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SHORT REPORT

Gastrointestinal mucormycosis: A success story and appraisal of concepts

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Summary Mucormycosis is an opportunistic, life-threatening fungal infection caused by fungi of the class Zygomycetes. The disease has traditionally been reported in immunocompromised patients, premature infants, diabetics, transplant recipients, prolonged use of corticosteroids or in condition associated with increased availability of serum iron such as acidosis or deferoxamine administration. The infection is progressive and associated with a high mortality unless treatment is initiated promptly. The number of cases of gastrointestinal mucormycosis indexed on PubMed over the past 2 decades has shown an alarming rise. Moreover, the infection is being increasingly reported in patients without the traditional risk factors.

We report successful management of an immunocompetent child with gastrointestinal mucormycosis who responded to aggressive treatment with surgical debridement and antifungal agents. The fungicidal activity of colistin (polymyxin E) has also been highlighted.

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Introduction

Mucormycosis is an increasingly common opportunistic, life-threatening fungal infection that affects immunocompromised hosts. Although rare,

it has been reported in low-birth-weight infants and has been shown to be associated with a high mortality rate. However, infection in healthy persons is unusual.

We report the successful management of an immunocompetent child with gastrointestinal mucormycosis who responded to aggressive treatment with surgical debridement and antifungal agents (amphotericin B and colistin).

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Case history

A 10-year-old boy weighing 16.3 kg presented with complaints of loose stools and progressively increasing distention of the abdomen for the previous five days. He also had bilious vomiting and an absence of stools or flatus for the previous two days. He had not passed urine for the last 13 h. He complained of colicky pain in the lower right quadrant of the abdomen for the previous 6 h. The patient appeared ill and was febrile and moderately dehydrated. His pulse rate was 126/min, his respiratory rate was 30/min and his blood pressure (mmHg) was 84/46. Abdominal examination revealed generalized tenderness and absence of bowel sounds. Preliminary laboratory investigations revealed hemoglobin of 8.8 g/dL with an abnormal coagulation profile. The erect abdominal radiograph revealed free intraperitoneal air.

While the patient was resuscitated and hemodynamically stabilized, bilateral flank drains were inserted under local anesthesia, and approximately 650 mL of thick, deep yellow, foul-smelling pus was drained. Vitamin K and fresh frozen plasma were administered. An exploratory laparotomy was performed after stabilization of the hemodynamic and coagulation parameters. Loculated pyoperitoneum with pus flakes densely adherent to the bowel wall were present. A 0.9 cm × 0.8 cm perforation was present along the lateral border of the ascending colon, approximately 18 cm distal to the ileocecal junction. The edges of the perforation were irregular, everted, swollen and covered with creamy white slough. The duodenojejunal junction was to the right side of the midline, and the mesentery was foreshortened. The margins of the ulcer were freshened, and the ulcer was repaired. Ladd's procedure was also performed. Because of severe sepsis and edema of the bowel wall, a loop ileostomy was performed 15 cm proximal to the ileocecal junction. Peritoneal lavage was performed, and the abdomen was closed.

The margins of the ulcer were submitted for histopathological examination. There were multiple fragments of tissue from the ulcer margin, revealing large, deep mucosal ulcers with marked submucosal edema (Fig. 1). Ulcer beds formed by dense acute-on-chronic inflammatory granulation tissue were observed to reach into the muscularis propria. Neuromatoid hyperplasia was noted in the myenteric plexus. Organized inflammation in the serosa and a few granulomas with foreign body giant cells were also present. Multiple broad non-septate hyperacute branching PAS-positive fungal hyphae (Periodic Acid Schiff stain) were noted both in the inflammatory exudates and within the giant cells.

The overall findings were consistent with mucormycosis.

The patient was initiated on intravenous amphotericin B. Further work-up included nasal and sputum swabs, which were negative for mucormycosis. An ELISA test for HIV was also negative. The patient remained in a catabolic phase and lost 35% of his body weight over the next three weeks, despite receiving full oral nutrition and a high-protein diet. He developed a burst abdomen with ileostomy retraction and fecal fistulae just proximal to the ileostomy site in the exposed bowel, which were repaired under general anesthesia. The patient also developed left corneal ulceration. Neither gram stain nor KOH stain of the corneal ulcer were suggestive of mucormycosis. The ulcer was managed with topical antibiotics and artificial tears. The patient also developed secondary sepsis with methicillin-resistant *Staphylococcus aureus* that was sensitive to vancomycin. The patient was initiated on injectable vancomycin, but no appreciable response was observed after five days of antibiotic treatment. Based on the report by Ben-Ami et al. [9], the patient was initiated on injectable colistin (polymyxin E). The patient began to gain weight on the third day of colistin treatment, and his condition improved rapidly. The patient recovered and was discharged with a functioning ileostomy. He is awaiting ileostomy closure.

Discussion

We report the successful management of a case of gastrointestinal mucormycosis in a 10-year-old child who was not immunocompromised and did not have any of the known predisposing or precipitating factors.

Mucormycosis is an opportunistic, life-threatening fungal infection caused by fungi of the class Zygomycetes and order Mucorales. *Rhizopus oryzae* (*Rhizopus arrhizus*) is the most common cause of mucormycosis [1]. Mucormycosis almost always occurs in patients with compromised immune function and under conditions associated with the increased availability of serum iron. The infection is progressive and is associated with a high mortality unless treatment is initiated promptly.

Immunity against mucormycosis is provided by phagocytes (both mononuclear and polymorphonuclear) through the generation of oxidative metabolites and cationic peptide defensins. Patients with neutropenia or dysfunctional phagocytes are therefore highly susceptible to mucormycosis.

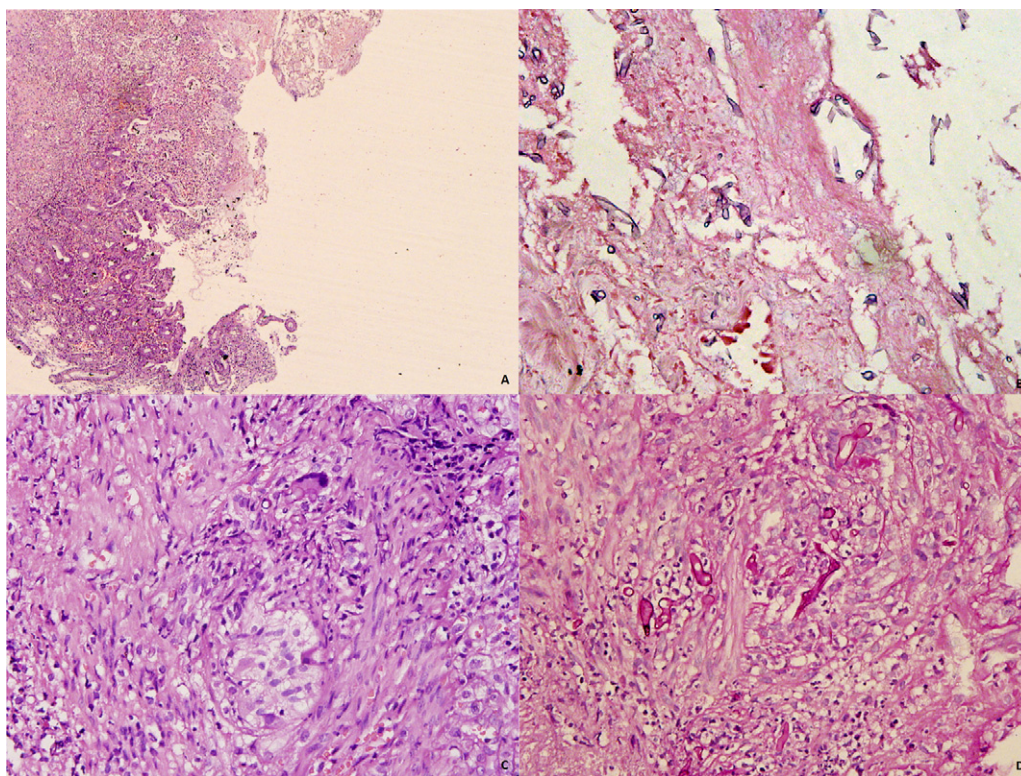


Figure 1 Photomicrographs show a large colonic ulcer (A, H&E 40 \times), with an acute inflammatory exudate containing many broad, aseptate, acute angle branching fungal hyphae (B, H&E 200 \times). In the granulation tissue below the ulcer base there are epithelioid cell granulomas with giant cells, engulfing fungal hyphae (C, H&E 100 \times). Periodic Acid Schiff stain with diastase brings out the fungal hyphae with the granulomas as well as in giant cells better (D, H&E 100 \times).

Ketoacidosis, diabetes and steroid use further impair phagocytic function through unknown mechanisms [2,3]. Furthermore, an increased availability of serum iron increases the susceptibility to mucormycosis. The clinical hallmark of mucormycosis is angioinvasion with consequential systemic dissemination of the fungal spores, thrombosis of the affected blood vessels and local tissue infarction/necrosis [5].

Mucormycosis may be classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated or miscellaneous. Rhinocerebral mucormycosis accounts for almost one-third to one-half of all cases [5]. Mucormycosis of the gastrointestinal tract is rare [4]. Predisposing factors include malnutrition, especially in infants and children [5]. The fungi typically enter the gastrointestinal tract through ingestion. The stomach is the most common site of gastrointestinal mucormycosis, followed by the colon and ileum. Gastrointestinal mucormycosis has been reported in premature neonates, with a presentation similar to that of necrotizing enterocolitis, and it is often associated with widespread dissemination.

Hepatic mucormycosis [6] has also been reported, particularly after the ingestion of herbal medicines. Maravi-Poma et al. [7] reported an outbreak of gastric mucormycosis associated with the use of wooden tongue depressors in critically ill patients.

Management includes prompt diagnosis, the reversal of underlying predisposing factors, aggressive surgical debridement of infected tissues and the initiation of antifungal therapy. The diagnosis is established by demonstrating characteristic broad, branching and non-septated hyphae in freshly infected tissues, usually in association with extensive angioinvasion, with resultant vascular thrombosis and infarction. Antigen detection is associated with low sensitivity and specificity.

Liposomal amphotericin B is the drug of choice for treatment of mucormycosis; posaconazole is considered a second-line therapy. Rifampicin [8] has been shown to enhance the fungicidal action of amphotericin B. Ben-Ami et al. [9] studied and demonstrated the fungicidal activity of colistin (polymyxin E) in vitro against Mucorales spores and mycelia.

Mucormycosis is uniformly associated with high mortality. Survival in neonates with gastrointestinal mucormycosis is rare [10–13]. The lack of clinical suspicion, its association with immunocompromised status and inadequate therapy account for the high mortality. The mortality in pulmonary mucormycosis approaches 65% at 1 year of age [14]. Disseminated mucormycosis is also associated with near-total mortality because the surgical removal of infected tissue is not feasible, and most of the affected patients are immunocompromised [1].

The successful management of gastrointestinal mucormycosis requires a high index of suspicion, diagnostic evaluation and the prompt initiation of antifungal and surgical therapy. Further research is required to establish the role of colistin (polymyxin E) in the management of this devastating infection.

Conflict of interest

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Competing interests: None declared.

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