Case Reports

Neonatal Colonic Mucormycosis—A Tropical Perspective

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Summary

Neonatal gastrointestinal (GI) mucormycosis is a rare, usually fatal, opportunistic fungal infection, which is difficult to diagnose early or preoperatively. We report three babies, only one of whom survived, with a review of the literature. All three had similar findings of necrosis of colon with multiple perforations. While the first baby was diagnosed as long segment Hirschsprung's, the second was treated as small left colon but went on to show signs of peritonitis. The third presented with pneumonia, which progressed to sepsis and peritonitis. All three were diagnosed by histology postoperatively and two of them succumbed, one in spite of amphotericin and the other as he was too sick to start antifungals and had a rapid downhill course. The one who survived did so even though she did not receive amphotericin, but had clear margins of resection. The only chance of survival in this fatal disease is early diagnosis and rapid institution of aggressive therapy inclusive of adequate surgical debridement and appropriate antifungal medications.

Introduction

Neonatal gastrointestinal (GI) mucormycosis is a rare, usually fatal, opportunistic fungal infection.[1–8] A third of the affected patients with mucormycosis present as necrotizing enterocolitis (NEC), as documented in two previous studies,[8] but a clinical presentation of intestinal obstruction has been infrequently reported.[9] This is a report of three neonates with colonic mucormycosis, two of whom presented as neonatal intestinal obstruction, with a review of the literature.

Case Reports

Case 1

A 4-day-old, term, small for date male, who had passed meconium on day 1, presented with abdominal distension, vomiting and dehydration. Investigations revealed thrombocytopenia and uraemia. The contrast findings were suggestive of long segment Hirschsprung's disease (HSD). At laparotomy, gangrene and multiple perforations of the sigmoid and descending colon were noted, the diseased segment was resected and end-stoma fashioned. Histology revealed transmural necrosis of the bowel wall with serosal and subserosal vascular thrombosis as well as marked serositis. Invasive fungal filaments of mucor, with the characteristic broad aseptate hyphae, branching at right angles, were seen amidst dense acute on chronic inflammation, at the site of perforation (Fig. 1) and within vascular thrombi (Fig. 2). The resected surgical margins were non-viable with transmural necrosis. The patient was started on amphotericin B, but had a downhill course and succumbed to secondary bacterial sepsis after 2 weeks.

Case 2

A 7-day-old, term female baby was admitted on day 2 with non-passage of meconium, vomiting and an episode of bleeding from the rectum. On examination the abdomen was distended with visible bowel loops. Abdominal X-ray revealed dilated bowel loops with paucity of rectal air. Contrast enema was suggestive of small left colon syndrome. The child was managed conservatively, but developed features of rapidly progressive peritonitis and was taken for an emergency laparotomy. She was found to have necrosis and multiple perforations involving the splenic flexure and the descending colon. Resection with the end stoma was performed. The histology of the colon at the site of perforation was similar to that of case 1. In this case, however, the resected margins were viable and free of fungal infiltration. The viable bowel was normally ganglionated. The parents declined further treatment and the child was discharged on oral fluconazole. Last seen at 3 months, the infant was doing well.

Case 3

This 16-day-old male was delivered by a caesarian section at term, due to fetal distress. On day 2 of life

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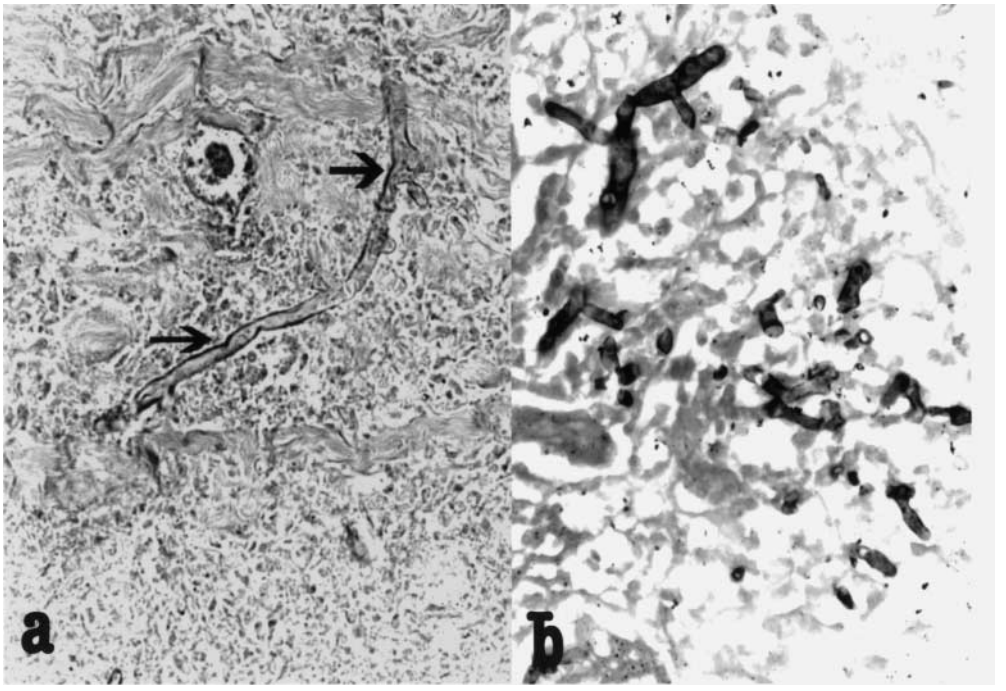

FIG. 1. (a) Characteristic broad hyphal filaments of mucormycosis (arrows) seen at the site of perforation (H & E ×400). (b) Branching fungal filaments clearly demonstrated by silver stain (GMS stain ×250).

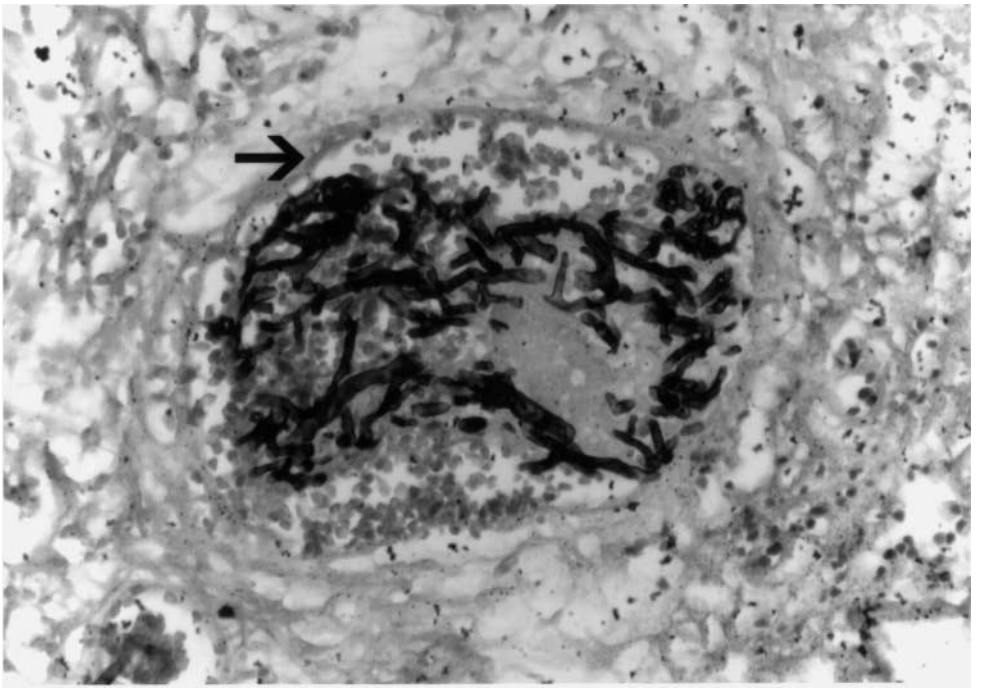

FIG. 2. Vasoinvasive filaments of mucor penetrating the vessel wall (arrow) (GMS stain ×250).

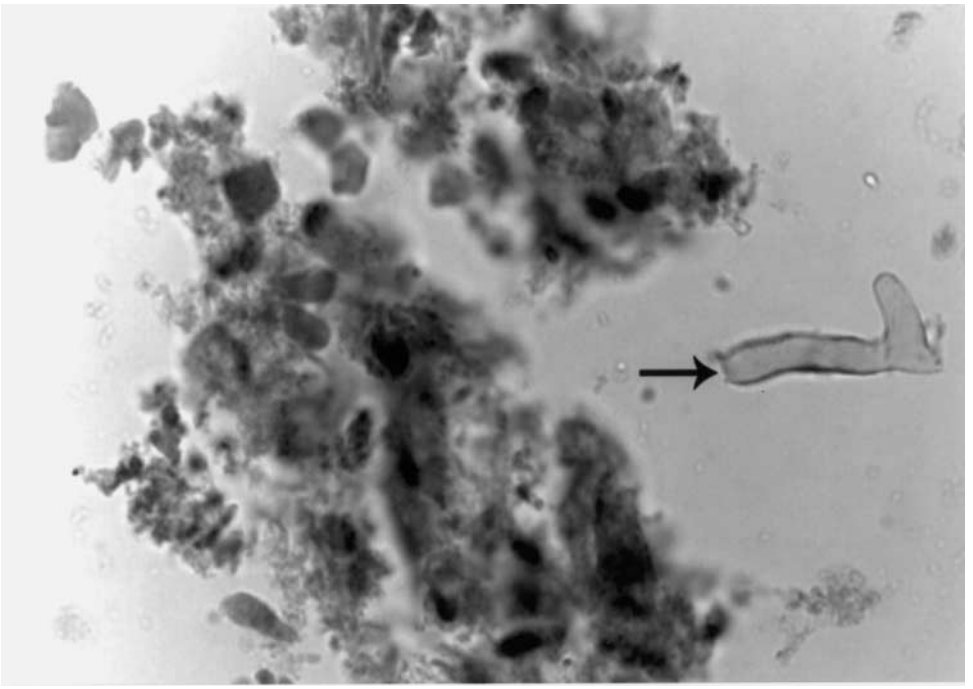

FIG. 3. Frozen section smears from necrotic tissue showing occasional characteristic hyphae of mucor (H & E ×400).

the child developed pneumonia with sepsis. He was treated with antibiotics, which included amoxicillin-clavilonic acid initially, ceftazidime, amikacin, and ciprofloxacin and required ventilatory support. Twelve days later the child developed abdominal distension and features of peritonitis. Aspirated peritoneal fluid showed yeast-like organisms morphologically resembling *Candida* species. At laparotomy, a segment of descending colon and sigmoid was resected which showed patchy necrosis with gangrenous perforation on histology. In view of the prior experiences, necrotic bowel was sent for frozen sections and smears (Fig. 3). In this case also, fungal hyphae of mucorales was found. In addition, a granulomatous response was also noted (Fig. 4). Amphotericin B could not be started since the newborn was hemodynamically unstable and had acute renal failure. He died within 48 h.

Discussion

Mucormycosis, which accounts for 10 per cent of all mycotic infections,[2] is caused by fungi of the order mucorales, which are ubiquitous saprophytic fungi, with little pathogenicity for the normal human host and causes infection through spores after inhalation, ingestion,[1] or inoculation through skin and blood.[2] The route of inoculation of the spores and host resistance determine the occurrence of pulmonic, rhinocerebral, cutaneous, gastrointestinal, or disseminated forms of the disease.[3,4,6]

Children account for a third of the patients with mucormycosis,[3] with 50 per cent occurring in infants.[1,3–7] Gastrointestinal (GI) involvement is rare accounting for only 7 per cent of mucormycosis, with stomach and colon being predominantly affected.[6] Colonic predilection has been observed in this study and two previous studies of Asian neonates.[8,9]

Most cases of GI mucormycosis have been reported from Africa and the USA.[1,7] There have been 12 reported cases of isolated GI mucormycosis from the Indian subcontinent,[2,8–10] including 10 children, six of which were neonates.[2] Five of these were diagnosed initially as necrotizing enterocolitis (NEC) and one as Hirchsprung's disease. Three of them were preterm babies, while the other three had either received prolonged antibiotics and/or undergone surgery (two of them for esophageal atresia).

Malnutrition, prematurity, concomitant infections, and immunosuppression are the common predisposing causes in children.[1,3,6] In our series, case 3 had sepsis and antibiotic therapy. Prior antibiotic therapy has been postulated to predispose to GI mucormycosis, possibly by altering the normal gastrointestinal flora and permitting the mucorales to invade the mucosa.[1] No major predisposing factors were

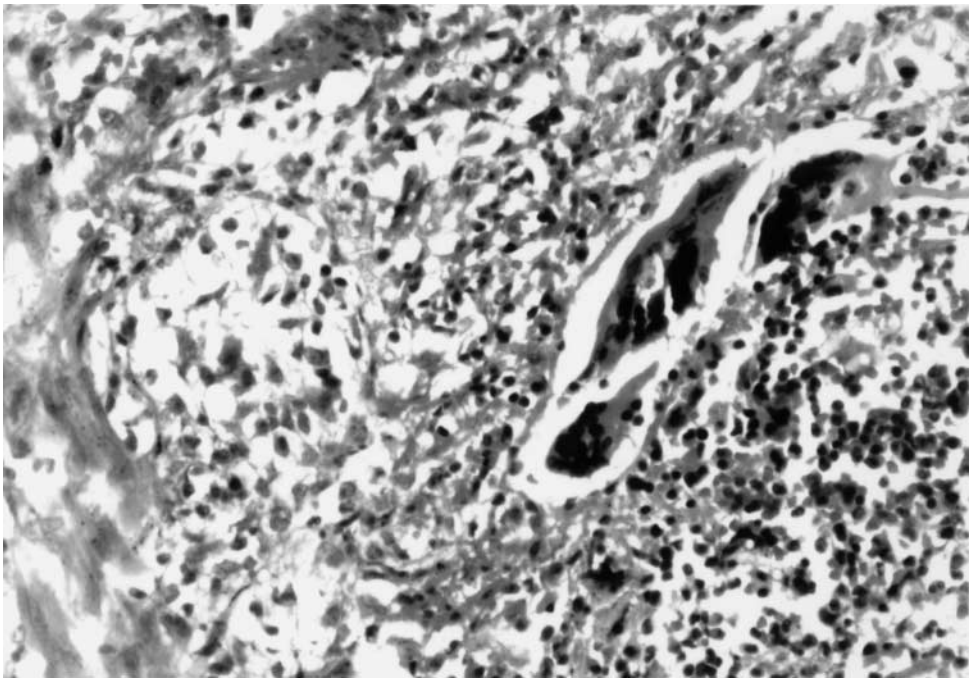

FIG. 4. Granulomatous inflammation with foreign body giant cells aggregate (H & E ×400).

identified in cases 1 and 2; however, both had prior barium enema, although at different time, and case 1 in addition was small for date. It has been suggested that GI diseases or procedures may result in altered mucosal defence or cause local tissue trauma and facilitate the establishment of the disease,[3,7] especially in those with already compromised GI mucosal barrier due to inflammation or sepsis. All three patients were negative for HIV.

The mode of presentation of gut mucormycosis is deceptive. Children often present with bloody diarrhea, intestinal obstruction, perforation, peritonitis,[2,3] and rarely with an abdominal lump.[11] Perforation and peritonitis, consistent findings in all our cases, have been reported in other studies.[2] Necrotizing enterocolitis is a frequent misdiagnosis and some authors have raised the possibility of neonatal GI mucormycosis being a variant of NEC.[8,12] The absence of submucosal pneumatosis and the identification of fungal elements, histologically, enables distinction of NEC from GI mucormycosis, as has been suggested by Woodward, *et al*.[12] The other pattern suggested by Kline,[4] is that of obstructive gastrointestinal pathology. Hirschsprung's and subacute intestinal obstruction[9] have often been erroneously diagnosed. Nevertheless, the possibility of a transient functional obstructive process, favoring colonization and invasion of mucormycosis in these children should be considered.

In our experience all the children had rapid deterioration of the GI tract with characteristic operative findings of gangrenous bowel loops with perforation. These findings should lead to a search for fungal filaments in the appropriate clinical setting. Mucor filaments are well seen on routine hematoxylin and eosin (H & E) stained sections. However, special stains like Gomori methanamine silver (GMS) stains help to highlight and clearly delineate the filaments and can be used when there is a paucity of organisms.[4,5] A comment on the nature of tissue invasion is critical. Thompson, *et al*. categorized mucormycosis into colonizing, infiltrating, and vaso-invasive forms.[7] All three cases in this study showed the vaso-invasive form of the disease, predictive of a poor prognostic outcome.

The pitfall of histological diagnosis is the inevitable delay of more than 24 h in routine paraffin processing, since a delay of a few hours impedes early institution of life saving anti-fungal chemotherapy. Direct microscopy of tissue exudates, contact smears taken from the cut surface of biopsies, or histology of frozen sections may confirm the diagnosis within a few hours,[13] as well as excluding invasive fungal filaments at the margins of resection. These techniques would ensure adequate surgical resection and result in prompt and early administration of anti-fungal therapy. In this case series, smears taken of the ulcerated bowel mucosa

TABLE 1
Summary of cases of neonatal GI mucormycosis in Asia

SI no.	Age/sex	Ref	Clinical features	Clinical diagnosis	Site	Predisposing factors	Outcome
1	9d/F	2	Abdominal distension	NEC	Colon	Prematurity	Died
2	4d/F	2	Constipation and abdominal distension	HSD	Colon	Prematurity	Died
3	6d/M	10	Abdominal distension	NEC	Ileum and colon	Antibiotic therapy	Died
4	4d/M	8	Post EA repair with abdominal distension and diarrhea	NEC	Colon	EA repair and antibiotic therapy	Died
5	9d/M	8	Constipation, abdominal distension, coagulopathy and shock	NEC	Colon	Prematurity	Died
6	1d/F	8	Post EA repair with leak and abdominal distension	NEC	Colon	EA repair	Survived
7	4d/M	Present study	Abdominal distension and vomiting	HSD	Colon	Small for date, barium enema	Died
8	7d/F	Present study	Abdominal distension and failure to pass meconium	Small left colon syndrome	Colon	Barium enema	Survived
9	16d/M	Present study	Abdominal distension	Peritonitis	Colon	Sepsis, antibiotics	Died

permitted early diagnosis in case 3, but the patient's condition did not permit the institution of appropriate therapy.

Currently adequate surgical resection of the involved intestine and amphotericin B therapy remains the mainstay of mucormycosis treatment.[1,3] Adequate resection not only reduces the fungal load but also eliminates the possibility of perforation or long-term sequelae-like strictures.[3] In case 2, where resection was adequate and margins were clear, the infant recovered in spite of not receiving amphotericin, while the other two cases with inadequate microscopic clearance succumbed to the fungal invasion. The patient who recovered was discharged on oral fluconazole, which has so far not been used in the treatment of GI mucormycosis, as the parents wanted to take the child home without further in-hospital management. However, whether response to therapy in this case was due to clearance at surgery or due to the drug is debatable. Other antifungals, such as ketoconazole, have not been shown to be effective. There have been no reports on the use of fluconazole for invasive fungal infections, although oral fluconazole is used prophylactically in cancer patients who are immunocompromised by chemotherapy.

Conclusions

We reiterate that GI mucormycosis, with its deceptive presentation and aggressive behavior, makes it hard to contend with, particularly in the neonate. The essence of successful management lies with early recognition and rapid institution of appropriate therapy. The surgeon should maintain a high index of suspicion in children who have a rapidly progressive onset of obstructive GI symptoms with necrotizing or perforating lesions of unknown cause, particularly involving the colon. Rapid diagnosis by utilization of simple procedures, such as microscopy of exudate smears, frozen section of necrotic tissue and margins of resection, would permit aggressive and adequate surgical debridement and catalyze effective anti-fungal chemotherapy.

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Primary Multiple Intracerebral Echinococcosis in a Young Child

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Summary

Primary multiple intracerebral echinococcosis is a very rare disorder particularly in children. In this case report we discuss the details of clinical presentation and management in a young child. We also highlight for the first time non-iatrogenic 'water lily' appearence of the lesion on computed tomography of the head.

Introduction

Cerebral hydatid disease is very rare. Brain involvement occurs only in 1–2 per cent of all *Echinococcus granulosus* infection.[1] Its incidence in India is reported to be 0.2 per cent of all intracranial space occupying lesions.[2] The cerebral cysts are usually single, spherical, and unilocular. Multiple primary brain cysts, as seen in this case, are reported sparingly in the literature.[3,4] To the best of our knowledge this is the first report that has shown the 'water lily' sign on computed tomography (CT) of the brain in a child without iatrogenic cyst rupture.

Case report

A 4-year-old boy presented with history of repeated right focal seizures for 2 years, intermittent episodes of headache and vomiting for 6 months, fever and excessive irritability for 15 days, and altered sensorium for 3 days prior to admission. Neurological examination revealed that he was comatosed, had unequal pupils, left-sided ptosis, bilateral papilledema, and had a right-sided Babinski's sign. He had repeated episodes of right focal seizures for which he was dilantinized. Computed tomography (CT) of the brain showed a large mass of multiple cystic space-occupying lesions in the left frontoparietal region with midline shift to the right side with ventricular distortion (Fig. 1). The margins of the lesions were smooth, the CT density of the cystic fluid and its absorption value were as for cerebrospinal fluid, and there was no edema surrounding this lesion. A collapsed cyst wall with a non-enhancing, faintly calcified wall was seen in the dependent part of the cyst i.e., 'water lily sign' (Fig. 2). Hemogram did not reveal eosinophilia and hydatid serology and Casoni's test were negative. Ultrasonography of the abdomen, chest X-ray, and echocardiography were normal.

The child was operated on and 30 hydatid cysts were evacuated using Dowling's technique. Histopathogical section of the cysts showed acellular laminated hyalinized membrane, along with scolex and hooklets. The postoperative period was marked with fever possibly due to an inflammatory response to cyst removal and aseptic meningitis for which he was appropriately managed. At discharge he was afebrile, had no neurodeficits but minor behavioral abnormalities. The CT, which was done 1 month into follow-up, revealed a subdural effusion without any pressure effect with reducing hydrocephalus. The child remained seizure-free with no neurodeficit at the end of 1-year follow-up.

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