the second day of inoculation.

Candida species are the most common causes of fungal peritonitis with *Candida albicans* being commonly encountered. Other filamentous fungi include *aspergillus sp.*, *Rhodotorula pilimanae*, *Paecilomyces variotii*, *Fusarium solani*, *Acremonium strictum curvularia sp.*, etc.¹³

There are over 185 species of aspergillus to which humans are constantly exposed but only few among them have been found to be associated with disease. More than 95% of infections are caused by mainly three species, namely, *Aspergillus fumigatus*, *Aspergillus flavus* and *Aspergillus niger*. The genus is characterized by septate hyphae from which non-septate conidiophores arise, which terminate in a vesicle. One or two rows of phialides arise from the vesicle, which in turn give rise to round or oval conidia arising from the tips.¹⁴

Currently, the initial diagnosis of fungal peritonitis is often based on a high index of clinical suspicion especially in a patient with predisposing factors. In a symptomatic patient, recurrent negative culture results, failure of antibiotic therapy raise the suspicion of fungal peritonitis. *Pseudomonas aeruginosa* can cause peritonitis in patients on CAPD. It is commonly associated with peritoneal catheter infections.¹² Both current and prior episodes of pseudomonas as exit site infection predisposes to peritonitis.² It has been observed that 22% of CAPD patients with exit site infections with pseudomonas developed peritonitis after resolution of infection.¹³ If exit site and tunnel are infected treatment involves catheter removal and simultaneous two anti pseudomonal antibiotics.¹⁵

Aspergillus peritonitis in patients of CAPD is rare and till date only 32 cases have been reported.⁵ Predisposing factors for the development of fungal peritonitis include underlying disease, use of immunosuppressive drugs, high concentration glucose solutions, presence of foreign body, gastrointestinal disease and antecedent antibiotic therapy.⁵

Here we report the occurrence and management of fungal peritonitis in a patient of diabetes, hypertension and ESRD. Management of aspergillus peritonitis includes catheter removal and anti mycotic therapy. In our patient, the catheter was removed immediately after we came to know the presence of aspergillus infection i.e., on day 7 of management. Although aspergillus are commonly considered environmental contaminants, repeated isolation and correlation between direct microscopy and culture is considered clinically significant. Different species of *Aspergillus* are reported to vary in their susceptibility to antifungal agents such as *Aspergillus terreus* is resistant to amphotericin B.¹⁶ In invasive aspergillosis, therapy with voriconazole is reported to be better tolerated and more efficacious than amphotericin B.¹⁴ Proper selection of antifungal agent is essential and it has been reported that sometimes their may be failure with the first drug, wherein shifting to another antifungal may be fruitful. In one report with fungal peritonitis two CAPD patients were successfully treated with voriconazole and cefsofungin after the initial therapy with amphotericin B had failed.⁶ In invasive aspergillosis, therapy with voriconazole is reported to be better tolerated and more efficacious than amphotericin B.¹⁷ Hence our patient was started on voriconazole.

We present this case to reiterate the ominous significance and outcome of fungal peritonitis specially in terms of morbidity and mortality. In addition this needs the change in modality as management from peritoneal dialysis to haemodialysis following catheter removal. The treatment is costly, prolonged and associated with side effects. A high

index of clinical suspicion, timely diagnosis and institution of appropriate antifungal treatment are essential for the successful management of fungal peritonitis in CAPD patients.

REFERENCES

1. Matuszkiewicz-Rowinska J. Update on fungal peritonitis and its treatment. *Perit Dial Int* 2009;29 Suppl 2:S161-5.
2. Uchida M, Sakemi T, Nagano Y, Mizuguchi M. Rectal stenosis associated with fungal peritonitis: a complication of continuous ambulatory peritoneal dialysis. *Nephron* 1989; 53:288.
3. Miles AM, Barth RH. Aspergillus peritonitis: therapy, survival, return to peritoneal dialysis. *Am J Kidney Dis* 1995;26:80-3.
4. Brunke M, Brier ME, Golper TA. Psuedomonas peritonitis in peritoneal dialysis patients: the Network #9 Peritonitis Study. *Am J Kidney Dis* 1995;25:769-74.
5. Eisenberg ES, Leviton I, Soeiro R. Fungal peritonitis in patients receiving peritoneal dialysis: experience with 11 patients and review of the literature. *Rev Infect Dis* 1986;8:309-21.
6. Ates O, Metan G, Dundar T, Kiziltepe M, Kocyigit I, Unal A, et al. Diagnosis of Aspergillus niger peritonitis in a peritoneal dialysis patient by peritoneal galactomannan and β -D-glucan detection. *Perit Dial Int* 2013;33:216-8.
7. Sridhar R, Thornley-Brown D, Kant KS. Peritonitis due to Aspergillus niger: diagnostic importance of peritoneal eosinophilia. *Perit Dial Int.* 1990;10:100-1
8. Scotter JM, Stevens JM, Chambers ST, Lynn KL, Patton WN. Diagnosis of aspergillus peritonitis in a renal dialysis patient by PCR and galactomannan detection. *J Clin Pathol* 2004;57:662-4.
9. Bordes A, Campos-Herrero MI, Ferdandez A, Vega N, Rodriguez JC, Palop L. Predisposing and prognostic factors of fungal peritonitis in peritoneal dialysis. *Perit Dial Int* 1995;15:275-6.
10. Michel C, Courdavault L, Khayat RA, Viron B, Roux P, Mignon F. Fungal peritonitis in patients on peritoneal dialysis. *Am J Nephrol* 1994;14:113-20.
11. Kazancioglu R, Kirici G, Albaz M, Dolgun R, Ekiz S. Fungal peritonitis among peritoneal dialysis patients. *J Ren Care* 2010;36:186-90.

12. Indhumathi E, Chandrasekaran V, Jagadeswaran D, Varadarajan M, Abraham G, Soundararajan P. The risk factors and outcome of fungal peritonitis in continuous ambulatory peritoneal dialysis patients. *Indian J Med Microbiol* 2009;27:59-61.
13. Bibashi E, Memmos D, Kokolina E, Tsakiris D, Sofianou D, Papadimitriou M. Fungal Peritonitis complicating peritoneal dialysis during an 11-year period: report of 46 cases. *Clin Infect Dis* 2003;36:927-31.
14. Richardson MD. Aspergillosis. In: Merz WG, Hay RJ, editors. *Topley & Wilson's microbiology and microbial infections*. 10th edition. London: Hodder Arnold; 2005.p.687-738.
15. Kazmi HR, Raffone FD, Kliger AS. Pseudomonas exit site infections in CAPD patients. *J Am Soc Nephrol* 1992;2:1498-501.
16. Verweij PE, Brandt ME. *Aspergillus*, *Fusarium*, and other opportunistic moniliaceous fungi. In: Murray PR, Baron EJ, Jorgensen JH, Pfaller MA, editors. *Manual of clinical microbiology*. 9th edition..Washington: ASM Press;2007.p.1802-38.
17. Bennett JE. Aspergillosis. In: Kasper DL, Braunwauld E, Fauci AS, Hauser SL,Longo DL, Jameson JL, editors. *Harrison's principles of internal medicine*. 16th edition. New York: McGraw - Hill;2005.p.1188-90.