CASE REPORT

Neonatal Mucormycosis with Gastrointestinal and Cutaneous involvement

R Usha Devi[1], Anitha Balachandran[1], CN Kamalarathnam[1] and S Pappathi[2]

From Departments of [1]Neonatology and [2]Pathology, Institute of Child Health and Hospital for Children, Egmore, Chennai, India.

Correspondence to: Dr M Anitha, Assistant Professor, Department of Neonatology, Institute of Child Health and Hospital for Children, Egmore, Chennai 600 008, India. drmanithadm @gmail.com.

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Background: Mucormycosis of the gastrointestinal tract is a rare fungal infection of neonates. **Case characteristics:** 48-hours-old term neonate presented with intestinal obstruction and perforation. No significant risk factors were present. Histopathological examination of the resected gangrenous bowel revealed mucormycosis. Cutaneous involvement due to systemic spread led to dermal necrosis in toes. **Outcome:** Though cutaneous lesions responded promptly to antifungal therapy, gastrointestinal manifestations required multiple antifungal therapy for prolonged period apart from surgical debridement. **Message**: Precise histopathological diagnosis and early appropriate therapy can prevent dismal outcomes in neonatal mucormycosis.

Keywords: *Gangrene, Intestinal perforation, Necrotizing enterocolitis, Neonate.*

Neonatal mucormycosis is a rare, fatal and opportunistic fungal infection [1,2]. Gastrointestinal mucormycosis is associated with high mortality, and most cases of cutaneous involvement need surgical debridement in addition to systemic antifungal drugs [3]. We report a case of neonatal mucormycosis with gastrointestinal and cutaneous involvement concurrently.

Case Report

A male neonate weighing 2.7 kg delivered at 39 weeks of gestation after normal transition had passed meconium and was on direct breast feeds. After 48 hours, he developed signs of intestinal obstruction and perforation. During laparotomy, two stricturous segments were noticed in the terminal ileum with friable gangrenous bowel about 20 cm from the ileocecal junction. After excision of stricturous segments, double barrel ileostomy was done. Thrombocytopenia and abnormal coagulogram persisted in the neonate even after receiving broad spectrum antibiotics, vitamin K and fresh frozen plasma transfusions. Subsequently, cutaneous necrosis was noticed in the great, second and third toes (***Fig.* 1**). Doppler study revealed normal blood flow pattern in the involved limb. Biopsy report of the excised bowel revealed necrotizing enterocolitis with presence of aseptate right angled fungal hyphae suggestive of mucormycosis (***Web Fig.* 1**). Urine analysis, renal imaging, eye examination and echocardiography did not reveal any evidence of fungal infection. The neonate was treated with Amphotericin B after the biopsy report. His cutaneous necrosis resolved completely after one week of Amphotericin B therapy. Ileostomy closure and re-anastamosis was done during the fourth week. Postoperatively after 72 hours, the infant deteriorated due to anastamotic leak and the entire small bowel had formed a cocoon (***Web Fig.* 1**). The abscess was drained and colonic reanastamosis was attempted during the relaparotomy. Infant continued to have low grade fever and weight loss despite total parenteral nutrition followed by enteral feeds. Considering that the gastrointestinal lesion was not responding to Amphotericin B, Caspofungin was started. Subsequently the infant became afebrile, started gaining weight and the wound healed without complications. The infant was discharged on direct breast feeds after six weeks. During follow-up, the infant was thriving well and work-up for immunodeficiency states was negative.

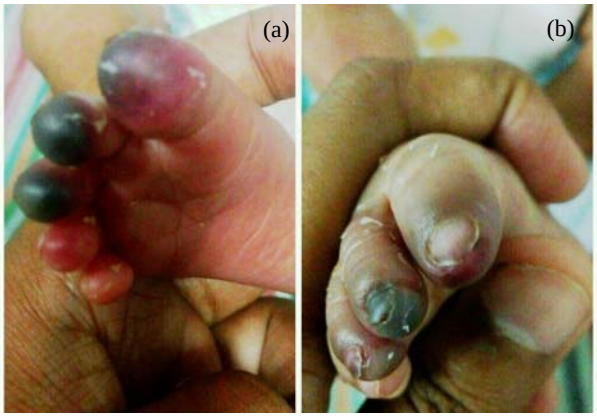

Fig. 1 *Cutaneous necrosis of toes noticed on day 2 of admission (a), and its resolution by 1 week of starting amphotericin B (b).*

DISCUSSION

Neonatal mucormycosis is rare, fulminant and often fatal [3]. Among neonates, gastrointestinal tract seems to be predominantly involved accounting for more than half (54%) of all the published cases of neonatal mucormycosis [4]. Colon is the most commonly affected organ among neonates. In our infant, terminal ileum was involved. The cutaneous lesions in mucormycosis may be caused by an infection at the primary site or secondary to dissemination from another site [3]. Dissemination from the gastrointestinal tract could have resulted in cutaneous mycosis in our neonate.

Due to their angioinvasive nature, these organisms penetrate through the endothdial cells and in that process can lead to rapid infarction of tissues. In almost all reported cases of neonates with gastrointestinal mucormycosis, the organism was identified by histopathological examination. Isolation of the organism by culture was possible in only less than half of reported [5]. Mucormycosis is considered as a variant of necrotizing enterocolitis with similar clinical presentation. However, neutropenia, absence of pneumatosis intestinalis and poor response to broad-spectrum antibiotics point towards mucormycosis [6]. The cutaneous lesion in our case responded well and healed after one week of systemic antifungal therapy unlike other cases reported in literature. Though cutaneous necrosis resolved with short course of Amphotericin B (1 week), gastrointestinal involvement in our case required prolonged therapy (5 weeks) for complete recovery. Ischemic necrosis of infected tissues prevents delivery of leukocytes and antifungal agents to the foci of infection making the infection extremely difficult to treat with medical therapy alone [7]. Thus gastrointestinal mucormycosis with severe necrosis of bowel is associated with high mortality in neonates. Prompt surgical intervention and institution of appropriate antifungal led to remarkable improvement and survival in our child preventing the dismal complications. The initial resection of necrotic bowel probably reduced the fungal load and improved the response to antifungal therapy in our case. Delayed anastamosis under the cover of appropriate antifungal therapy probably helped in better healing. Primary anastamosis is undesirable as it may lead to extensive gangrene of abdominal wall following closure.

The median (IQR) age for onset of neonatal mucormycosis is 12 (8, 18) days [8]. Dhingra, *et al*. [5] reported a very early presentation at 24 hours in a neonate with no risk factors, similar to our case . The risk factors for gastrointestinal mucormycosis are prematurity, low birth weight, poor nutritional status, diarrhea, acidosis, hyperglycemia, corticosteroid use, antibiotic administration, major surgery, oral or nasogastric tube placement, endotracheal intubation, indomethacin therapy, asphyxia and contaminated dietary supplements [9]. Placement of nasogastric tube to the check patency of esophagus in the delivery room was the only identified risk factor in our infant. This insertion could have caused local tissue damage and permitted subsequent early mycotic invasion. Improvement in clinical status after therapy and normal blood counts did not favour an immunodeficiency state during the hospital stay. The work-up for immunodeficiency done subsequently on follow-up was also normal.

We conclude that the neonates presenting with clinical features of necrotizing enterocolitis but without pneumatosis intestinalis, neutropenia and unresponsive to conventional treatment should arouse suspicion of mucormycosis. Early surgical intervention and appropriate adequate and prolonged coverage with antifungal therapy can prevent the dismal outcomes of this treatable condition.

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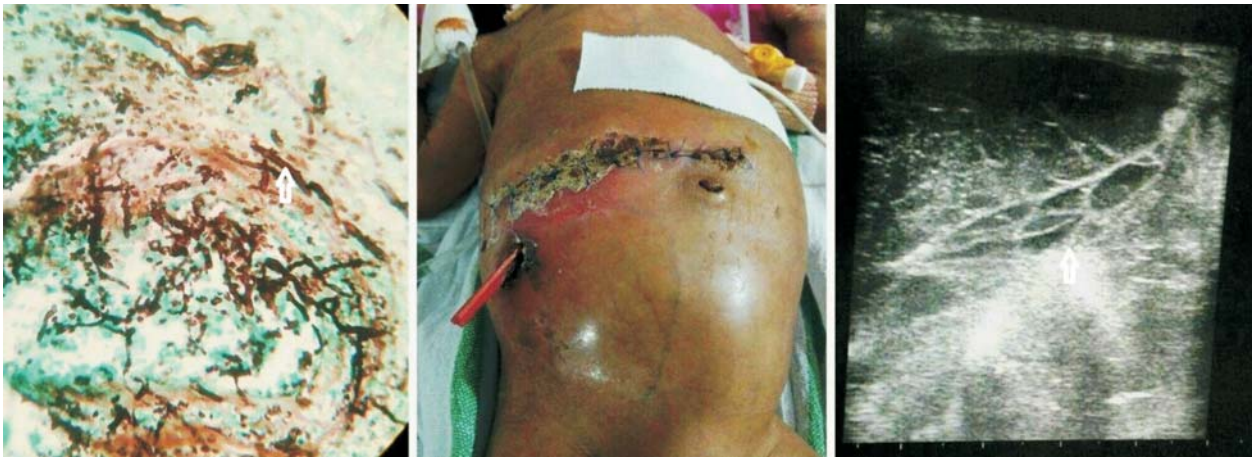

(*a*) (*b*) (*c*)

WEB FIG.1 *Gomori methenamine stain showing fungal hyphae* (*a*), *wound gaping* (*b*), *and Ultrasound showing loculated collection following anastamotic leak* (*c*).