Gastrointestinal Mucormycosis: A Rare but Lethal Mimicker of Necrotising Enterocolitis

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Abstract

Neonatal Gastrointestinal mucormycosis is a rare fungal infection carrying high morbidity and mortality. Clinically, it is not easily distinguishable from the more common necrotizing enterocolitis. Diagnosis is made by histopathology of the involved bowel. We report a neonate with gastrointestinal mucormycosis, bringing to notice the fatality of this infection.

Key words: Gastrointestinal mucormycosis, Necrotizing enterocolitis, neonatal bowel perforation

Introduction

Mucormycosis is an opportunistic fungal infection seen classically in patients with diabetes, lymphoma, leukemia, burns, malignancy, steroid usage, renal impairment on peritoneal dialysis and immunomodulatory usage due to organ transplant[1]. Neonatal *mucormycosis* is a rare infection which is difficult to diagnose and hence carries a high mortality[2]. Here we report a case of neonatal gastrointestinal *mucormycosis*, outlining the management and diagnostic dilemma, which the case presented.

The Case

An extramural, 33 weeks, baby girl, 1st of triplets, presented with sudden onset respiratory distress and lethargy from second day of life. After admission and stabilization in the neonatal intensive care unit, she was started on broad spectrum intravenous antibiotics and tube feeds. She developed distension of abdomen on the fifth day of life. Plain x-ray of abdomen showed non-specific bowel dilatation without evidence of pneumatosis or pneumoperitoneum.

With a provisional diagnosis of necrotizing enterocolitis, conservative management was planned with nil per oral and intravenous fluids. Subsequently, the abdominal distension was progressive and repeat x-ray of abdomen was found to have hollow viscus perforation on day 13 of life (Fig 1). With this, the child was referred to us for further management. At presentation, her activity was poor, capillary filling time was more than three seconds, heart rate was 164/min, respiratory rate was 35/min. Systemic examination including cardiovascular and respiratory system examination was normal. On palpation, abdomen was tense and tender. Laboratory parameters were Hb 12.3g/dl; total white cell count was 7150/mm^3

with neutrophils 81% and platelet count 1.56 lakhs/ mm^3. She was diagnosed as Necrotizing Enterocolitis stage IIIb and was planned for emergency surgery after resuscitation. Informed written consent for exploratory laparotomy was obtained from parents.

Intra-operatively, about 40 ml of feculent peritoneal fluid was present. Distal half of transverse colon and descending colon was found to be gangrenous. Unhealthy colon was resected and peritoneal lavage was given. The proximal part of right transverse colon was brought out as end stoma with the healthy sigmoid colon as mucus fistula. Post operatively, the child was ventilated. Her vitals were unstable in spite of inotropic support and close monitoring in the neonatal intensive care unit. Finally, she succumbed to multi-organ dysfunction on 2nd post-operative day. Intra-operative pus grew pan-resistant *Enterococcus faecalis* and *Candida*.

Histopathology of resected segments revealed extensive ulceration of bowel with serositis. Broad fungal elements were seen with angio-invasion at places. Features were consistent with gastrointestinal *mucormycosis* (Figure 2 and 3).

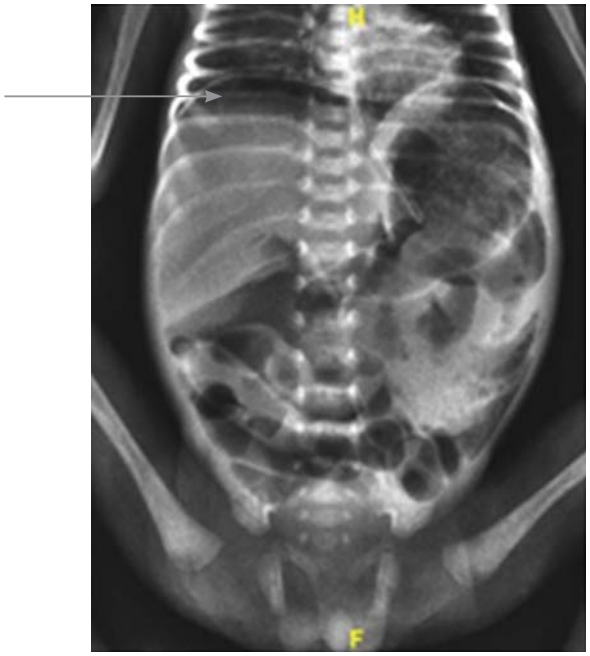

Fig 1: X-ray abdomen showing pneumoperitoneum

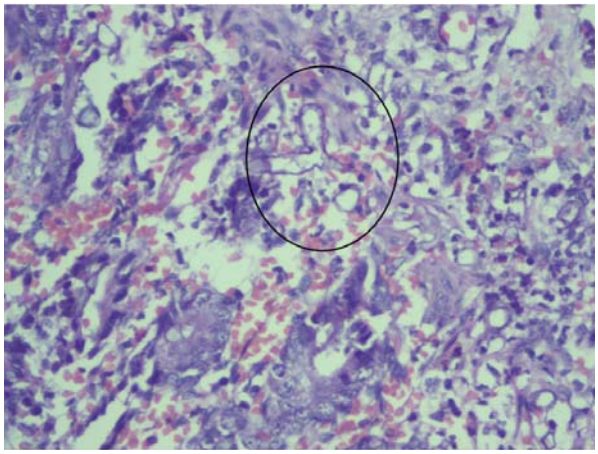

Fig 2: Section from colon showing few colonic glands and broad aseptate basophilic fungal profiles of *mucormycosis* at the muscularis mucosae H & E X 200

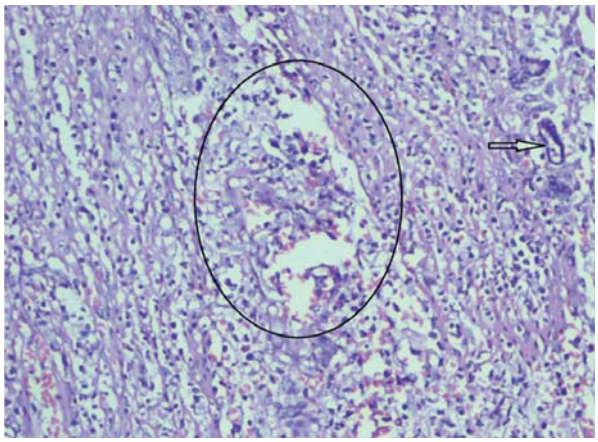

Fig 3: Muscularispropria showing broad aseptate basophilic fungal profiles of *mucormycosis*with a gaint cell reaction (arrow) H & E X200

Discussion

Zygomycosis is a rare, life-threatening fungal infection caused by *Zygomycetes* seen in immunocompromised hosts. *Mucor, Rhizomucor* and *Absidia* are the *zygomycetes* affecting humans. These are ubiquitous saprophytes, found in the soil and decomposing organic substance. The airborne spores formed by these fungi are infective which when inhaled, ingested or injected leads to cerebral, respiratory, gastrointestinal or cutaneous infections.[1,2]

Gastrointestinal *mucormycosis* is the rarest form of *zygomycosis* constituting 7% of all cases. Till date around 60 cases have been reported with only 25-30% survival rate. Stomach is the most commonly affected organ in children and adults while colon is the most commonly affected organ in neonates[3,4].

Premature and low birth weight (LBW) neonates are at high risk as the immune system is immature and skin is fragile making them highly susceptible. Approximately 83% of gastrointestinal *mucormycosis* occurs in preterm neonates[5]. The humid neonatal intensive care unit environment enhances the growth of these fungi. Broad spectrum antibiotics and steroids affect healthy gastrointestinal flora whereas naso or oro-gastric tube, endotracheal tube and indomethacin damage the gut increasing the risk of *Mucor* invasion[3,4]. Co-existing congenital heart disease with splanchnic hypoperfusion, nil oral status with avoidance of breast milk, acidosis and low gastric pH (≤ 6.5) also carry a high risk for mucormycosis[5]. Our patient had most of the risk factors.

It's difficult to differentiate gastrointestinal *mucormycosis* from necrotizing enterocolitis (NEC) in view of their similar clinical presentation. Neutropenia, absence of pneumatosis intestinalis and poor response to broad-spectrum antibiotics can give a clue towards *Mucormycosis*, but all these are non-specific features[3,4]. Fungal cultures are positive in only 33% cases.[5] Colonic involvement with sparing of rest of the small bowel, as in our case, points towards *Mucormycosis*.[4] As these fungi have an affinity towards arterial involvement, the resultant arterial thrombosis leads to extensive ischaemic necrosis of the bowel which is out of proportion to the degree of infection.[5] Widespread angio-invasion and presence of fungal hyphae in histopathology is diagnostic of *Mucormycosis*[3,4,5].

Early, aggressive and adequate surgical resection followed by intravenous Amphotericin- B is the mainstay of treatment. Antifungal agents cannot reach the infected tissue as the agent is blocked by the presence of mycotic thrombi[3,5]. Adequate resection reduces the fungal load and improves the efficacy of antifungal therapy. Adequate resection also reduces the risk of perforation and stricture formation. Primary anastomosis is undesirable while there are reports of extensive gangrene of abdominal wall post-stoma[5]. Hence clip and drop, keeping laparotomy incision as laparostomy to inspect tissues is recommended by a few authors[5]. This is followed by delayed primary anastomosis, once general condition improves. It is of note that the commonly used antifungal agent, fluconazole and even newer agents like caspofungin and voriconazole are not effective against *Mucormycosis*.[3]

The prognosis of gastrointestinal *Mucormycosis* is grim with high mortality. Poor outcome is due to lack of clinical suspicion, inadequate surgery and ineffective antifungal therapy. The survival depends on the virulence of the organism, timely intervention and immune status of the individual. Though our patient underwent adequate surgical resection, adequate antifungal therapy was not initiated. In addition, contributing factor for our patient's mortality was also the late presentation with bowel perforation.

Conclusion

A high index of suspicion of gastrointestinal *mucormycosis* is a must in preterm and low birth weight neonates with clinical features of necrotizing enterocolitis having neutropenia. Early aggressive adequate surgery followed by commencement of amphotericin-B is the mainstay of treatment. We suggest frozen section as a modality to quicken diagnosis and initiate appropriate treatment.

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