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# NECROTIZING FASCIITIS IN PEDIATRIC PATIENT DUE TO APOPHYSOMYCES VARIABILIS-REPORT OF TWO CASES.

Clinical Microbiology

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## ABSTRACT

Mucormycosis due to *Apophysomyces* species belonging to order Mucorales is increasingly being reported. We report two cases of mucormycosis following intramuscular injections in infants, leading to severe necrotizing fasciitis. Despite rigorous surgical debridement and antifungal treatment, the patients succumbed to mucormycosis. Delay in diagnosis leads to fatal outcome. The risk factors for *Apophysomyces species infections* in healthcare facilities could be due to poor infection control practices, accidental inoculation, lack of awareness and delay in diagnosis. *A. variabilis* infection should be considered in the differential diagnosis of rapidly progressing necrotizing fasciitis. Early diagnosis and treatment will help in reducing disease progression and improve the outcome.

## KEYWORDS

Necrotising fasciitis, Mucorales, Apophysomyces species, Healthcare associated.

**INTRODUCTION:**

Mucormycosis is caused by fungi belonging to the order Mucorales. Morphologically, they appear as broad, aseptate or sparsely septate ribbon-like hyphae. Prominent infarcts, angioinvasion and perineural invasion characterize mucormycosis. Humans acquire infection mainly by inhalation of sporangiospores, occasionally by ingesting contaminated food or traumatic inoculation. Risk factors are diabetes mellitus, haematological malignancy, solid organ transplants, corticosteroid therapy, and trauma.[1]

Necrotizing fasciitis is a rapidly progressive inflammation of fascia with secondary necrosis of the skin and subcutaneous tissues. It may occur following trauma, post-operative incision, intramuscular injections or burn.[1] Etiological agents for necrotizing fasciitis are bacteria and fungus, the latter belonging to the order Mucorales are being increasingly reported.[1] Worldwide, 80% of Mucormycosis is caused by *Rhizopus, Lichtheimia and Mucor* and rarely by Cunninghamella*, Syncephalastrum, Apophysomyces, and Saksenaea* species.[2] *Rhizopus spp. is the most common cause of Mucormycosis in India. Apophysomyces spp.* accounts for 60% of the reported cases after *Rhizopus* spp. worldwide.[2,3,4] *A. variabilis* predominantly affects immunocompetent individuals.[5] Most common causes for mucormycosis in children are due to road accidents, burns etc. [1] Rarely, it may be due to accidental inoculation during intramuscular injections in paediatric population. Here, we report two cases of necrotizing fasciitis among infants due *to A. variabilis* following intramuscular injections.

**Case Report:**

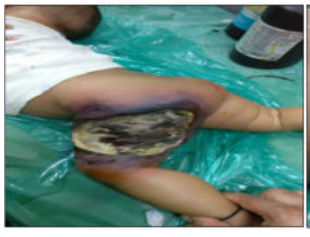
A 4-month-old male child hailing from Uttar Pradesh came with chief complaints of fever with chills, swelling and rash at the site of intramuscular injection in the left side of gluteal region, which extended as a necrotic lesion about 10x10 cm in size on to the posterior aspect of the left buttock, which was extending to the thigh. No other associated complaints or history of trauma or application of soil was present. WBC counts were 18,900/cumm with neutrophilic predominance. The blood culture was sterile. A clinical diagnosis of necrotizing fasciitis was made. The wound was debrided, and samples were sent for histopathological and microbiological investigations. Bacterial and mycobacterial cultures of the tissue were negative. KOH mount showed broad, aseptate hyphae. On Sabouraud's dextrose agar(SDA) cottony white fluffy colonies at 25°C and 37°C were observed(Fig.1) Lactophenol cotton blue (LPCB) mount of the growth showed broad aseptate hyphae suggestive of Mucorales. Slide culture did not show any sporulation even after seven days. Sporulation was induced by using water agar at 25°C. Growth was observed on the eighth day of incubation with branching broad aseptate hyphae with distinct foot cells on LPCB (Fig.2).

Sporangiospores arising singly as unbranched, of variable length, and slightly tapering towards the apex were observed. Sporangia were pyriform in shape and multispored, with hemispherical columella and distinctive funnel-shaped apophyses suggestive of *Apophysomyces* species(Fig.2). Histopathology of the tissue suggested a fungal inflammatory pathology suggestive of mucormycosis.

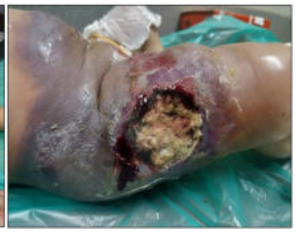
Extensive tissue debridement of the wound along with Vancomycin, Imipenem, Amphotericin B, and Voriconazole were given. Despite all efforts, the patient succumbed within a month of infection.

We encountered a similar case in a 3-month-old female child from another city in Uttar Pradesh with a similar history of necrotic lesions on the right anterior aspect of the thigh following some intramuscular injection. A swelling which then extended to form a necrotic lesion and necrotizing fasciitis.

This patient also had fungal growth of Apophysomyces species from tissue biopsy. The patient immediately underwent extensive debridement and was started on Amphotericin B and Voriconazole. Ultimately this patient also succumbed. These isolates were genomically identified as *Apophysomyces variabilis*. (PGIMER, Chandigarh)



**Case no 1:** 4-month-old male child showing necrotising fasciitis on thigh region



**Case no 2:** 3-month-old female child showing necrotising fasciitis on thigh region

**Fig. 1:** Cottony white fluffy growth on Sabouraud's dextrose agar.

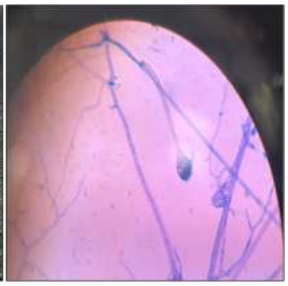


**Fig. 2:** Lactophenol cotton blue (LPCB) mount of Apophysomyces sp.

**DISCUSSION:**

Necrotizing fasciitis is a rare and often rapidly fatal soft tissue infection.[1] It can involve any body region; however, the most common sites are the abdominal wall, perineum, and extremities. Clinical manifestations involve fever, cellulitis, oedema, crepitus, bullae, necrosis of fascia and subcutaneous tissue with or without myonecrosis and sepsis.[2,5] Most common cause being *Streptococcus pyogenes,* necrotizing fasciitis may also occur due to polymicrobial synergism of both aerobic and anaerobic Gram-positive and Gram-negative organisms. Fungal necrotizing fasciitis is a rare entity.[5]

Class Zygomycetes includes three orders, i.e. *Mucorales, Mortierellales* and *Entomophthorales.* Human infections are mainly caused by order *Mucorales* and rarely by order *Entomophthorales.* Order *Mortierellales* cause disease among animals. Apophysomyces species complex includes *A. elegans, A. variabilis, A. piriformis*, and *A. trapeziformis* based on genetic studies.[3,5,8,9] *Apophysomyces infections* are rare. Infections with Zygomycetes are usually seen in immunocompromised individuals, but few cases have also been reported in immunocompetent individuals. Contaminated soil with such organisms acts as a reservoir. *A.variabilis* is abundant in Indian soil with low nitrogen content and can be a source of infection.[2,3,4] The thermotolerant nature of this fungus permits its proliferation in deep tissues, even in febrile patients. The primary mode of acquisition could be accidental inoculation of this organism at the trauma site, surgical wound, burn or intramuscular injections.[5] Cutaneous Zygomycosis occurs as a localized, deep or disseminated disease of which almost 50% of patients with cutaneous zygomycosis have their disease confined to the cutaneous and subcutaneous tissue. In comparison, in 24% of cases, the disease may extend to bone, tendon, muscle, and deeper tissues.[1–5]

Histologically, class Zygomycetes exhibit broad, thin-walled hyaline, often aseptate or pauciseptate hyphae with frequent angioinvasion. Identification becomes problematic since *Apophysomyces spp* and *Saksenaea spp* do not sporulate by routine methods. Methods like the water agar technique and internal transcribed spacer sequencing (ITS) helps in identifying these non-sporulating Mucorales.[1–5]

Healthcare-associated mucormycosis (HCM) are defined as cases associated with any healthcare procedure (medical devices and surgery, including solid organ transplant or diagnostic or therapeutic invasive procedures) with an identified or suspected source of infection. In our case series, two infants were reported with necrotizing fasciitis after an intramuscular injection.[5,15,16,17] Majority of the patients with HCM presenting with cutaneous involvement either have direct inoculation from contaminated wound dressings, bandages, medical devices, instruments, tongue depressors, catheters, or following procedures like intramuscular injections, which is the matter of concern in developing countries. Poor infection control practices are the major risk factors.[5,15,16,17] Breakdown in the mucocutaneous barrier because of injections may have caused inoculation of fungal agents, iatrogenically at the site, which leads to zygomycosis infection.

Most cases have successful outcomes when managed by extensive surgical debridement and liposomal amphotericin B instead of amphotericin B deoxycholate therapy. Even with surgical intervention alone, a cure has been reported in small lesions.[8–14] Other treatment options are posaconazole, itraconazole, and hyperbaric oxygen therapy, which depends on the extent of spread in a case.[8–14] In these cases both the infants succumbed even after rigorous debridement and Amphotericin B treatment. However, the mortality associated with cutaneous mucormycosis due to *Apophysomyces* species remains high, even if this condition is diagnosed and treated (28.5%– 80%). One of the reasons could be a lack of awareness among doctors, who primarily manage necrotizing fasciitis cases, delay in sending the specimens for microscopy, culture and histopathology including a work up of fungal infections. Since necrotising fasciitis is most commonly associated with bacteria followed by fungus there may be delay in starting antifungals which may further worsen the prognosis. *Among all Mucorales, the Apophysomyces* species complex is considered more virulent due to the high mortality rate and affects healthy individuals.

In these cases, *Apophysomyces species infection* probably could have occurred due to poor infection control practices or due to accidental inoculation of this fungus. Otherwise in a healthy patient who is not responding to antibacterial therapy and has a progressive necrotizing infection, *Mucorales*, especially *Apophysomyces* aetiology should be considered. Early and prompt diagnosis would help reduce the cost of treatment and improve patient outcomes.

**Conflicts of Interests:** None

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**Ethics Approval:** Received from the Institutional ethics committee.

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