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CASE REPORT | COLON

Invasive Gastrointestinal Mucormycosis

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ABSTRACT

Invasive mucormycosis is an opportunistic fungal infection that can be devastating in immunosuppressed patients. Gastrointestinal infection is rare, but carries among the highest mortality rates of its major clinical presentations. We present a case of invasive gastrointestinal mucormycosis in a patient who underwent recent chemotherapy and autologous stem cell transplant. Initial histopathology revealed cytomegalovirus infection, which was treated before subsequent diagnosis of mucormycosis on repeat bowel biopsy. Our case highlights a myriad of risk factors that increase the potential for serious infection by this pervasive fungus.

KEYWORDS: mucormycosis; disseminated; cytomegalovirus; immunosuppressed

INTRODUCTION

Mucormycosis is caused by a group of molds from the order *Mucorales*, most commonly from the genera *Rhizopus* and *Mucor*.[1] Spores from these fungi are ubiquitous in our environment, often found in soil and decayed matter. The infection generally spreads through inhalation, through ingestion, iatrogenically, or through open-wound exposure to spores. Invasive mucormycosis infection is characterized by tissue infarction and necrosis from the invasion of a host vasculature with its hyphae that result in subsequent thrombosis.[2] Predisposing factors include uncontrolled diabetes mellitus, particularly in diabetic ketoacidosis, and those related to immunosuppression, such as hematologic malignancy, hematopoietic stem cell or solid organ transplantation, chronic corticosteroid use, and severe neutropenia.[3] Mucormycosis has 5 major clinical forms that include rhinocerebral, pulmonary, cutaneous, gastrointestinal (GI), and disseminated. Most frequently reported sites of invasion have been rhinocerebral and pulmonary, with GI as the rarest presentation.[4] Diagnosis of mucormycosis requires identification of the mold by histopathology of the affected tissue and confirmation by fungal culture. Treatment of all clinical forms necessitates the combination of early intravenous antifungal therapy and surgical debridement of infected tissue.[5]

CASE REPORT

A 40-year-old man with immunoglobulin A deficiency and refractory, progressive, chronic, inflammatory, demyelinating polyneuropathy was admitted for chemotherapy, followed by autologous stem cell transplantation. Initial hospitalization was complicated by neutropenic fever, ileus, and enteritis with *Clostridioides difficile* colonization treated with fidaxomicin 200 mg twice daily for 10 days. One month later, he was admitted for nausea and vomiting due to a focal jejunal stricture with diffuse small bowel wall thickening seen on computed tomography enterography. Single-balloon push enteroscopy revealed 2 circumferential deep small bowel ulcerations, which were biopsied (Figure 1); however, the stricture noted on imaging was too distal to be reached. Pathology showed granulation tissue-containing cells with cytologic features suspicious for cytomegalovirus (CMV), although no viral inclusions were identified. Biopsy CMV polymerase chain reaction revealed greater than 3 million UI/mL, and serum polymerase chain reaction also identified mild viremia with 920 copies/mL. He was treated with IV ganciclovir 300 mg twice daily before transitioning to oral valganciclovir 900 mg daily for 20 days and total parenteral nutrition initiated on discharge. The patient was admitted a third time for recurrent nausea and vomiting. Imaging revealed new small bowel obstruction with a transition zone at a known jejunal stricture. Nasogastric tube decompression was attempted, but was unsuccessful and eventually required surgical intervention. Diagnostic laparoscopy revealed 5 strictures in the small bowel approximately 15 to 100 cm distal to the ligament of Treitz, which were all resected and reanastomosed. Histopathology showed mucosal

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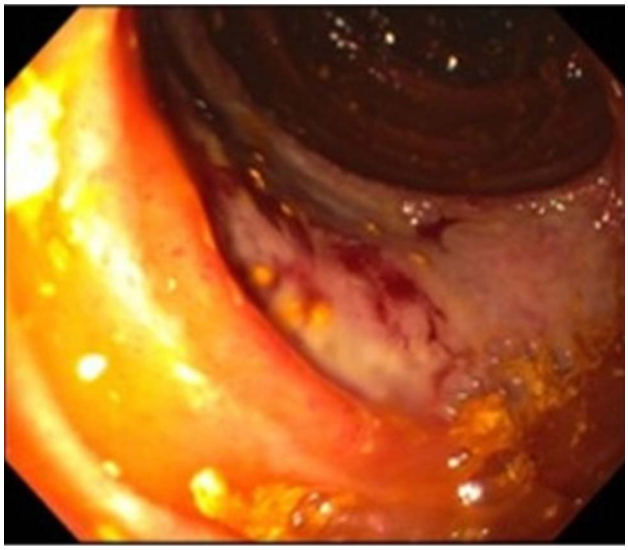

Figure 1. Circumferential ulcerations seen in the jejunum on push enteroscopy.

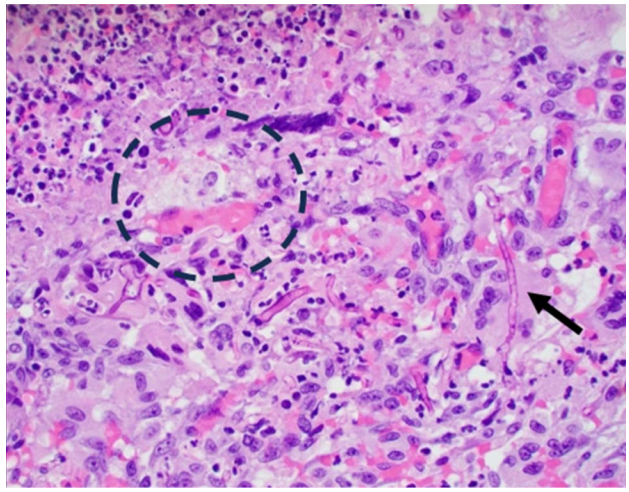

Figure 2. Mucosal ulceration with underlying necrotizing granulomatous inflammation (circle) with nonseptated fungal hyphae (arrow) (hematoxylin and eosin stain, 200× magnification).

ulceration with underlying necrotizing granulomatous inflammation and nonseptated fungal hyphae concerning for mucormycosis (Figure 2). Serum fungal culture was negative for fungemia. The patient remained on oral antiviral treatment, and CMV was not identified on jejunal biopsy or polymerase chain reaction testing. He was treated with liposomal amphotericin B 290 mg daily before transitioning to oral isavuconazole 372 mg daily for 6 months and advanced off total parenteral nutrition. The patient is currently 1 year out from his autologous stem cell transplantation with complications resolved, neutrophil recovery, and reduction in intravenous immunoglobulin requirement.

DISCUSSION

Mucormycosis is an angioinvasive fungal infection associated with high morbidity and mortality in the immunocompromised population. Major predisposing factors for infection are in patients with poorly controlled diabetes mellitus, especially those with diabetic ketoacidosis because the fungus favors the hyperglycemic and acidotic state. Recent literature has reported that patients with hematological malignancies and hematopoietic stem cell transplantation were the 2 most rapidly increasing populations developing mucormycosis.[4,6] GI infection is rare in living patients and estimated to occur in only around 7% of all cases, yet carries a mortality rate as high as 85%.[4] The stomach is the most frequently affected portion of the GI system, followed by the colon. Just 10% of documented cases have involved the small bowel, further signifying the rarity of our case.[7] Only 25% of GI mucormycosis is diagnosed antemortem because of its rapid progression and diagnostic challenges.[2] GI infection can present as variable nonspecific abdominal complaints which, without a high index of suspicion, can delay early endoscopic evaluation. On computed tomography, mucor may mimic ischemic bowel with wall thickening, lack of enhancement, and mucosal defects.[8] Current recommendations for diagnosis depend on tissue histopathology with culture confirmation. Endoscopy-guided biopsy can improve histologic sensitivities up to 80%; however, in more than 50% of cases, there is no growth in culture.[9,10] As such, even with timely analysis, establishing the diagnosis may be impeded by morphologic mimics, sampling difficulties, and inconsistent fungal growth.[11]

Interestingly, our patient was diagnosed and treated for CMV GI infection before the discovery of mucor invasion. There have been reports of mixed CMV and mucormycosis coinfection seen in renal transplant recipients.[12–14] There were significant quantities of CMV identified on tissue and serum polymerase chain reactions, but the absence of viral inclusions stratified our patient as low-grade CMV based on the criteria set by Jones et al.[15] Our case aligns with their findings that low-grade patients were more likely to require surgical resection, yet antiviral therapy was still effective. It is difficult to confidently state whether CMV and mucor infections were concurrent for our patient. We suspect that they occurred individually based on the absence of organisms seen concomitantly on repeated biopsies and rapid resolution of initial CMV after treatment.

In this case, invasive mucormycosis likely stemmed from a combination of immunosuppression therapy, stem cell transplant, prolonged neutropenia, surgical and endoscopic interventions, and recent infections of the GI tract. Diagnosis was made on histologic observation of nonseptated fungal hyphae present in mucosal ulceration of the resected jejunum. Although uncommon, GI mucormycosis should be considered in immunocompromised patients with unexplained, recurrent GI symptoms and multiple risk factors, as presented in this case. Early diagnosis is important because rapid progression in susceptible patients is associated with serious complications and high mortality. We hope that this case will encourage clinicians to keep mucormycosis in their differential and seek histologic diagnosis if clinically warranted.

DISCLOSURES

Author contributions: B. Zhong contributed to acquisition and interpretation of data and drafting of the manuscript and is the article guarantor. T. Amundsen contributed to drafting and editing of the manuscript. C. Farmer contributed to interpretation of data and editing of the manuscript.

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