Fatal peritonitis caused by Rhizopus microsporus

HERVÉ HYVERNAT*, BRIGITTE DUNAIS†, FANNY BUREL-VANDENBOS‡, SARAH GUIDICELLI*, GILLES BERNARDIN* & MARTINE GARI-TOUSSAINT§

*Medical Intensive Care Unit, Archet 1 Hospital, Nice, †Department of Infectiology, Nice, ‡Department of Pathology, Pasteur Hospital, Nice, and §Laboratory of Parasitology-Mycology, Archet 2 Hospital, Nice, France

A 52-year-old woman with a history of Crohn’s disease was admitted due to peritonitis which followed an intestinal perforation. After transitory treatment with voriconazole, resolution of the infection was complicated by recurring peritonitis resulting from necrosis and perforation of the left colon which ultimately lead to the death of the patient. Microscopic examination of the peritoneal fluid revealed the presence of broad, irregular hyphae and culture of the fluid yielded Rhizopus microsporus. The identification of the fungus was confirmed by its characteristic microscopic morphology and sequencing of the ITS region of the rDNA. The histopathologic examination of the colon tissue demonstrated the presence of broad, non-septate hyphae and the same fungus was again isolated in culture.

Keywords zygomycosis, Rhizopus microsporus, peritonitis, voriconazole, nosocomial infection

Introduction

Rhizopus microsporus, phylum Zygomycota, order Mucorales, is a saprophytic fungus found in forest soil and on wooden surfaces. Zygomycosis occurs in immunocompromised hosts, patients receiving deferoxamine therapy, those with diabetes mellitus, burns, trauma, and solid organ transplant recipients. Mucorales induce dramatic angio-invasive infections with mortality rates exceeding 60% [1]. Clinical localizations may be rhino-orbital, cerebral, pulmonary, cutaneous, disseminated, gastrointestinal or miscellaneous. Peritonitis is rarely described and its occurrence has been associated with continuous ambulatory peritoneal dialysis (CAPD) [2,3]. We report a fatal case of probable nosocomially-acquired peritonitis due to Rhizopus microsporus.

Case report

A 52-year-old woman with a 2-year history of Crohn’s disease, treated with corticosteroids and azathioprine, presented to the local emergency department with abdominal pain and intestinal occlusion. A CT scan of the abdomen revealed peritoneal effusion with peri-hepatic air. Peritonitis resulting from perforation of the small intestine was confirmed upon surgical treatment involving ileo-caecal resection with ileostomy and right colostomy. Histological examination of tissue demonstrated Crohn’s disease with no further anomalies. On day 15 following admission, the patient presented with septic shock and was transferred to the medical intensive care unit in Nice University Hospital. She exhibited multiple organ failure with hemodynamic dysfunction requiring high doses of norepinephrine infusion. Furthermore, a large area over the colostomy was covered with mould. Culture of the mould-like material on Sabouraud’s medium yielded Aspergillus fumigatus. This fungus was found through the use of the E-test to be susceptible to amphotericin B and voriconazole, i.e., minimal inhibitory concentration (MIC) of 0.125 μg/ml and 0.25μg/ml, respectively. To avoid further dissemination of the fungus, and despite negative evidence of Aspergillus galactomannan antigenemia (index value = 0.19; threshold = 0.5-Pastorex Aspergillus kit; Biorad, Marnes-la Coquette, France), preventive treatment with intravenous voriconazole was initiated (400 mg bid as a loading dose followed by 300 mg bid). Treatment was discontinued six days later on the basis of renewed negative Aspergillus galactomannan antigenemia (index value = 0.06) and
negative *Aspergillus* serology. During the following week, the patient’s clinical condition gradually improved and norepinephrine was discontinued. Unfortunately, 2 days later the patient’s condition deteriorated and treatment with voriconazole was restored (300 mg bid). Abdominal CT scan and multiple samplings in search of secondary foci were negative. Six days later, the patient developed haemodynamic instability and a lesion on her left flank suggesting cellulitis. A CT scan showed intra-abdominal collections associated with infiltration of the left flank. Laparotomy revealed encapsulating peritonitis covering a necrotic perforated left colon. The patient died on the 18th day following admission. Histological examination of the intestine showed lesions of ischemic necrosis of the left colon and omentum and vascular thrombosis due to invasive fungal infection. Examination of Grocott-Gomori methenamine silver stained sections demonstrated large, irregular, right-angle branched, aseptate hyphae suggestive of a zygomycete in the vessels, the tunica muscularis and the sub-serous colon membrane (Fig. 1). Microscopic examination of the intra-abdominal fluid also showed large and irregular hyphae and culture of the fluid on Sabouraud’s dextrose agar incubated at 28°C yielded *Rhizopus* spp. within 48 h. The colonies were dark, grayish-brown and microscopic examination showed rhizoids and brownish sporangiospores. The isolate was sent to the French National Reference Center for Mycosis and Antifungal Agents and was identified as *R. microsporus* by sequencing of the ITS regions [4]. It was found to be susceptible to amphotericin B (MIC = 0.03 μg/ml) and resistant to voriconazole (MIC >8 μg/ml) by the micromethod in liquid medium, EUCAST.

Further investigations

A search for airborne fungi in our intensive care unit did not reveal the presence of either *A. fumigatus* or *R. microsporus*. However, various *Aspergillus* species (but not *R. microsporus*) were recovered from the central air-conditioning system of the local hospital in which two recent cases of post-operative aspergillosis had been diagnosed.

Discussion

Post-mortem data obtained from haematology patients indicate that zygomycosis accounts for 8–13% of the fungal infections associated with patients, with only 2–11% of gastrointestinal (GI) involvement [5]. *R. microsporus* is the second most frequently isolated zygomycete, and may be found in the stomach and ileum. In this case, endoscopic examination shows extensive hemorrhagic ulcerations with black, necrotic, fundi and infiltration of the surrounding tissue [6]. Zygomycosis of the large bowel is less frequent. Bloody diarrhoea or massive hematochezia are frequently reported [7]. However, until now, no case of colonic zygomycosis due to *R. microsporus* has been described, probably because, in most cases, the diagnosis is made *post-mortem* without species identification. Peritonitis caused by *R. microsporus* is usually described in CAPD [2,3] and only one case has been reported after primitive peritonitis caused by perforation of the sigmoid colon [8]. Circumstances of contamination appear different between GI and peritonitis-associated zygomycosis. In the former, contamination is due to ingestion of contaminated foods, the use of contaminated wooden tongue depressors. For example, hospital-acquired infections due to *Rhizopus* spp. have been described following the use of wooden tongue depressors [9]. Similarly, gastric mycosis appeared after naso-gastric intubation or other conditions leading to development of gastric or colonic ulcers, suggesting that an initial ulceration may trigger fungal infection. In peritonitis, infection appears to be due to direct contamination of the peritoneum by catheters in CAPD or by faecal flora containing *R. microsporus* [2,3,8]. In our case, the infection might have been acquired due to contamination of the operation area by the fungus as the result of a possibly defective air-conditioning system.

Because of its vascular tropism, rapid diagnosis of zygomycetes is essential. Biopsy of the target organ is the best method, but this is often difficult in immunocompromised patients with coagulation disorders. Indeed, ante-mortem diagnosis was made in only 9% of 185 cases of disseminated zygomycosis [10]. Similarly, in post-CAPD peritonitis, mycological cultures are often negative, requiring concentration of the peritoneal fluid.

Treatment often requires surgery followed by antifungal therapy. In our patient, initial treatment with voriconazole for local aspergillosis appeared as a suitable option because
voriconazole is recommended as first line therapy to treat this fungal infection. Moreover it has a limited toxicity and can be administered orally. Recent guidelines recommend systemic voriconazole for cutaneous lesions following disseminated infection [11]. _Aspergillus_ peritonitis occurring as a complication of CAPD may also be treated with voriconazole as primary therapy although most of these cases have been treated initially with amphotericin B deoxycholate as described in individual case reports [11]. In all cases of CAPD infection, catheters must be withdrawn. However voriconazole has a narrower spectrum than amphotericin B and is not effective in limiting the development of zygomycetes [12]. Thus, many authors observe a resurgence of zygomycosis among patients with risk factors [13]. Posaconazole could be an alternative therapy. In a retrospective study including 91 cases of zygomycosis refractory or intolerant to prior antifungal treatment, posaconazole had a 60% success rate 12 weeks after treatment initiation [14]. In this series, two patients had gastrointestinal zygomycosis and both had a favourable outcome.

In conclusion, the present report describes an unusual case of peritonitis due to _R. microsporus_ complicated with invasion of the colon and highlights the limitations of the currently used antifungal agents.

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**References**


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