

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

Biomedical Journal

journal homepage: [www.elsevier.com/locate/bj](http://www.elsevier.com/locate/bj)

## Brief Communication

# Esophageal mucormycosis in an immunocompetent child: A rare presentation



Jenna Blah Bhattacharya<sup>a,\*</sup>, Seema Kaushal<sup>a</sup>, Satish Kumar Aggarwal<sup>b</sup>

<sup>a</sup> Department of Pathology, Maulana Azad Medical College, New Delhi, India

<sup>b</sup> Department of Paediatric Surgery, Maulana Azad Medical College, New Delhi, India

## ARTICLE INFO

## Article history:

Received 2 January 2015

Accepted 4 November 2015

Available online 20 June 2016

## Keywords:

Esophageal mucormycosis

Fungal infection

Gastrointestinal fungal infection

Mucormycosis

## ABSTRACT

Invasive mucormycosis of the esophagus (rare) and gastrointestinal tract is emerging as an important cause of concern in children. It usually affects immunosuppressed individuals. However, infection of immunocompetent children is also seen. The diagnosis of mucormycosis is difficult both at the clinical and the laboratory level, hence leading to unsatisfactory treatment and high mortality rates. The infection is usually life threatening so an early diagnosis and prompt administration of antifungal therapy is imperative.

Mucormycosis refers to fungal infection seen in immunosuppressed individuals caused by a ubiquitous saprophytic mold growing in soil and organic matter which produce hyphae after inhalation or ingestion. They belong to the order mucorales. While *Mucor* is mostly seen in immunosuppressed; some fungi of the genus mucorales (*Apophysomyces elegans* and *Saksenaia vasiformis*) are seen infecting immunocompetent ones. The prevalence and incidence of opportunistic mycoses have increased owing to several factors, including longer survival of immunosuppressed individuals and advances in laboratory-based diagnosis of these diseases. Mucormycosis is the third most frequent mold infection in immunocompromised patients after *candida* and *aspergillus* [1] and may disseminate to rhinocerebral, pulmonary, cutaneous and gastrointestinal (GI) areas. Unfortunately, diagnosis of

mucormycosis in both the clinical and the laboratory levels remains difficult, leading to unsatisfactory treatment and high mortality rates. Early diagnosis, surgical debridement, systemic antifungal therapy, and control of underlying conditions are the key elements in the successful management of this infection. Most common predisposing factors are malnutrition, prematurity, HIV, diabetes mellitus, leukaemia and induced immunosuppression.

## Case report

A 1 year old boy was presented to the Pediatric Out-Patient Department with complaints of dysphagia (more to solids than liquids) and a recent history of difficulty in breathing for

\* Corresponding author. Department of Pathology, Maulana Azad Medical College, B-126, Second floor, Sector-50, Noida, Uttar Pradesh 210301, India. Tel.: +91 09899840023

E-mail address: [jennamamc@gmail.com](mailto:jennamamc@gmail.com) (J.B. Bhattacharya).

Peer review under responsibility of Chang Gung University.

<http://dx.doi.org/10.1016/j.bj.2015.11.001>

2319-4170/© 2016 Chang Gung University. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

2 months. The child, a normal vaginal term delivery with a birth weight of 3.5 kg, was born in a remote hospital. The child had not undergone invasive procedures of any kind or been hospitalized before for any disease. The mother gave history of a single episode of diarrhea when the child was a month old and was given some local medication. Since then, he had been experiencing the same symptoms on and off for which he took treatment at various centers. The child was weaned at 6 months of age; however, proper weaning practices could not be performed due to poor socio-economic status. At the age of 11 months the child developed inspiratory stridor due to tracheal compression with regurgitation of feeds.

On examination the patient was sick-looking, conscious, and afebrile with drooling of saliva. His weight was 9 kg (25th percentile) and height was 75 cm (85th percentile). The pulse rate was 120 beats/min and the respiratory rate was 40 breaths/min with chest retraction. The oxygen saturation was 86% under 100% oxygen inhalation. Laboratory investigations showed hemoglobin 16 g/dl, total leukocyte count 12,000/mm<sup>3</sup> with polymorphs 60%, lymphocytes 25%, eosinophils 8%, and monocytes 7%. Platelet count was 2.8 lakhs/mm<sup>3</sup> and erythrocyte sedimentation rate was 20 mm/h. The peripheral smear showed normal red blood cell picture (mean corpuscular volume (MCV) – 98 fl, mean corpuscular hemoglobin (MCH) – 27 pg and mean corpuscular hemoglobin concentration (MCHC) – 32 g/dl. Tests for HIV and hepatitis C virus serology were non-reactive. Upper GI contrast study showed mild persistent luminal narrowing in cervical and thoracic esophagus while the distal esophagus was normal. [Fig. 1] Contrast enhanced computed tomography (CT) Neck and Thorax showed asymmetrical diffuse wall thickening/mass in the submucosal location involving cervical and thoracic vertebrae (C4-T12) leading to esophageal narrowing. Maximum esophageal wall thickness was 1.7 cm. There was anterior displacement and compression of trachea. Based on radiological findings diffuse leiomyomatosis or inflammatory lesion or lymphoma was impressed.

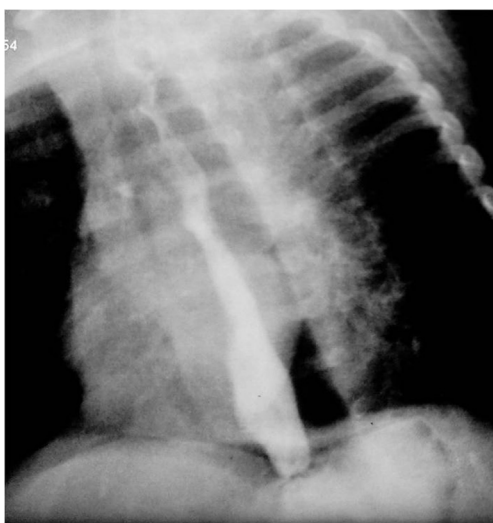


Fig. 1 – Upper gastrointestinal contrast study showing persistent luminal narrowing in cervical and thoracic esophagus.

At the time of admission, the child was treated with antibiotics, and then injectable steroids added due to worsening respiratory distress. Upper GI endoscopy was planned after CT scan but due to the patient's deteriorating condition and difficulty in performing endoscopic procedure in severely strictured esophagus an urgent resection of cervical and thoracic esophagus with tracheostomy and feeding gastrostomy was performed.

On histopathological examination the specimen was received as a part of esophagus 9 cm long with a luminal diameter of 2 cm. The entire wall was thickened up to 1 cm without a well-defined growth.

Multiple sections were taken and the esophageal wall demonstrated granulomatous inflammation composed of histiocytes, lymphocytes and many eosinophils along with many giant cells some of which contained broad, aseptate and branching hyphae [Fig. 2 high power view]. These hyphae also presented in the subepithelium surrounded by granulomas. These fungal hyphae were positive for periodic-acid Schiff and silver stains. Stain for acid fast bacillus was negative. The above pictures suggested mucormycosis.

## Discussion

Mucormycosis is a rare infection seen mostly in immunocompromised individuals causing a granulomatous inflammation attributed to the prolonged course of infection. Known for its vascular invasion, it is one of the leading causes for invasive infection causing high morbidity and mortality. In a large review of 929 patients with zygomycosis [2], diabetes was the most common underlying risk factor (36%), followed by malignancy (17%), solid organ transplantation (7%), desferrioxamine therapy (6%), and bone marrow transplantation (5%). Most of these conditions are associated with impairment immune function. Hematological malignancy associated mucormycosis has been seen as an emerging problem. In a study done by Pagano et al., 59 cases of the leukemic patients, the majority of whom were neutropenic, developed mucormycosis with a mortality of 80% [1]. Premature neonates having an immature immune system are known to be associated with

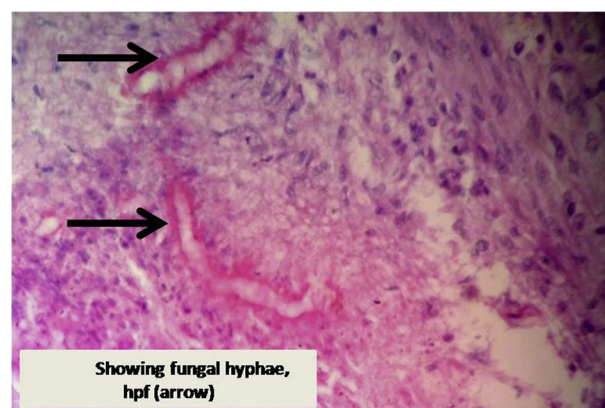


Fig. 2 – Microscopy showing a granulomatous inflammation composed of chiefly many eosinophils along with broad, aseptate, branching hyphae (high power view).

necrotizing enterocolitis (NEC) and get treated for a long period with intravenous antibiotics and steroids which alter the already compromised gut flora leading to easy susceptibility to mucorales [3]. In a study done by Agarwal et al. they noticed that three neonates who had no radiological findings of NEC were diagnosed to have GI mucormycosis [4]. Risk of contracting mucormycosis increases with instrumentation of any kind (oro-gastric instrumentation, endotracheal intubation) leading to mucosal injury. Our patient had none of the above risk factors; however, improper weaning was speculated to play some role.

Clinical and radiological pictures of mucormycosis often mimic aspergillosis, but the antifungal treatments are different. Culture is the definitive mode to identify the species since many sub species other than *Mucor* (such as pathogenic *Rhizopus*, *Absidia*, *Mortierella* and *Cunninghamella* and *Basidiobolus*) have also been seen to infect children. In tissue sections, all of these species appear the same, so culture is imperative. When affected, stomach, colon, small intestine is seen in decreasing frequency, however, esophageal involvement although seen, is rare. In a review study done by Mooney and Wagner, 34 children presented between ages 2 days and 15 years and the most common affected being <1 year of age. Of 34, 26 involved the GI tract, of which 18 were gastric, 14 were large bowel, 10 as small bowel and 5 in esophagus [5].

Because GI mucormycosis is almost uniformly fatal in both adults and children, diagnosis is usually made at autopsy and is frequently missed during life. A clinical diagnosis of the condition has never been made [6]. An early diagnosis in such cases either by an endoscopy-guided biopsy or surgery plays an important role to administer therapy early. Aggressive treatment in the form of IV amphotericin followed by surgery is the mainstay of the treatment. Adequate resection to reduce the fungal load and further complications is vital; however, surgical resection depends on the general condition, platelet count and neutrophil count. Survival of the patient depends on the immunity of the patient and virulence of the infecting organism. The commonly used antifungals such as fluconazole are not effective in removing mucorales, and hence the symptoms persist or even worsen. First-line antifungal agents suggested by European Conference on Infections in Leukemia are liposomal amphotericin B (L-AMB) and amphotericin-B lipid complex (ABLC). AMB is challenged by its potentially severe side effects. L-AMB is more effective, as it attains good concentration in the brain as well as in the reticuloendothelial system. Posaconazole and combinations of L-AMB/ABLC with caspofungin have been suggested as second-line treatment. Even though posaconazole exhibits good efficacy and has been used successfully in few cases, it is not reliable as a first-line therapy, as it has unpredictable bioavailability in patients with GI involvement [7]. The prognosis of mucormycosis is grave with neonatal mortality being 40% and in patients with hematological malignancies, it is 65–90% [7] owing commonly

to misdiagnosis and wrong treatment with extensive surgery in an already compromised child. Until date, only seven children of GI mucormycosis have been survived [3]. Our patient received antifungal therapy (AMB and posaconazole) and responded during the hospital stay; however, esophageal reconstruction could not be performed due to against advice discharge and loss of follow-up.

---

## Conclusion

Esophageal mucormycosis is a rare presentation in children. It is difficult to diagnose as the clinical presentation may point towards a more common different diagnosis. Hence, a high suspicion in dysphagic patient with non-corrosive, non-congenital, and non-peptic esophageal narrowing is crucial. A thorough investigation with early surgery/biopsy for histopathological diagnosis aided by microbiological or molecular methods and aggressive antifungal treatment is mandatory in both immunocompromised and immunocompetent individuals to reduce morbidity and mortality.

---

## Financial support and sponsorship

Nil.

---

## Conflicts of interest

There are no conflicts of interest.

---

## REFERENCES

- [1] Pagano L, Offidani M, Fianchi L, Nosari A, Candoni A, Piccardi M, et al. Mucormycosis in hematologic patients. *Haematologica* 2004;89:207–14.
- [2] Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. A review of 929 reported cases. *Clin Infect Dis* 2005;41:634–53.
- [3] Sarin YK. Intestinal mucormycosis in a neonate: a case report and review. *J Indian Assoc Pediatr Surg* 2010;15:98–100.
- [4] Agarwal K, Sharma M, Singh S, Jain M. Antemortem diagnosis of GI mucormycosis in neonates: report of two cases and review of literature. *Indian J Pathol Microbiol* 2006;49:430–2.
- [5] Mooney JE, Wanger A. Mucormycosis of the gastrointestinal tract in children: report of a case and review of the literature. *Pediatr Infect Dis J* 1993;12:872–6.
- [6] Thomson SR, Bade PG, Taams M, Chrystal V. Gastrointestinal mucormycosis. *Br J Surg* 1991;78:952–4.
- [7] Radhakrishnan N, Yadav SP, Oberoi J, Kulshreshtha R, Bhalla S, Sachdeva A. Intestinal mucormycosis: a rare entity in pediatric oncology. *Pediatr Hematol Oncol* 2013;30:178–83.