Infection (2013) 41:723–726
DOI 10.1007/s15010-013-0429-8

CASE REPORT

Cerebral *Scedosporium apiospermum* infection presenting with intestinal manifestations

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Received: 22 October 2012 / Accepted: 12 February 2013 / Published online: 26 February 2013

Abstract We present a case of cerebral *Scedosporium apiospermum* infection presenting with intestinal manifestations in a 64-year-old male patient on immunosuppression for orthotopic liver transplantation. At admission, the patient's chief complaint was chronic watery diarrhea and he was found to have colonic ulcers on endoscopy. His hospital course was complicated by a tonic–clonic seizure caused by a left frontal brain abscess, with the causative agent being identified by culture. He was treated with lobectomy, high-dose intravenous voriconazole, and liposomal amphotericin with clinical, endoscopic, and histologic improvement. To our knowledge, *S. apiospermum* has not been previously described as a cause of colitis. The septate branching appearance of the *Scedosporium* species is similar to the more common *Aspergillus* species. This case of gastrointestinal *Scedosporium* brings into question previously reported cases of isolated gastrointestinal aspergillosis diagnosed by histopathology. Clinical suspicion for *S. apiospermum* must be maintained in immunosuppressed patients presenting with neurologic and gastrointestinal symptoms.

Keywords Colitis · Brain abscess · Immunocompromised · *Scedosporium apiospermum* · Fungal · Hyphae · *Aspergillus* · Aspergillosis

This case report was collected from a patient treated in 2012 at the Michael E. DeBakey Veterans Affairs Medical Center.

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Introduction

Scedosporium apiospermum, the asexual (anamorph) form of *Pseudallescheria boydii*, is found in soil, sewage, and polluted water. It has increasingly been recognized as an opportunistic fungal pathogen, generally in immunocompromised patients [1]. *S. apiospermum* is known to cause localized and disseminated disease [2]. To our knowledge, it has not been identified as a cause of colitis. We report a case of cerebral *S. apiospermum* infection that presented with intestinal manifestations suggestive of colitis.

Case report

A 64-year-old male with an orthotopic liver transplantation presented with 1 month of diarrhea. His liver transplant was performed 5 months prior to admission for cirrhosis, secondary to hepatitis C and alcohol abuse, and hepatocellular carcinoma. His transplant course was complicated by renal insufficiency; however, no infectious complications were noted. His post-transplant course was complicated by acute rejection, which was managed with the addition of tacrolimus (0.5 mg PO every 12 h) and mycophenolate mofetil (1,000 mg PO every 12 h) to his

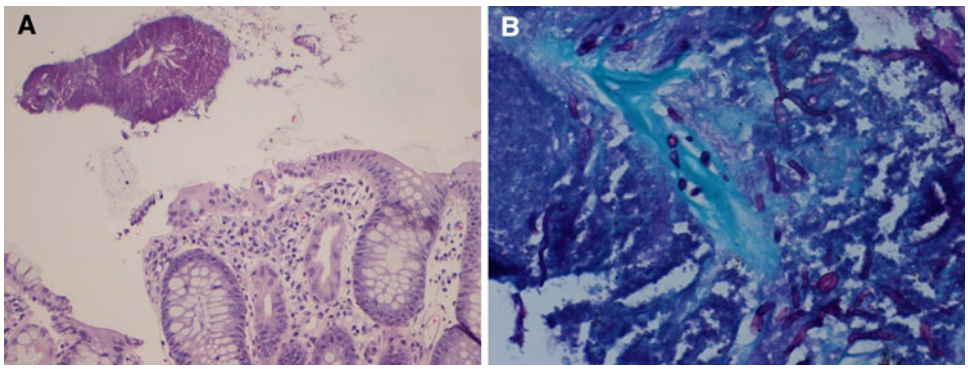

Fig. 1 **a** Colonic mucosal biopsy showing degenerated epithelium with rare neutrophils and detached debris (hematoxylin and eosin stain, ×200 magnification). **b** High magnification of debris containing straight and branched hyphae with septae and oval conidia (periodic acid-Schiff stain, ×1,000 magnification)

previous prednisone (10 mg PO daily) and sirolimus (1 mg PO daily). He was receiving no antifungal prophylaxis. The diarrhea was watery, non-bloody, and associated with mild crampy abdominal pain and decreased appetite. He reported no recent travel and lived in San Antonio, TX, where he was retired and spent most of his time doing yard work.

On admission, his vital signs were normal but he appeared hypovolemic. His white blood cell (WBC) count was 5,600/mm^3. Both his tacrolimus level of 7.9 ng/mL and sirolimus level of 14.5 ng/mL were within therapeutic ranges. Fecal occult blood test was positive. Stool studies were negative for fecal leukocytes, ova and parasites, and *Clostridium difficile* toxin. Blood cultures throughout his hospitalization were negative. Flexible sigmoidoscopy and colonoscopy showed multiple small shallow ulcers throughout the colon. He was started empirically on ganciclovir, and tacrolimus and mycophenolate mofetil were held. Immunostains were ultimately negative for cytomegalovirus (CMV) and herpes simplex virus (HSV), and ganciclovir was discontinued after 7 days of treatment.

On the eighth day of hospitalization, the patient had a witnessed generalized tonic–clonic seizure and was noted afterwards to be confused, with mild weakness of the right upper extremity. Magnetic resonance imaging (MRI) of the brain with contrast showed a left frontal enhancing mass of 3.2 × 3.1 × 3.3 cm. A left frontal craniotomy was performed and 10 cc of purulent material was aspirated. Frozen section showed necrotic material and acute inflammation. Septate branching fungal hyphae were seen on Gomori methenamine silver stain and voriconazole treatment (200 mg by mouth every 12 h) was started.

The patient's mental status continued to wax and wane. Repeat imaging demonstrated further enlargement and a left frontal lobectomy was performed. The original organism was identified through culture as *S. apiospermum* and high-dose intravenous voriconazole (6 mg/kg IV every 12 h) and liposomal amphotericin (4 mg/kg IV daily) were added after 7 days of treatment with oral voriconazole. Culture sensitivities were not performed. Colonic biopsies were now re-examined, using Periodic acid-Schiff stain, demonstrating the presence of septate branching fungal hyphae consistent with *S. apiospermum* (Fig. 1).

On discharge, the patient was clinically stable, with resolution of his diarrhea and improved cognition and memory. He had completed 2 weeks of liposomal amphotericin and was switched to a maintenance dose of oral voriconazole (400 mg PO every 12 h). Repeat flexible sigmoidoscopy 8 days after discharge revealed healing ulcers. Biopsies showed healing and special stains were negative for fungal organisms. Six months following discharge, the patient continued to do well, with no further complications from his central nervous system (CNS) infection.

Discussion

S. apiospermum is a filamentous fungus with worldwide distribution. It is recognized as a cause of infection in solid organ transplant recipients on immunosuppressive drugs, with a trend of higher incidence in lung transplant recipients [3].

Infection results from the inhalation of spores or through direct inoculation, and has the potential for invasion with lymphatic and hematogenous dissemination [4]. The most common site of infection is the lungs and respiratory tract, but other localized infections include keratitis, brain abscesses from near-drowning episodes, and soft tissue infections.

Disseminated disease is seen primarily in immunocompromised patients and is associated with mortality approaching 70 % [5, 6]. Hematogenous dissemination commonly causes endophthalmitis, brain abscesses, meningitis, endocarditis, osteomyelitis, and septic arthritis [2]. Nevertheless, autopsy of patients with disseminated *S. apiospermum* have shown the involvement of multiple organs in the abdominal cavity, including the kidney, stomach, pancreas, and liver [3].

Additionally, a recently reported case of disseminated *Scedosporium prolificans* demonstrated fungal infection of

the gastrointestinal tract on histopathology of autopsy specimens [7]. *S. prolificans* is the other medically important species of the genus *Scedosporium*, and it shares a similar pathogenesis and clinical presentation with *S. apiospermum* [2].

The diagnosis of infection due to *S. apiospermum* is difficult [8, 9] and requires histopathologic examination and culture. In this case, culture of the patient's brain abscess identified the organism. Although colonic tissues were not cultured, microscopic examination revealed septate branching hyphae consistent with *Scedosporium* in a bed of inflammatory tissue. Septate branching hyphae can also be seen with *Aspergillus* and other filamentous fungi [10]. However, this patient most likely had disseminated *S. apiospermum* infection, given that isolated gastrointestinal aspergillosis would be a most unlikely finding, especially without underlying neutropenia [11].

Assuming fungal stains were performed on his colonic biopsies without the identification of his brain abscess, septate hyphae would have been seen and most likely identified as *Aspergillus*. This questions the reported cases of gastrointestinal *Aspergillus* for which diagnosis was based upon histopathology [12–14], but, given the low culture yield of *Aspergillus* spp., controversy exists over the optimal diagnostic criteria [15]. Future methods may be able to more rapidly and accurately diagnose *Scedosporium* infections. Molecular technologies being examined include polymerase chain reaction (PCR) [16] and monoclonal antibodies [8].

The treatment of *S. apiospermum* brain abscesses combines medical management with adjunctive surgery [17–19]. Voriconazole is regarded as the antifungal agent of choice [19, 20], although the largest series published to date, by Troke et al. [20], showed that voriconazole therapy led to a successful response in 61 % of patients compared to 56 % of those receiving other antifungal medications. Additionally, solid organ transplant patients were associated with higher rates of response to voriconazole therapy (63 %).

In this case, the patient received both voriconazole and liposomal amphotericin B treatment. While amphotericin B has high minimum inhibitory concentration (MIC) values among the available antifungal agents [21], the concern with one-drug therapy with voriconazole is widely variable drug interactions with calcineurin inhibitors [22] and erratic metabolism by hepatic enzyme polymorphisms [23]. A recent study examining the in vitro activity of antifungal agents against *Scedosporium* showed no evidence of antagonism with any drug combinations, including amphotericin B with azoles [24]. The decision was made to add liposomal amphotericin B to assure therapeutic doses.

In conclusion, this report demonstrates a unique case of cerebral *S. apiospermum* infection in an immunocompromised patient whose original presentation was with symptoms of colitis and who had diffuse colonic lesions due to this fungal agent.

Conflict of interest The authors have no conflicts of interest or financial disclosures. There are no other concurrent submissions.

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