

Peritonitis Due to *Blastobotrys proliferans* in a Patient Undergoing Continuous Ambulatory Peritoneal Dialysis[∇]

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***Blastobotrys proliferans* is an ascomycetous yeast never previously reported as a human pathogen. Here we report a case of peritonitis due to *Blastobotrys proliferans* in a 46-year-old man undergoing peritoneal dialysis.**

CASE REPORT

A 46-year-old Melanesian man undergoing continuous ambulatory peritoneal dialysis (CAPD) had a past medical history that included chronic bronchitis due to cigarette smoking and a certain state of malnutrition. He had been on CAPD for the past 3 years and had already had three episodes of peritonitis (two due to *Staphylococcus aureus* and one to *Klebsiella pneumoniae*), from all of which he had recovered with adapted antibiotherapies.

On 3 January 2007, he was admitted to the community clinics in Lifou Island (northeast of the New Caledonia main island, Grande Terre) for abdominal pain and cloudy peritoneal dialysis bags, which clinically presumed peritonitis. The peritoneal dialysate fluid white blood cell count at admission confirmed peritonitis with more than 100/mm³ (90% polymorphonuclear neutrophils), and a Gram stain revealed numerous gram-positive cocci. The patient was started on a peritonitis protocol consisting of vancomycin (2 g/5 days) together with ceftazidime (2 g/day), both intraperitoneally. Ceftazidime was stopped when *S. aureus* was identified in cultures from the initial dialysate.

In spite of antibiotherapy, the patient continued to deteriorate with persistent abdominal pain. He was referred to the New Caledonia Territorial Hospital on 11 January 2007. Repeated sampling of the dialysate fluid showed persistent elevation of white blood cell count at 220/mm³ (35% neutrophils, 34% lymphocytes, and 17% eosinophils) and the presence of numerous yeasts and hyphae growing on Sabouraud agar in less than 24 h. The isolate was sent to the French National Reference Center for Mycoses due to an unusual microscopical aspect (rare segmented hyphae and unusual size and shape of conidia) and lack of identification using carbon assimilation patterns (ID32C; bioMérieux, Marcy-l'Étoile, France).

It was then decided to remove the Tenckoff catheter and to start antifungal therapy with oral fluconazole (100 mg/day), which resulted in a quick clinical improvement and the resolution of the patient's symptoms. However, treatment was

switched to amphotericin B (3 mg/kg of body weight/day) for 3 weeks after antifungal drug susceptibility testing results (ATB-Fungus3; bioMérieux) showed decreased susceptibility to all of the antifungals tested, except amphotericin B. MICs of amphotericin B (0.5 µg/ml), flucytosine (8 µg/ml), fluconazole (64 µg/ml), voriconazole (2 µg/ml), posaconazole (0.5 µg/ml), and caspofungin (>8 µg/ml) were determined according to the EUCAST microdilution broth reference method (28). The inflammatory markers then returned to normal levels. The clinical symptoms resolved completely with a follow-up of 4 months.

Identification of the species *Blastobotrys proliferans* Marvanová was done based on the carbon assimilation pattern (ID32C and 50CH; bioMérieux) and microscopic morphology after slide culture in 2% malt agar medium after 6 days at 25°C using the keys established by de Hoog and colleagues (8, 9). Sequences were determined for the internal transcribed spacer 1 (ITS1)-5.8S-ITS2 regions (GenBank accession no. EF584542) and the D1/D2 variable region of the ribosomal DNA gene (GenBank accession no. EF58451) using universal primers V9D/LS266 (7, 21) and NL1/NL4 (24). Identification of the ascomycetous yeast *B. proliferans* was confirmed by comparison of the D1-D2 region nucleotide sequence with those published in GenBank (accession no. U40098 and DQ442684) (15–17), with 99% similarity over 590 bp.

Discussion. Peritonitis remains a common complication of peritoneal dialysis and occurs at an overall average rate of one episode every 29 months (32). The most common etiology is bacterial peritonitis, with *S. aureus* being the most frequently implicated species. However, in New Caledonia, the frequency of peritonitis is higher, due to poor housing conditions, reaching the rate of one episode every 16 to 20 months. Fungal peritonitis is a less frequent (4 to 6% of all peritonitis in this context) (1) but a more severe complication, requiring Tenckoff catheter removal and a switch to definitive hemodialysis. A history of antibiotherapy for bacterial peritonitis within the 4 weeks preceding fungal peritonitis is often but not systematically reported (29). Risk factors also identified for development of fungal peritonitis include recent bacterial peritonitis (3) and lupus (13, 30). Our patient's history thus conforms to

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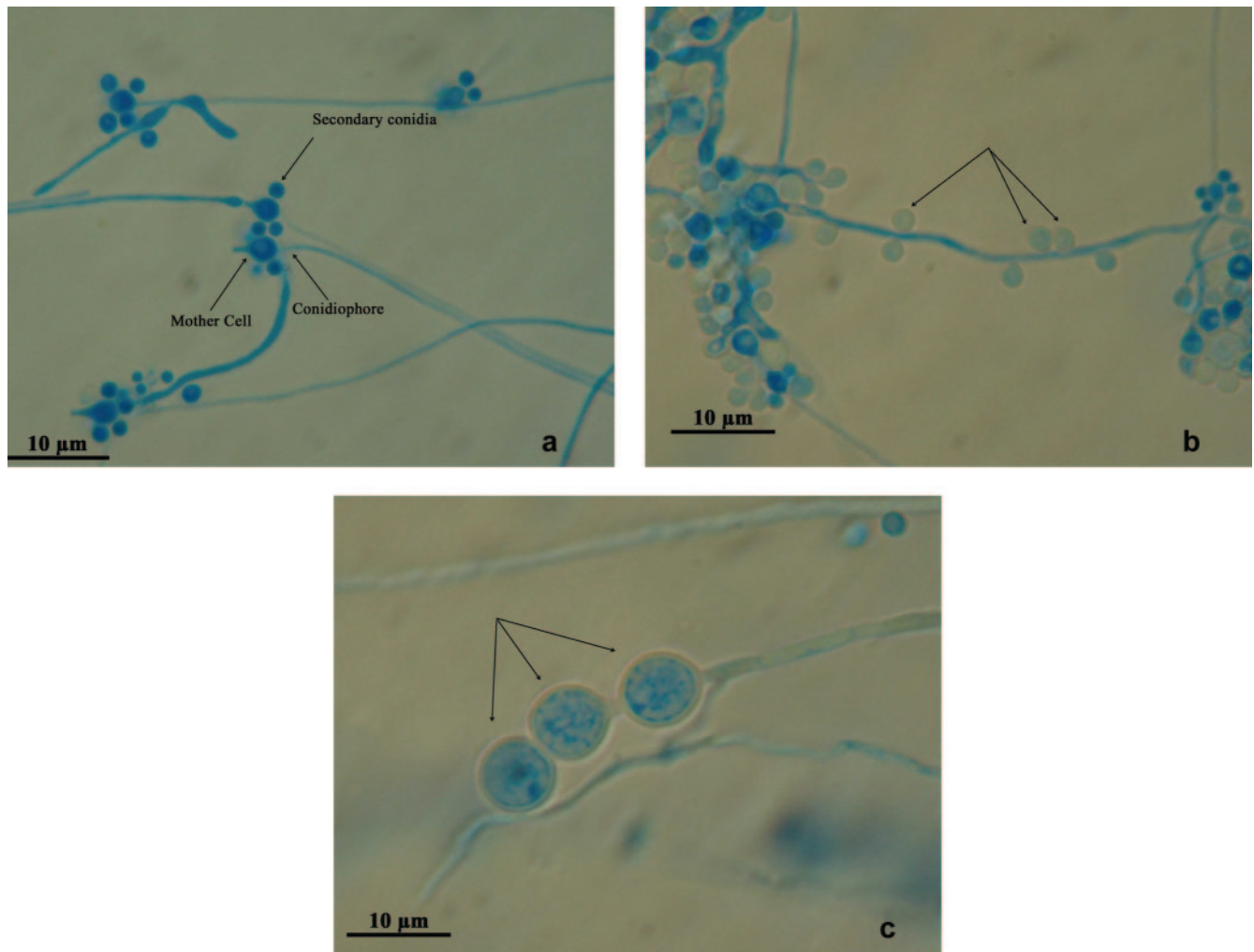


FIG. 1. *Blastobotrys proliferans* from a culture on 2% malt agar examined with Nomarski interphase contrast ($\times 100$). (a) Conidiophores bearing the mother cell with refractive body and secondary conidia. (b) Lateral conidia (arrows). (c) Chlamydospores (arrows).

these reports. Outcome of fungal peritonitis appears to be more favorable in children (33) and in patients with residual renal function (18).

Candida species are the most common fungi isolated (6, 26, 27). Peritonitis due to various filamentous fungi is also reported. *Aspergillus* spp. are responsible for a severe form of peritonitis, frequently lethal, and require prompt removal of the Tenckhoff catheter while starting intravenous amphotericin B (2, 22, 23). Zygomycetes remain an uncommon cause of peritonitis associated with a high mortality rate of 57% (23). Other filamentous fungi and yeasts are even less frequently reported (*Fusarium*, *Trichoderma*, *Penicillium*, *Paecilomyces*, *Curvularia*, *Acremonium*, *Rhodotorula*, and *Trichosporon*) (4, 5, 10–12, 14, 19, 20, 25, 31). To our knowledge, *B. proliferans* has never been reported as a cause of infection in humans or animals, even though strain CBS 293.84 stored at the Centraal Bureau voor Schimmelcultures (Utrecht, The Netherlands) is indicated as recovered from a “cystic lesion of ankle in a man.” The reservoir of *B. proliferans* is unknown.

Until recently, the dimorphic genus *Blastobotrys* was treated as a hyphomycete, close to the ascomycetous genus *Sporothrix*.

What distinguishes both genera is conidiogenesis. In fact, *Blastobotrys* species have distinct mother cells (primary conidia) and secondary conidia, whereas in *Sporothrix* species there is no visible differentiation between conidia of the first and second orders. The species *B. proliferans* has conidiophores bearing pear-shaped mother cells containing a conspicuous body (Fig. 1a). The mother cells are single, each crowned with secondary conidia. Globose, lateral conidia (Fig. 1b) and hyaline, thick-walled, terminal and intercalary chlamydospores (Fig. 1c) are present. *Blastobotrys proliferans* is different from all other *Blastobotrys* species by its proliferating mother cells and the refractive bodies in those mother cells (8). It grows with most carbon sources, does not assimilate nitrate, and ferments glucose. Growth in the presence of melibiose, raffinose, and at 37°C is characteristic of *B. proliferans* isolates in the genus.

For the purpose of phylogenetic analysis, Kurtzman and Robnett (17) have reexamined the relationship between *Blastobotryx*, *Arxula*, *Sympodiomyces*, and several *Candida* species with a multigene analysis. They have demonstrated that *Blastobotryx*, *Arxula*, *Sympodiomyces*, and some *Candida* species were members of the same clade. The multigene sequence

analysis showed also *Trichomonascus* to represent the ascospore state of this clade. Finally, *Blastobotrys* spp. are considered as anamorphic members of the Saccharomycetales treated under the yeasts, while *Sporothrix* belongs to the Ophiostomatales.

Of note, despite the decreased in vitro susceptibility of the isolate to fluconazole assessed by two techniques, clinical improvement was observed rapidly after the introduction of oral fluconazole. This corroborates the usual lack of correlation between in vitro susceptibility testing results and clinical efficacy. However, it does not mean that fluconazole should be the first choice for the treatment of fungal peritonitis due to uncommon species.

Conclusion. Clinical features of fungal peritonitis are not different from those of bacterial peritonitis but are less frequent. Persistence of clinical or biological abnormalities despite adequate antibiotherapy for bacterial peritonitis should prompt new sampling and suspicion of fungal peritonitis. Identification of the pathogen is always required to adapt the treatment. Infections due to uncommon fungi are most frequently seen in immunocompromised patients but are also an emerging threat in those with end-stage renal failure. Whether *B. proliferans* represents a new source of human infection is unknown.

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