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Case Report

A fatal case of gastrointestinal mucormycosis in immunosuppressed host

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ARTICLE INFO

Article history:

Received 26 September 2012

Accepted 20 May 2013

Available online 5 July 2013

Keywords:

Gastrointestinal mucormycosis

Antifungal therapy

Opportunistic infections

On examination, vitals were; Temp 96.6, BP 110/65, PR 105; he appeared malnourished, lethargic but in no acute distress. Abdominal examination showed epigastric tenderness, guarding with sluggish bowel sounds. Rectal examination was guaiac negative. CT abdomen showed free peritoneal air with possible distal ileal perforation (Fig. 1). At exploratory laparotomy, multiple areas of full thickness perforation involving the proximal jejunum and the distal ileal were seen requiring segmental resection. Histopathological examination revealed ischemic necrosis of the bowel wall with gross and microscopic evidence of perforation, infarction and transmural infiltration by nonseptate, fungal hyphae consistent with *Rhizopus* species. The patient died within 24 h from overwhelming sepsis despite aggressive surgical intervention and antifungal therapy (Fig. 2).

Case report

A 62-year-old white male patient with history of compound inherited coagulopathy (heterozygous factor V Leiden and MTHFR) and 6 months history of biopsy proven Wegener's granulomatosis with lung and renal involvement, presents to the ER with severe abdominal discomfort, fever and loss of appetite. He was admitted to an other facility a month prior to this hospital admission for dyspnea for a right-sided pneumothorax requiring tube thoracostomy. He also underwent bronchoscopy with biopsy of the cavitating pulmonary lesion for suspicion of infection. Biopsy results conformed to invasive aspergillosis and he was started on Voriconazole and Caspofungin. His other medications include warfarin, Rituximab, Prednisone and Cyclophosphamide.

Discussion

Mucorales is a ubiquitous saprophytic fungus, present in soil and decaying organic material that have little pathogenicity in normal hosts. Over the past few years due to reclassification, the order zygomycetes has been replaced with mucorales under the subphylum mucormycotina.¹ In the last decade there has been an increased trend toward diagnosis of mucormycosis especially among the recipients of hematopoietic stem cell transplant (HSCT), though the exact incidence is unknown. They cause opportunistic infections in acidotic states such as diabetic ketoacidosis, immunosuppression following solid and hematopoietic stem cell transplant and also iron overload states with or

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<http://dx.doi.org/10.1016/j.mjafi.2013.05.006>

Fig. 1 – CT abdomen showing extravasation of the oral contrast into the mesentery with dilated small bowel and free air.

without deferoxamine therapy.² The hallmark of mucormycosis is angioinvasion with vessel thrombosis, extensive tissue necrosis and propensity to hematogenous dissemination. They cause deep tissue disease after inhalation, accidental inoculation or ingestion of the fungal spores.

Based on clinical presentation and anatomical involvement, mucormycosis are classified into six categories: 1) rhinocerebral 2) pulmonary 3) cutaneous 4) gastrointestinal 5) disseminated 6) miscellaneous. Gastrointestinal mucormycosis is relatively rare, with stomach and the colon being the most frequent sites of involvement.³ Hepatic mucormycosis after herbal medication ingestion has been reported previously. Typical risk factors for gastrointestinal mucormycosis include malnutrition (kwashiorkor), premature birth, intrinsic gastrointestinal tract abnormalities or immunosuppression.³ Other reasons for proposed increase in the incidence of mucormycosis include widespread use of newer, broad-spectrum antifungal agents such as Voriconazole (unknown is association vs. causation) in the prophylaxis and treatment in select patients.

Gastrointestinal involvement can usually present with invasion of the mucosa, submucosa and along with pathognomonic demonstration of angioinvasion. Clinical presentation

include that of acute abdomen such as pain, distention, nausea and vomiting but can also be with hematemesis, hematochezia or intestinal perforation with peritonitis. Many of these signs and symptoms can also be present as part of vasculitis syndrome with tissue ischemia in patients with known systemic vasculitis which may further delay the diagnosis. The CT abdomen and intra-operative findings can be nonspecific and may be suggestive of ischemic enteritis as in our case. Diagnosis relies on direct identification of the fungal elements in the tissue specimen and cultures. Blood cultures may rarely be positive but usually remain negative.

Infections remain one of the leading causes of death in patients with known small vessel vasculitis including WG.⁴ The cause of gastrointestinal mucormycosis in this patient is likely multifactorial including severe immunosuppression and malnutrition. The association of Voriconazole as a causation of invasive mucormycosis is of debate with preliminary studies from animal model demonstrating increased virulence of the fungus when exposed to the drug.⁵ In addition, mucormycosis is often diagnosed in the background of patients undergoing concurrent treatment for aspergillosis majority of the antifungal agents used in the treatment of the later being ineffective.⁶ Additionally, the data from Chamilos et al showed a two-fold increase in mortality at 12 weeks when treatment was delayed when Amphotericin B was initiated > 6 days after diagnosis (82.9% vs. 48.6%).⁶ Angioinvasion with vessel thrombosis leading to tissue necrosis is the hallmark of mucormycosis, which is identified, in the pathological specimen. Treatment for gastrointestinal mucormycosis like other organ specific forms of mucormycosis, remains early surgical debridement along with administration of Amphotericin B, though the overall survival remains poor. This being said early surgical debridement of the dead and devitalized tissue may have mortality benefit though survivors in the surgical group in retrospective case series could be a result of selection bias with sicker patients not considered as good surgical candidates.⁷ Amphotericin B deoxycholate (AmB) at doses of 1 mg/kg/day remains the antifungal therapy of choice in mucormycosis. Additionally, limited data exists on combination AmB-echinocandins in rhinocerebral mucor.⁸ Whether this combination offers mortality benefit in other organ involvement remains unknown and has to be addressed in additional randomized control studies. In conclusion early diagnosis, surgical debridement when possible along with prompt initiation of AmB seems to improve survival in

Fig. 2 – Angioinvasion; nonseptate, irregular branching fungal hyphae with thrombosis (a); along with extension into the epiploic appendages (b) with infarction.

patients with mucormycosis but data is limited to gastrointestinal involvement.

Conflicts of interest

All authors have none to declare.

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