Case Report

Ileo-cecal mucormycosis in an immune competent adult: Treating successfully a rare disease with high mortality

P.K. Thatoi,[1] S. Khadanga,[2] Ujjawal Khurana,[3] D. Dugar,[4] S. P. Satapathy,[5] T Karuna[6]

[1]Post Graduate Dept of Medicine, SCB Medical College, Cuttack, Odisha, India.
[2]Department of Medicine, AIIMS Bhopal, India.
[3]Department of Pathology, People's College of Medical Sciences, Madhya Pradesh, India.
[4]Department of Surgery, Hitech Medical College, Bhubaneswar, Odisha, India.
[5]Aditya Care Hospital, Bhubaneswar, Odisha, India.
[6]Department of Microbiology, AIIMS Bhopal, India.

ABSTRACT

Mucormycosis is common in immunocompromised patients. Among the various clinical spectrum of mucormycosis gastrointestinal mucormycosis has been documented in about seven percent of cases, more commonly in pediatric population. In large studies (mostly in immunocompromised) the mortality has been documented even up to 100%. Only nine cases have been described so far in immune competent adults globally including ours. We present here a case of successful treatment of ileo-cecal mucormycosis in an immunocompetent middle age man from eastern part of India. This case will enlighten the clinicians and broaden their vision of differential diagnosis while dealing with cases of non- specific pain abdomen. This case also highlights the importance of microbiological studies in addition to conventional biopsy and histopathology alone.

Keywords: Gastrointestinal mucormycosis, Ileo-cecal, Immunocompetent

INTRODUCTION

Mucormycosis is a rare and severe infection caused by members of family Mucoraceae, order Mucorales and class Zygomycetes. The class Zygomycetes includes *Rhizopus*, *Mucor*, *Absidia* and *Cunninghamella* species which are ubiquitous fungi. *Rhizopus* species is the most common organism affecting humans. *Rhizopus* alone is responsible for 60% of total mucormycosis.[1] Zygomycetes are commonly found on soil and the most common route of transmission is through respiratory tract. Other routes of transmission can be ingestion or direct inoculation of the wound by fungal spores.[2] Humans are usually resistant to infection with spores of Mucorales. Mucormycosis is a very aggressive, often fatal, disease almost exclusively affecting patients with an underlying immunosuppressive disorder, like diabetes mellitus, hematological disorders, hemato-poietic stem cell transplantation, solid organ transplantation and immunosuppression.[3]

Clinically mucormycosis has been reported as rhino-orbital-cerebral, pulmonary, cutaneous, gastro-intestinal (GI), central nervous system and miscellaneous.[4] Rhino-orbital-cerebral mucormycosis is the most common presentation. GI mucormycosis is rare and have been documented in about 7% cases in the largest series of Roden *et al*.[4] Mortality has been reported from 85-100% by various authors in gastro intestinal mucormycosis.[4,5] All parts of the GI tract may

Corresponding Author: Dr. Sagar Khadanga
E-mail: sagarkhadanga@yahoo.com

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be involved, but the stomach and the colon are the most commonly affected regions. Other sites such as duodenum, jejunum and ileum are infrequently involved. Affection of liver, pancreas and spleen has also been documented. [4]

Intestinal mucormycosis is more commonly described in malnourished pediatric population. Only a few hundred of cases have been reported in adults worldwide. GI mucormycosis in adults have been more commonly reported from immune compromised individuals. Till date, only 9 cases of intestinal mucormycosis, including the present one have been reported in immune competent adults.

CASE REPORT

A 42 year old gentleman from eastern coastal region of India, a shopkeeper by profession, non-diabetic, non-hypertensive and non alcoholic, was hospitalized with complaints of dull aching pain abdomen for one month which increased in severity gradually over the last two-three days. He had lost seven kilograms of weight during the illness. He had altered bowel habit in the form of constipation to start with, followed by loosely formed stool admixed with mucus. He developed hematochezia intermittently over the last week, seven to eight times. On examination he was of thin body built and markedly dehydrated. His temperature was 100^0F, heart rate was 110/min and regular, respiratory rate was 20/min and blood pressure was 90/60mmHg. Cardiovascular system and respiratory system examination did not reveal any abnormality. On examination of abdomen, it was distended with diffuse tenderness, more at the right iliac fossa, without any organ enlargement or free fluid. Routine hematological investigations revealed 7.2 g/dl hemoglobin, neutrophilic pleocytosis with total leukocyte count 16,000/cmm, neutrophils 80%, lymphocyte 14% without any premature cells and hemoparasites. The point of care biochemical parameters revealed random blood glucose 120 mg/dl, HbA1c - 5.8% and negative urine ketone body. Arterial blood gas analysis showed respiratory alkalosis. He was provisionally diagnosed to be having ileo-cecal malignancy with sepsis. Patient was shifted to intensive care unit (ICU) and managed conservatively with piperacillin-tazobactam and adequate intravenous (IV) fluids. Liver enzymes were

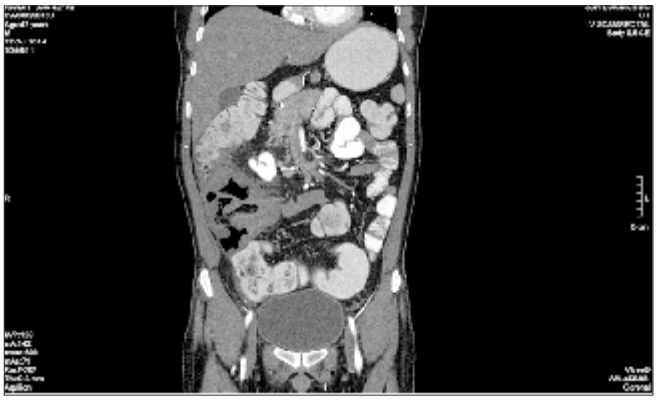

Fig.1 : Coronal section CT scan of abdomen showing non enhancing distal ileum with surrounding edema and features of sub acute intestinal obstruction.

mildly elevated; aspartate transaminase - 64 U/L, alanine transaminase-78 U/L, and alkaline phosphatase -156 U/L. Blood urea nitrogen -32 mmol/L and creatinine -1.1 μmol/L, sodium - 134 mEq/L and potassium -3.4 mEq/L. Serum amylase and lipase levels were normal. Routine urine examination was normal. Tests for HbSAg, anti-hepatitis C virus and HIV were negative. CT scan of abdomen revealed thick walled ileum, not enhancing with contrast with surrounding fat edema and features of sub acute intestinal obstruction in the form of dilated bowel loops with air fluid level (Fig.1). Blood and urine were sent for aerobic culture and the report was awaited. On third day the patient was taken up for exploratory laparotomy. Abdomen was opened with lower midline incision. Terminal ileum was found to be gangrenous around 2-3 cm from ileo-cecal junction extending about 10 cm proximally. Vascularity of rest of the bowel was normal. Ileo-cecal resection was done with two layer ileo-ascending anastomosis. The resected segment was sent for histopathology and microbiological study. Thorough peritoneal lavage was done. The wound closure was done in a single layer. Post operatively the patient developed respiratory distress and was shifted to ICU. The patient was intubated and mechanically ventilated under sedation. On 2nd post operative day (POD) the kidney function deteriorated (blood urea nitrogen -37 mmol/L and creatinine -2.1 μmol/L) and the antibiotic was switched over to meropenem one gram IV eight hourly. On the 1st POD the direct potassium hydroxide mounts revealed broad hyaline aseptate hyphae, branching at right angles. The microbiological culture report of biopsy specimen was

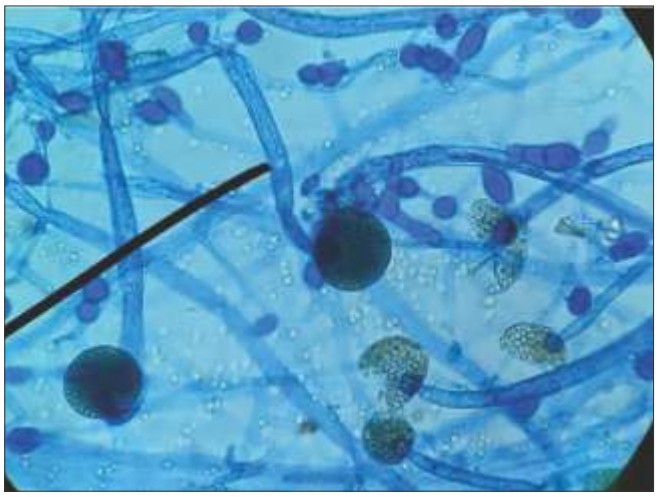

Fig. 2: Lacto phenol cotton blue mount showing broad hyaline, aseptate hyphae with sporangiospores.

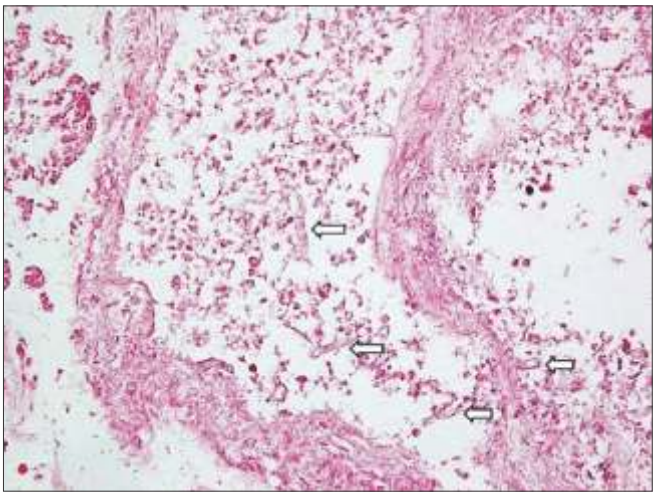

Fig. 3: The lumen and the wall of the vessel shows broad aseptate, weakly basophilic hyphae suggestive of intestinal mucormycosis (H&E).

received on 5th POD. Lacto phenol cotton blue mount of cottony white growth from Sabouraud dextrose agar showed broad aseptate hyaline hyphae with sporangiophores and sporangia filled with sporangiospores (Fig. 2). The sporangiophores appeared erect, branched, forming large terminal spherical multispored sporangia, without apophyses and with well-developed subtending columellae. Phenotypically the genus was confirmed to be Mucor due to absence of rhizoids. With the above mentioned fungal characteristics a diagnosis of ileo-cecal mucormycosis was made and conventional amphotericin B (AmB) emulsion was started in a dose of 1.5 mg/ kg/day diluted in 500 ml of 5% dextrose and transfused over a period of 3-4 hours. On 10th POD the histopathology report was obtained. Gross examination revealed thinned out distal ileum with many small yellowish grey masses over the mucosal aspect of distal ileum. Microscopic picture revealed serosa which was edematous and infiltrated by polymorphonuclear (PMN) cells. Muscularis mucosa had scattered infiltration of mononuclear cells, PMN cells and plasma cells. The mucosa was edematous and necrotic at many areas. The mucosal stroma and glandular architecture was disrupted with granular debris. Scattered in the necrotic debris, there were numerous PMN lymphocytes and fungal elements. The submucosa was also seen with fungal elements at many places. At several places the blood vessel walls showed areas of necrosis, infiltration by PMN cells and fungal elements in between. In most of the instances the fungal extension did not extend beyond submucosa (Fig. 3). AmB was continued for 16 days. The patient gradually improved over the days. He was out of mechanical ventilation on 15th POD and was shifted out of ICU on 18th POD. He was discharged from the hospital on 28th POD. He was last seen 6 months after the operation and was doing fine.

DISCUSSION

GI mucormycosis is a rare and fatal disease. Only a few hundred cases of GI mucormycosis has been documented worldwide predominantly in pediatric population. The diagnosis of GI mucormycosis is often delayed as most of the symptoms are non specific and insidious in onset. Abdominal pain, mass, distension, nausea and vomiting are the usual accompaniment with fever, loss of weight and bleeding per rectum documented occasionally. A definite diagnosis of mucormycosis requires direct identification of characteristic hyphae and/or recovery of the organism in the culture from specimen obtained from the site of infection. Histopathology of a biopsy material from deep tissue if available is characterized by angio-invasion of broad aseptate hyphae with acute angle branched filaments. Genera from the order Mucorales (*Rhizopus, Rhizomucor, Mucor, Absidia, Apophysomyces, Cunninghamella,* and *Saksenaea*) are the etiologic agents for rapidly progressive, angio-invasive infections with

rhinocerebral, orbital, pulmonary, disseminated, cutaneous, or (rarely) GI involvement (mucormycosis). In contrast, entomophthoromycosis from *Basidiobolus ranarum* and *Conidiobolus coronatus* involves indolent and slowly progressive subcutaneous infections in immunocompetent persons who reside in tropical and subtropical climate. Within the past three decades, sporadic cases of GI involvement with *B. ranarum* have been reported worldwide. As both Mucorales and Entomophthorales are rapid growers with similar clinical presentation and cultural characteristics it is important to confirm the genus by phenotypic or genotypic methods. Being in a resource poor setting we could not prove the genus genotypically. Considering the phenotypic characteristics and histopathology the isolate was confirmed to belong to genus *Mucor.*

Though this is a disease of immune compromised hosts, a few cases have been documented in immune competent patients in the last decade. After an intensive search eight number of cases in immune competent adults have been reported from all over the world and of them two cases are from India.[6-8] To the best of our knowledge, the present case is the ninth one in the global literature. A few more have been documented in alcoholic dependent and cannabis addict patients.[9,10] Of these nine cases, five cases have survived including the present one. Though the mortality has been claimed to be 85-100% in most of the immunocompromised patient series, the mortality seems to be less in immune competent patients.

Optimal therapy requires prompt institution of appropriate antifungal therapy, reversal of underlying predisposing condition and surgical debridement of devitalized tissues. Medical management alone is not effective because of poor drug delivery to the site of infection due to extensive vascular thrombosis.[11] The medical management varies and no guideline exists for GI mucormycosis. Liposomal amphotericin B (LAmB) has been used by most of the clinicians probably because of its better central nervous system penetration and greater efficacy in murine models. But for financial constraints we used conventional AmB. Role of combination therapy with one of the echinocandins is controversial. The duration of treatment is also a matter of debate as there is no published comparative data. Most clinicians believe antifungal therapy should be continued till the resolution of symptoms and signs.

CONCLUSION

With the epidemic of diabetes in India, more and more cases of mucormycosis are seen. Though it is a disease of immunocompromised patients, immunocompetency does not rule out its existence. In the absence of a rapid test, high index of suspiciousness and microbiological examination, in addition to histopathology is absolutely necessary in timely diagnosis and successful treatment of the disease.

CONFLICT OF INTEREST: Nil

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