Case Report

Successive Treatment of Gastrointestinal Angio-Invasive Mucormycosis in an Adult With Acute Leukemia During Hematopoietic Stem Cell Transplant: A Rare Case Report

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ABSTRACT

Mucormycosis is an opportunistic fungal infection caused by common pathogen of Class Zygomycetes including Mucor, Rhizopus and Absidea species. It is an uncommon disease but is associated with high mortality in immunocompromised host, as in uncontrolled diabetes, and patients with solid and hematologic malignancies, septicemia, and renal disease or on long term treatment with steroids and immunosuppressant.

Systemic Mucormycosis usually involves nasopharynx, lungs, gastrointestinal tract and rarely even pericardium. Gastrointestinal Mucormycosis is rare and causes considerable morbidity and mortality due to non-specific presentation often resulting in delayed diagnosis and treatment. We report a case of successive treatment of gastrointestinal angio- invasive Mucormycosis in an adult with acute leukemia during hematopoietic stem cell transplant who recovered with surgical debridement and appropriate intravenous antifungal therapy.

Key words: Mucormycosis; Gastrointestinal; Immunocompromised host; Hematopoietic stem cell transplant

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INTRODUCTION

Mucormycosis is an invasive and rapidly progressing fungal infection caused by filamentous fungi within Order Mucorales found in soil, decaying organisms. These organisms are pathogenically of low virulence but are fulminant and may cause fatal infection in immunocompromised host, as in hematological malignancies or uncontrolled diabetes [1]. The treatment of acute leukemia has resulted in immunosuppression due to prolonged neutropenia caused by potent chemotherapy, iron overload related to multiple transfusion (iron is a growth stimulant for Mucorales) [2].The successful management of Mucormycosis in neutropenia patients requires multimodal combination of serial surgical debridement and intravenous antifungal therapy.

CASE HISTORY

A 28-year-man presented with weakness and fever in August 2019. He was diagnosed as Acute Myelomonocytic Leukemia, based on blood investigations followed by bone marrow examination with immunophenotyping and cytogenetic evaluation. He underwent treatment with 7:3 Induction chemotherapy (Cytarabine 100 mg/m^2 for 7 days and Daunorubicin 60 mg/m^2 for 3 days) which was then followed by 5:2 chemotherapy (Cytarabine 100 mg/m^2 for 5 days and Daunorubicin 60 mg/m^2 for 2 days) and then completed 3 cycles of consolidation with high dose Cytarabine (3 g/m^2).

Within a period of less than 6 months of completion of treatment, he relapsed, and presented with hyper leukocytosis (blood leucocyte count of 172 × 10^9/L). He was advised salvage chemotherapy followed by consolidation with hematopoietic stem cell transplant.

Salvage chemotherapy consist of FLA- IDA chemotherapy (Fludarabine 30 mg/m^2 for 5 days, Idarubicin 10 mg/m^2 and Cytarabine 2 g/m^2 for 5 days. The cytopenic period after chemotherapy was adequately supported with antibiotics, antifungals, blood products and Granulocyte Colony Stimulating Factor (GCSF). Antifungal prophylaxis was done with oral Posaconazole suspension 200 mg three times daily. On day +20 post chemotherapy during peak cytopenic period, he developed abdominal distension with obstipation. Computed Tomography (CT) imaging of abdomen revealed dilated small bowel loops. Conservative management measures failed hence he underwent laparotomy and 7.5 cm of obstructed small bowel was resected.

Histopathology of the resected bowel revealed angio-invasive mucor mycosis (Figure 1). He was then started with intravenous liposomal amphotericin B 3 mg/kg daily. Upon completion of Amphotericin B for a course of 14 days followed by oral Posaconazole 300 mg once daily.

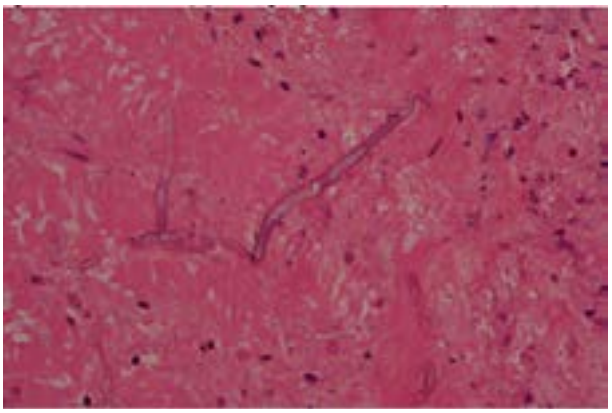

Figure 1: Gastric biopsy showing angio-invasive mucormycosis.

Post salvage bone marrow examination, done on Day+35 post FLA IDA chemotherapy, he was in complete remission (Both morphology and measurable residual disease status). Since he had a matched sibling, he was recommended allogeneic peripheral blood stem cell transplantation.

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Conditioning chemotherapy regimen was Fludarabine 30 mg/m^2 for 5 days along with Treosulfan 14 g/m^2 for 3 days. Antifungal prophylaxis was started with oral Posaconazole suspension 200 mg three times daily. Post-transplant, during the neutropenic phase, he was restarted on intravenous liposomal Amphotericin B 3 mg/kg daily from Day+5 to Day+12 for a period of 8 days with successfully prevented the recurrence of Mucormycosis. Upon count recovery liposomal Amphotericin B was stopped and oral Posaconazole suspension 200 mg three times daily was restarted.

RESULTS AND DISCUSSION

Mucormycosis is a rare but life threatening opportunistic angioinvasive infection caused by saprophytic filamentous fungus belonging to order Mucorales within class Zygomycetes. The commonly found pathogens for causing Mucormycosis in humans include Mucor, Rhizopus and Absidia species [3]. These fungi are ubiquitous in nature, are common inhabitants of decomposing plant and animal matter and are released via airborne sporangiospores [4]. The resistance to innate host defense and angioinvasive growth leading to tissue necrosis and hematogenous dissemination attributes to high morbidity and mortality for the condition [5].

Since mid-1990s, Mucormycosis has emerged as an important invasive fungal infection in immunocompromised hosts including poorly controlled diabetes mellitus, extreme malnutrition, hematopoietic stem cell transplant recipients, solid-organ transplant recipients, and patients with hematologic malignancies [2]. It is also found in hemodialysis patients with end stage renal disease and patients with iron overload as iron is a growth stimulant for Mucorales. Additional risk factors include male gender, trauma, burns, chronic steroid use, intravenous drug abuse, underlying rheumatologic disorders and antifungal azole prophylaxis in patients undergoing chemotherapy [6].

On the basis of clinical presentation most frequent form of Mucormycosis are sinus (39%) Pulmonary (24%), cutaneous (19%), cerebral (9%), gastrointestinal (7%), disseminated (3%), and kidney [7]. Gastrointestinal Mucormycosis though rare may occur due to ingestion of contaminated food or drink where the most compromised organ is the stomach (58%) followed by the colon (32%) small intestine and the esophagus [1,7].

The symptoms are typically nonspecific and can range from fever, abdominal pain, nausea, vomiting, hematemesis, melena, hematochezia or gastrointestinal perforation [3]. The diagnosis involves imaging and histopathologic confirmation based on biopsy of the suspected area by means of surgery or endoscopy [7]. Successful management of Mucormycosis includes aggressive metabolic support, antifungal therapy and surgical debridement of all necrosis-involved tissues [7]. Antifungal for primary treatment is intravenous Amphotericin B with its lipid formulation preferred due to less nephrotoxicity at a dose of 3-5 mg/kg followed by Posaconazole for step down therapy. The length of the treatment in usually till 4-6 weeks. For adult patients having Gastrointestinal Mucormycosis with underlying hematological malignancies, survival was better among those who underwent surgical management to debulk or resect all infected tissue accompanied with appropriate pharmacological management [2,5].

CONCLUSION

Mucormycosis in immunocompromised patients can be managed successfully with appropriate metabolic support, antifungal therapy and surgical debridement of all associated tissues. Often the high fatality is associated with delayed recognition due to nonspecific presentation making diagnosis difficult. Hence the susceptible patients with underlying malignancy have to be approached with careful assessment from diagnosis via imaging, histopathological confirmation and surgical intervention with early initiation of antifungal therapy.

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