Original Article

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Unveiling the fungal frontier: Exploring pediatric surgical cases with bowel mucormycosis through a retrospective lens

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ABSTRACT

Background: Bowel mucormycosis is common among high-risk surgical neonates and has high fatality. This study was done to study the clinical profile and outcome of pediatric surgical patients operated at our center who had bowel mucormycosis on histology.

Methods: It was a retrospective observational study. The data was collected from the medical records department. The files of surgical patients with tissue diagnosis of bowel mucormycosis operated at Chacha Nehru Bal Chikitsalaya from June 2018 to May 2021 were retrieved. The data was tabulated on Microsoft Excel sheet®.

Results: A total of 11 surgical patients with bowel mucormycosis on histology were traced. The study had male preponderance. The majority were neonates and had low platelet counts with raised CRP levels. All but one expired, with severe sepsis and septic shock as major causes of death.

Conclusion: The invasive mucormycosis is more common among neonates (but older children are not immune) with male preponderance. It may affect any part of GIT and the counts and sepsis screen may be normal. It has a high fatality rate.

INTRODUCTION

Mucormycosis is a term used for various ailments caused by all the fungi of the family Mucoraceae, class Zygomycetes. They are ubiquitous and can cause invasive infections, especially in immunocompromised patients. Children are especially prone in hospital environment, due to the warm humid environment of intensive care units, preterm gestation, contamination of fluids, and various foreign bodies including feeding tubes, catheters, endotracheal tubes etc.[1,2,3,4] It can be acquired in the gastrointestinal tract via inhaling or ingesting fungus spores from the air or contaminated hospital environment. By doing this study, we wished to find out the rate of bowel mucormycosis in our surgical patients and their clinical profile along with the outcome.

METHODS

It was a retrospective observational study at the Department of Pediatric Surgery, Chacha Nehru Bal Chikitasalaya, New Delhi. The data was collected from the medical records department. The files of surgical patients with tissue diagnosis of bowel mucormycosis operated at our centre from June 2018 to May 2021 were retrieved. The clinical case files were screened for incidence, age, gender, clinical presentation, biochemical and microbiological investigations, surgery done, and outcome. The data was tabulated on Microsoft Excel sheet®. Institutional committee clearance was taken for the study.

RESULTS

A total of 11 surgical patients with bowel mucormycosis on histology were traced. The study had male preponderance, with M:F ratio of 10:1. The Majority were neonates (n=8) with 2 infants and 1 toddler. All had term gestation except 2 neonates. The mean weight among neonates was 2.3 kg and had a mean age of 14 days at presentation to our hospital. The clinical presentation included abdominal distension (n=11), fever (n=5), bilious vomiting (n=5), diarrhea and not passing stools since birth in 1 each. Two of them had pneumo-peritoneum at the presentation. The associated findings had cardiac anomaly in 2, and Down phenotype in 1 case. Out of them, 3 were outside-operated neonates with ileal atresia, Low ARM and bowel gangrene. Among laboratory investigations at presentation, 5 had anemia (3 needed pre-op blood transfusion), raised total leukocyte counts (>21000/cmm) in 2, raised C-

reactive proteins (>10 mg/L) in 8, thrombocytopenia (<1.5L/cmm) in 6 (2 needed pre-op platelet transfusion) and deranged Na and K levels in 7 cases. The blood culture was positive in 2 patients, while 2 had skin contaminants. The days to stabilize before undertaking surgery ranged from 0 to 10 days with a mode of 1 day and mean of 2 days. At surgery, bowel gangrene was present in 6 cases (54.5%), multiple perforations in 5 (45.5%). The small intestine was involved in 7, the large intestine in 6 and stomach necrosis and NEC totalis in 1 case each. Three underwent re-explorations. The stoma was created in 8 cases, while 3 had resection and anastomosis. Antifungal therapy was received in 8/11, and started empirically in 3. The total length of stay ranged from 5 to 22 days, with a mean stay of 10 days. Of a total of 11 patients, nine expired, one took leave against medical advice which we considered as potential mortality, and only one survived. Severe sepsis and septic shock were significant causes of mortality. The stoma has been reversed for survivors and doing good at 3 years of follow-up.

DISCUSSION

Family Mucoraceae include many opportunistic pathogens including Mucor, Rhizopus, Absidia and Rhizomucor. They have a unique affinity property for arterial wall invasion and causing extensive ischemic necrosis of tissues.[5] The gastro-intestinal mucormycosis (GIM) often mimics necrotizing enterocolitis but damage is often disproportionate to the degree of infection. The common features of abdominal distension, bilious vomiting and thrombocytopenia are found in both. The clinical clue to differential diagnosis lies in the nosopoietic mechanism of NEC and GIM in neonates and has been very well explained by Raveenthiran V.[6] GIM has predilection in the hospital environment and preterm gestation. In fact 83% of GIM occur in preterm neonates.[7] In our series, both pretermers had GIM. The additional risk factors of GIM are steroid therapy, overzealous broad-spectrum antibiotics, co-existing congenital heart disease with splanchnic hypoperfusion etc.[8,9] A few of our cases had these risk factors. Antemortem and preoperative diagnoses of GIM are exceptions rather than the rule.[10] GIM has predilection for colon in neonates.[11] In our series, 54.5 % had large intestine involvement but less than small intestine (in 63.%).

The fungal hyphae need to be demonstrated in tissue for correct diagnosis. There is need of special stains such as Periodic Acid Schiff (PAS) or Gomori silver methenamine as it can be easily missed on Hematoxylin-Eosin staining on routine microscopy.[8] Fungal blood cultures are not routine and do not distinguish invasive or innocuous colonization. The positivity rate of fungal cultures is about 33 %.[12] Due to delay in reporting of blood or tissue cultures and lesser yield, Patra et.al recommended frozen sections in addition to the routine paraffin preparations.[8] Direct microscopy of tissue using KOH mount and fluorescence brightener such as calcofluor white is a tool for rapid diagnosis. It has about 90% sensitivity.[13] We followed our institutional protocol for histopathological diagnosis of mucormycosis. In clinically suspected cases, KOH mounts were sent in normal saline. The histopathological examination (HPE) showing hyphae with tissue invasion is confirmatory of invasive mucormycosis. The hyphae may vary in width from 10 to 50 um with varying angles at branching or may be pseudo-septae because of foldings and no true branching appreciable. Wider, irregular, ribbon-like hyphae are more reliable diagnostic features. HPE accounts for about diagnosis in 80 % of cases.[13] The sample/tissue needs to be obtained from clinically active lesions and not necrotic areas, to increase the diagnostic yield. This is the reason for wide surgical debridement as the backbone of therapy for invasive mucormycosis. It would remove the dead tissue and simultaneously provide samples from active lesions for improving diagnostic yield. The species identification is usually not reported in the majority of cases, due to the retrospective nature of studies.[7].

Timely institution of antifungal therapy is said to be paramount in the management of bowel mucormycosis. It should be started empirically in high-index lesions. Amphotericin B and fluconazole are the most commonly used antifungal agents. However, there are case reports of recovery even without any specific antifungal therapy.[14,15] We started empirical therapy in 3 cases soon after exploration (including the survival case) and a total of 8 cases received it (after HPE confirmation). Rest expired before a diagnosis could be confirmed. It is postulated that the mycotic thrombus may prevent the effect of antifungals in affected tissue and thus wide surgical debridement remains the backbone of treatment in mucormycosis.[16]

Diversion after surgical excision of the affected bowel is favored over primary anastomosis.[4] The mortality in mucormycosis of gastrointestinal tract is high, especially in neonates (as high as 75%). It may be attributed to delayed diagnosis, or inappropriate or inadequate treatment.[5,8,17,18] A systematic review of case reports from 2015 to 2021 done by Didehdar M et al revealed only 10 neonatal cases of GIM, with a mortality rate of 70 %.[19] Our series has 8 neonates with a mortality rate of 87.5% (7 out of 8 neonates expired).

The rise of various sites of mucormycosis cases at times during the Covid era may be due to various possibilities like indiscriminate use of steroids in immunocompromised states, unhygienic sources for

O2 delivery, industrial O2 use (bypassing sterilization processes), non-humidified O2 delivery (potential erosion of mucosa linings), raised glucose and ferritin levels in covid (needed for fungus proliferation) etc

CONCLUSION

The invasive mucormycosis is more common among neonates (but older children are not immune) with male preponderance. It may affect any part of the gastro-intestinal tract and the counts and sepsis screen may be normal. Early surgical excision/debridement should be done to confirm the diagnosis by HPE, and diversion should be done against anastomosis. It has a high fatality rate.

Take home message

1. Mucormycosis is potentially lethal, with a high fatality rate.
2. Though more common in neonates, older children are not immune.
3. The counts and sepsis screen may be normal.
4. Surgical debridement is the backbone of treatment.
5. Diversion should be done as against anastomosis.

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