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Mucormycosis in a Child with all- A Rare and Difficult Case

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ABSTRACT

Opportunistic infections pose a serious threat during treatment of paediatric malignancies due to prolonged immune compromised states. Mucormycosis is one of the less common infections, but has been recently emerging as the third leading cause of invasive fungal infections after aspergillosis and candida.⁽¹⁾ We report a case of intestinal mucormycosis in a child with Pre B-acute lymphoblastic leukaemia (ALL) during the second week of induction phase chemotherapy who finally succumbed to death due to the progressive nature of the disease despite appropriate and aggressive multimodal treatment approach. This case is being reported for its rarity and to increase the awareness about colonic mucormycosis in paediatric oncological practice.

Keywords: mucormycosis, child, malignancies.

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INTRODUCTION

Diagnosis and management of Acute Lymphoblastic Leukemia in children living in third world countries with limited resources is a challenge. Giving tailored chemotherapy balancing toxicity and efficacy in such a setting is also a challenge. When they develop reactions to the routinely administered least expensive protocol based drugs it becomes all the more challenging. Managing such cases is a great stress and strain for the patient and the parents, and for the doctors too. We are reporting one such case here.

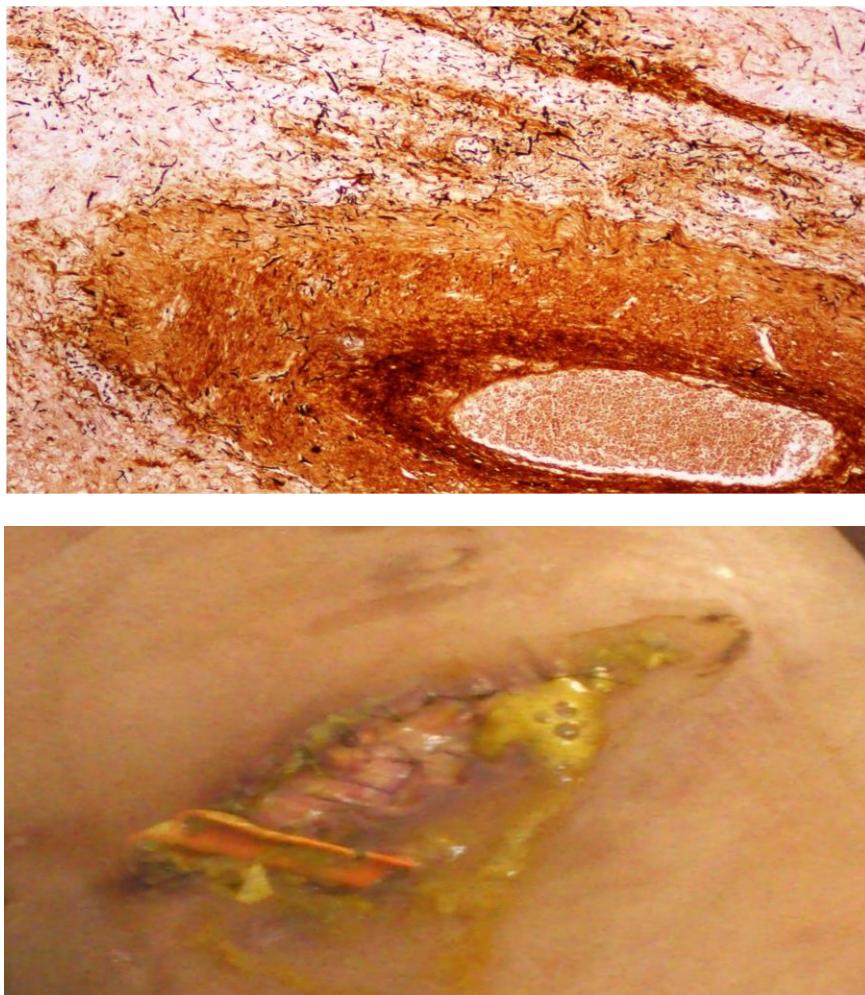
CASE REPORT

A 4 ½ year old male child presented with multiple swellings over the neck, axilla and inguinal region for 2 months associated with low grade intermittent fever for 2 months, abdominal distension for 1 month with loss of weight and loss of appetite. Clinical examination revealed generalised lymphadenopathy and hepatosplenomegaly. Complete blood counts revealed Hemoglobin 6.5 gm%, total white blood cell count (WBC) of 18300 cells per cu.mm with differential count of 7% neutrophils, 50% lymphoblasts and 43% lymphocytes, RBC 2.17/cu.mm, and platelet count 35000/cu.mm, and serum lactate dehydrogenase (LDH) 221.8 units/dl.

Bone marrow aspirate smear study was suggestive of ALL L2/L3 morphology. Immuno-phenotyping of peripheral blood confirmed it as Pre B cell-ALL. As per the ALL treatment protocol for induction of remission Vincristine, dexamethasone and intrathecal methotrexate were administered. L-asparaginase could not be administered as the child developed severe anaphylactic reaction with the test dose itself. On day 12 of treatment child developed fever with abdominal pain and distension. Repeat blood counts showed Hemoglobin 7.5gm%, WBC 700cells/cu.mm, with neutrophils 2%, lymphocytes 98% and platelet count 4000/cu mm. Plain X-ray of the abdomen showed multiple air fluid levels in the small intestine in a step ladder pattern suggestive of intestinal obstruction for which immediate exploratory laparotomy was done. Child was started on vancomycin, meropenem and fluconazole. Exploratory laparotomy revealed a mesenteric mass causing closed loop obstruction in the ileum proximal to the ileo-caecal junction. A typhilitic ulcer was noted in the terminal ileum. Histopathological examination of the mass revealed mucor species. Hence antifungal treatment was changed to liposomal amphotericin B. On post operative day 6 child again developed abdominal distension. Hence re-laparotomy was done and it showed multiple adhesions throughout the ileum and concealed perforations throughout the terminal ileum and a fungal mass in the mesentery. 6 days later the child developed a faecal fistula.

Despite two surgeries involving resection and adhesionolysis along with appropriate antifungal therapy for mucormycosis child succumbed to death due to progressive course of the infection.





DISCUSSION

The incidence rate of invasive fungal infections in children with cancer is 4.9-7.2% but have a much higher mortality rate of 21.7-59%[2] The unique feature of this infection is its angioinvasive property causing vasculitis and thrombosis leading to infarction. It carries an overall mortality rate of 58% when occurring in concurrence with paediatric malignancies.(1)It occurs in 5 different patterns of which the GI involvement is the least common type.[1,3,5]They are known to occur usually during the late stages of chemotherapy following prolonged neutropenia. Mucormycosis is steadily increasing in patients with immunocompromised states. This rising trend has been attributed to the use of aggressive chemotherapy leading to prolonged neutropenia, the use of empirical antifungal agents which do not have coverage for mucor species and the use of aggressive approaches like haematopoietic stem cell transplantation.

The commonest form of mucormycosis is rhinocerebral type with an incidence of 50%[4]. 10% are pulmonary, cutaneous and disseminated forms. Mortality rates are least with the cutaneous form and is around 10%[5].The disseminated form has maximum mortality of 95% and is more common among immunocompromised patients.[6] Gastro intestinal mucormycosis has an incidence of 2% [4]. Stomach is most commonly affected followed by colon and small intestine[1]. Interestingly, in leukaemic patients small intestine is most commonly involved. To the best of our knowledge only 12 cases of intestinal mucormycosis has been reported in children in the world so far with leukaemia of whom only 5 have survived[1]. Mucormycosis occurring during early induction phase in children is very rare. Only 7 such cases have been reported. Our literature search for the combination of small intestinal mucormycosis occurring during early induction phase of chemotherapy revealed that **only 3 other such cases have been reported so far in the world.** Ryan et al reported a case of rhino-cerebral mucormycosis during induction phase⁽⁷⁾Parkyn et al reported a case of sinonasal mucormycosis during the third week.[7] Boopathy et al reported colonic mucormycosis in a 10 year old boy with Down's syndrome with pre B ALL during induction phase who later

died of disseminated mucormycosis with a radiological evidence of central nervous system involvement[7]. Jhuma Shankar et al reported a case of cutaneous mucormycosis during induction phase. [8]

To diagnose intestinal mucormycosis a high degree of suspicion is necessary, and it poses a diagnostic challenge because various chemotherapeutic agents used in ALL may cause abdominal pain due to their side effects for eg. gastritis caused by steroid use, pancreatitis caused by L-asparaginase and abdominal neuropathy caused by vincristine and all of this may mimic intestinal mucormycosis.[7]

Successful management of such cases involves early diagnosis, appropriate antifungal therapy and surgical debridement [1] Liposomal amphotericin B (L-AMB) and Amphotericin B lipid complex (ABLC) are considered to be first line drugs for mucormycosis. The usual azoles like fluconazole, voriconazole and itraconazole do not act against Mucormycosis. Posaconazole and combination of L-AMB/ABLC with caspofungin are recommended as second line agents⁽¹⁾. Combination therapy with liposomal Amphotericin B and posaconazole have a more favourable outcome.⁽¹⁾ One of the limitations of posaconazole is its unpredictable bioavailability in gastrointestinal infection⁽³⁾. Early initiation of anti fungals within 6 days of diagnosis favours a high cure rate.

Recovery from neutropenia seems to be the most important factor influencing cure from invasive infections[1] Granulocyte-Colony Stimulating factor may be supportive in facilitating faster recovery. Early surgical debulking helps in control of disease progression. Complications include intestinal perforation in colonic type. Hard palate perforation is a complication of rhinocerebral type due to angioinvasion[4]. A case of hyperthyroidism has been reported due to involvement of thyroid gland secondary to mucormycosis in a leukaemic patient. [9]

Our patient developed intestinal mucormycosis early in the induction phase of ALL treatment thus creating a diagnostic and therapeutic problem. Achieving a balance between control of fungal infection and inducing remission of underlying disease was a difficult one.

SUMMARY

It is hoped that this article conveys the fact that intestinal mucormycosis occurring during early induction phase of leukemia in children is a very rare entity and **so far only 3 such cases have been reported in the world**. It requires a high degree of suspicion and must be considered in the differential diagnosis for intestinal obstruction in paediatric leukaemias even in the early phase of treatment.

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