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CASE REPORT

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# A fatal *Acremonium falciforme* peritonitis

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**Abstract**

A case of Acremonium falciforme peritonitis in a 50-year-old man with a 10-year history of end stage renal disease that was on Continuous Ambulatory Peritoneal Dialysis for 8 years is reported. The aim of this report is to remind the clinician that in resistant and life-threatening peritonitis, A. falciforme may be the cause. This fungus was identified as A. falciforme in culture by its characteristic colonies and microscopic morphological findings. In vitro fluconazole and amphotericin B minimum inhibitory concentrations (MICs) were found as 6 and 0.125 µg/mL respectively. First fluconazole and then amphotericin B was administered, but patient was deceased on day 10 of amphotericin B therapy. This indicates that more antifungal susceptibility studies should be done before making a comment about in vivo and in vitro concordance of susceptibility of filamentous fungi.

**Keywords:** *Acremonium falciforme*, peritonitis, amphotericin B, fluconazole, itraconazole, voriconazole, ketoconazole

## Introduction

The genus *Acremonium*, formerly called Cephalosporium, includes many species associated with soil, insects, sewage, rhizophores of plants, and other environmental substrates. Many reports concerning *Acremonium* species involve nail, skin, eye infections, or mycetoma. Localized or disseminated infections occur in patients following valve replacement, dialysis, transplantation, or in patients with hematological or solid organ malignancies. Fungemia is common. Recognition of *Acremonium* species in culture is not too difficult, but identification to species is very challenging, and many reports of infection are based on unidentified species.

The aim of this study is to report a rare case of peritonitis caused by *A. falciforme* in a patient on Continuous Ambulatory Peritoneal Dialysis (CAPD) and suggest an approach to therapy.

## Case Report

A 50–year-old man with a 10-year - history of end stage renal disease and on CAPD for 8 years was admitted with nausea, vomiting, abdominal pain, and cloudy peritoneal dialysis (PD) effluent to emergency service on May 16. On examination, he was found to be febrile (37.8°C) with a tense abdomen, rebound tenderness, and decreased bowel sounds. The Tenckhoff catheter site was clean with no sign of inflammation. The dialysate fluid had a leucocyte of 500/mm3. The PD fluid was sent for microscopy and culture. No organisms were observed on the Gram stain slide, therapy was started on a peritonitis protocol consisting of i.p. cephazolin, amicasin. On day 4 after admission, peritoneal dialysate culture for bacteria was negative, but Sabouraud dextrose agar (SDA) incubation, tufted white colonies could be observed. Fluconazole 2x100 mg intravenously (iv) was started and Tenckhoff catheter was removed on the same day. A central venous catheter was placed for hemodialysis. Fluconazole was given for 6 days. Immediately after *A. falciforme* was identified in the culture, amphotericin B was substituted for fluconazole (1x50 mg iv). In the following three cultures of peritoneal effluent, *A. falciforme* was grown. The patient's condition deteriorated, he became febrile and tachycardic. Soon after abdominal ultrasonogram showed intraabdominal effluent, a drainage catheter was placed and 300 cc cloudy effluent per day had come.

On the culture of this effluent, P. aeruginosa and K. oxytoca were isolated. Antibacterial therapy (meropenem 2x1 g) was also started on day 12 after admission. The patient's condition continued to deteriorate despite amphotericin B and meropenem therapy. He had continuous fever and mental confusion. His blood pressure was hypotensive. On day 20 after admission, he was deceased due to respiratory failure. His blood culture was negative for bacteria and fungi on the day of death.

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**Diagnosis**

A 10-ml sample of peritoneal dialysate fluid was centrifuged at 3,000 rpm for 10 min, and the supernatant was removed. The deposit was then inoculated onto blood agar, incubated at 35°C. In addition, 3 ml of dialysate fluid was inoculated into a BACTEC Aerobic Plus/F (Becton Dickinson, Sparks, MD) blood culture bottle and the bottle was incubated in a BACTEC 9240 incubator (Becton Dickinson) at 35°C. A Gram stain was made from the spun dialysate, and the cell count was determined for the noncentrifuged specimen

No fungi were recovered from the primary culture plates. However, when the BACTEC 9240 signaled positive growth, fungal colonies were visually observed within the BACTEC Aerobic Plus/F bottles after Gram staining of a syringe-drawn sample revealed no bacterial organisms. The time to detection of positive growth ranged from 2 to 4 days. The fluid from these bottles was then subcultured on Sabouraud agar plates incubated at 28°C. These plates grew colonies of a kind of fungus. The same fungus was isolated from three separate samples of PD fluid.

On the third day of Sabouraud dextrose agar incubation, tufted white colonies could be observed. Further incubation revealed a pink-orange pigment. A microculture slide preparation was examined. Microscopically, the hyphae were hyaline, septate, smooth, and branched and 1.5-2.5 µm in diameter. They developed erect, undifferentiated, and unbranched repeatedly septate conidiophores. The conidia were slightly curved, non-septate and among in mucoid clusters at the end of conidiophores. This fungus was identified as *A. falciforme* in culture by its characteristic colonies and microscopic morphological findings.

Antifungal susceptibility test was performed by gradient test (Biomerieux, France), and we found MICs as follows: Amphotericin B, 0.125 µg/ mL; fluconazole, 6 µg/ mL; itraconazole, 0.32 µg/ mL; voriconazole, 0.125 µg/ mL; ketoconazole, 0.32 µg/ mL.

**Discussion**

Fungi of the genus Acremonium are opportunistic microorganisms that are found as environmentally-widespread saprophytes in soil but are rarely pathogenic in humans.[1]

Among the many species of Acremonium, about 80 % of infections in humans have been caused by only a few species, namely: *A. falciforme, A. recifei, A. kiliense, A. potronii, A. roseogriseum, A. strictum, and A. Alabamensis*.[2]

Although infection caused by Acremonium is rare, there are several reports in the literature. Many of them are described in immune-compromised patients; the others are exposed to trauma or several surgical attempts such as prosthetic heart valve or peritoneal catheters[1,3] .

There have only been a few cases of *A. falciforme* infection in the literature: a fatal *A. falciforme* fungemia in an immune-compromised patient, an invasive gastritis in an 11-month-old girl with severe combined immunodeficiency, endophthalmitis and diskitis and a mycetoma, an invasive *Acremonium falciforme* infection in a patient with severe combined immunodeficiency, and our case, a fatal CAPD peritonitis in a patient with end stage renal failure Acremonium spp is not a very rare cause of fungal peritonitis. There are several reported peritonitis cases of *Acremonium. Acremonium* kiliense peritonitis complicating CAPD, an 8-year-old boy and a 48-year-old man, peritonitis due to *Acremonium* strictum in a patient of continuous ambulatory peritoneal dialyses, an *Acremonium* spp. peritonitis in an infant, another case of Acremonium strictum peritonitis. [4] Our report is an *A. falciforme* peritonitis in an end stage kidney failure patient with an 8-year CAPD history. Optimal treatment of Acremonium infection is not well defined. There are several reports suggesting combination of different antifungals or using adjuvant therapies such as surgery or removal of the catheter.

In vivo response varies due to different doses of antifungal regimen or the different antifungal applications, e.g. intravenous/ intraperitoneal or the patient's other ongoing diseases. An endophthalmitis and lumbar diskitis due to *A. falciforme* was administered Amphotericin B and Amphotericin B plus itraconazole respectively and was cured. In another case, an invasive *A. falciforme* infection with severe immunodeficiency was cured with Amphotericin B plus itraconazole plus GMCSF. A case of A. strictum peritonitis was treated with combination of oral fluconazole substituting intravenous and intraperitoneal Amphotericin B and catheter removal. On the other hand, a case with *A. falciforme* fungemia passed away on day 4 after initiation of Amphotericin B therapy.

Although it is generally understood that in vitro susceptibility to antifungal agents has a limited value in the absence of in vitro versus in vivo correlations of drug efficacy, the results of in vitro susceptibility tests can be at least a useful guide to clinicians confronted with infections caused by rare agents. There are not many susceptibility studies involving more strains, and their results appear to be different. Koc et al.[3] reported a MIC of 0.5 µg/mL for Amphotericin B for *A. falciforme* fungemia, while Lau et al.[1] indicated a MIC of 1 µg/mL for invasive *A. falciforme* infection .

Rotowa et al.[5] reported a MIC90 of >32 µg/mL for Amphotericin B for 10 isolates, while Fincher et al.[6] indicated a range of MICs of 1-2 µg/mL for the same drug for 6 isolates .

Guarro et al.[4] studied in vitro activity of Amphotericin B against

33 Acremonium isolates and reported an MIC90 of 4.62 µg/mL . We found a MIC of 0.125 µg/mL as a lower result.

The other antifungal agents showed different susceptibility patterns in different studies, but nearly all the studies report fluconazole ineffective with a range of MICs of >256 - >32 µg/mL ( Koc AN et al.[3], Lau YL et al.[1], Guarro JG et al.[4])

Guarro et al.[4] reported fluconazole MIC >80 µg/mL and ineffective in all cases. We found a MIC of 6 µg/mL for fluconazole. Other azoles showed lower MICs against Acremonium species. Lau et al. indicated a MIC of 0.05 µg/mL for itraconazole, while Koc et al. reported a MIC of >32 µg/mL for the same drug. We showed a MIC of 0.32 µg/mL for itraconazole.

The different results of these susceptibility studies may alter on the strain studied or the method used for susceptibility.[4,7] Until the methods for susceptibility testing of filamentous fungi are standardized, the results of comparative studies will not be reliable .[8]

Although Acremonium infections are rare, they are life-threatening. Early diagnosis and rational therapy is, therefore, essential. Although this patient was deceased during Amphotericin B therapy, clinical failure may be correlated to the way of administration (intraperitoneal/intravenous) or the doses of the drug used. We believe Amphotericin B is still the best choice for treatment because cultures were observed to be negative after the therapy. *Acremonium falciforme* should be recognized as a rare cause of fungal peritonitis in patients with CAPD.

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