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CASE REPORT

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Necrotizing fasciitis in neonate by *Lichtheimia ramosa* : A case study

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Abstract

Zygomycetes have been known to cause life-threatening infections in humans which are often difficult to treat. We present a rare case of cutaneous mucormycosis in a premature neonate admitted with neonatal sepsis and necrotizing fasciitis. He was diagnosed with *Lichtheimia ramosa* infection and managed surgically along with Amphotericin B. Low birth weight, prematurity, respiratory distress, administration of corticosteroid and broad spectrum antibiotics were identified as the potential risk factors in this case which had led to the fungal infection. Early diagnosis and prompt management is critical in prevention of morbidity and mortality associated with the disease.

INTRODUCTION

Cutaneous mucormycosis is the third most common clinical form of the disease, after pulmonary and rhino-cerebral. Very few cases of invasive cutaneous mucormycosis occurring in neonates have been reported in the literature of corticosteroids for respiratory distress.

Mucormycosis is a fungal infection that has been increasingly associated with serious disease in immunocompromised hosts. The causative agent belongs to the class Zygomycetes and order Mucorales [1]. The most common infections by this class of fungus are rhino-cerebral and pulmonary mucormycosis followed by cutaneous mucormycosis. Till now among neonates, very few cases have been recorded worldwide of the invasive cutaneous form of mucormycosis [2]. These neonates diagnosed with mucormycosis usually have predisposing factors like weakened immune status, prematurity, very low birth weight and history of trauma to skin [3].

There are various genera under Zygomycetes which are responsible for the invasive infections. These are *Absidia*, *Mucor*, *Rhizomucor*, *Rhizopus*, *Apophysomyces*, *Saksenaea*, *Cunninghamella*, *Cokeromyces* and *Syncephalastrum*. Most of the infections are caused by the genus *Rhizopus*. The other common genera are *Mucor* and *Lichtheimia*. These three genera account for 70–80% of all mucormycosis cases [4]. There are four species in genus *Lichtheimia*. These include: *Lichtheimia corymbifera (syn. Absidia corymbifera, Mycocladus corymbifera), Lichtheimia ramosa (syn. Absidia ramosa, Mycocladus ramosus), Lichtheimia blakesleeana (syn. Absidia blakesleeana, Mycocladus blakesleeanus*) and *Lichtheimia hyalospora (syn. Absidia hyalospora, Mycocladus hyalosporus)* [5]. The human infections among genus *Lichtheimia* are caused by *L. corymbifera* and *L. ramosa*. These species though being ubiquitous saprophytes of soil, plants and decomposed food, cause rapid and severe infections (mucormycosis) in patients who are immunocompromised and their pathogenicity evolves as host immunity gets weakened [6, 7].

In the present case report, we have described a rare presentation of primary cutaneous mucormycosis due to *L. ramosa* in premature low birth weight neonate with necrotizing fasciitis.

Cutaneous mucormycosis is the third most common clinical form of the disease, after pulmonary and rhino-cerebral. Very few cases of invasive cutaneous mucormycosis occurring in neonates have been reported in the use of corticosteroids for respiratory distress.

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Abbreviations: KOH, potassium hydroxide; LPCB, lactophenol cotton blue.

Fig. 1. Child with necrotizing fasciitis on right side of neck.

CASE

We present a case of an 11 day old male premature neonate who was admitted to the neonatal ICU on 2 February 2021 after he was brought in to hospital with a history of recurrent episodes of apnoea and bluish discolouration of peripheries. The parents also gave history of poor feeding. He was delivered in a hospital to a non-diabetic mother at 30 weeks of gestation with birth weight of 1.8 kg. On examination, the baby was lethargic and his general condition was poor. His pupils were bilaterally reacting to light. His heart rate was 74 min^{-1}. He was gasping on respiration as there were no spontaneous respiratory efforts. His peripheral pulses were palpable but severe hypothermia was seen. The fontanelles were not bulged. FiO2 was 60% and grunt was present. After unsuccessful improvement on bag and mask ventilation, the child was intubated. The abdomen was soft. It was observed that there was a large ecchymotic patch on the right side of neck extending from left maxillary area to the clavicle.

The investigations showed that the child had severe thrombocytopenia, hyperkalemia. Platelets were transfused to relieve thrombocytopenia. His blood tests including coagulation profile, liver function tests, TORCH profile, viral markers showed normal results and cardiovascular examination was remarkable. After surgical consultation it was observed that there was development of necrosis over the ecchymotic patch which further led to necrotizing fasciitis on the third day of admission (Fig. 1). He was started on empirical antibiotics after being given provisional diagnosis of neonatal sepsis. The antibiotics included Augmentin and Meropenem. The platelets were also transfused along with wound care of the necrotic patch. Severe hypothermia was corrected. SpO2 improved from 68–92%. Heart rate improved to 118 min^{-1}. The child was extubated.

On fourth day of admission, the debridement of necrotizing fasciitis was planned and done. The dressings were done regularly. His blood was sent for culture and *Enterococcus* species were isolated from it.

On eighth day of admission, the child developed pneumonia (Fig. 2) with decrease in SpO2 and increased respiratory distress for which he was intubated. He was febrile on examination. The antibiotics were changed to Vancomycin, Colistin and Amphotericin B. His routine investigation showed hypocalcemia. The subsequent debridement were done and the tissue was sent for fungal culture.

The KOH mount of tissue specimen was made which had shown many aseptate, broad, ribbon shaped hyphae with right angle branching suggestive of mucormycosis. The specimen was inoculated onto two sets of Sabouraud dextrose agar supplemented with chloramphenicol and gentamicin and without antibiotics. One set of tubes was incubated at 25 °C and other one at 37 °C. After 24 h of incubation, macroscopically a white floccose growth (effuse) was obtained in both the tubes which turned grey on further incubation within 2–3 days (Fig. 3). The lactophenol cotton blue mounts were made and on microscopic examination broad, aseptate branching hyphae were seen. The sporangia were pyriform shaped, hyaline and had prominent conical columella

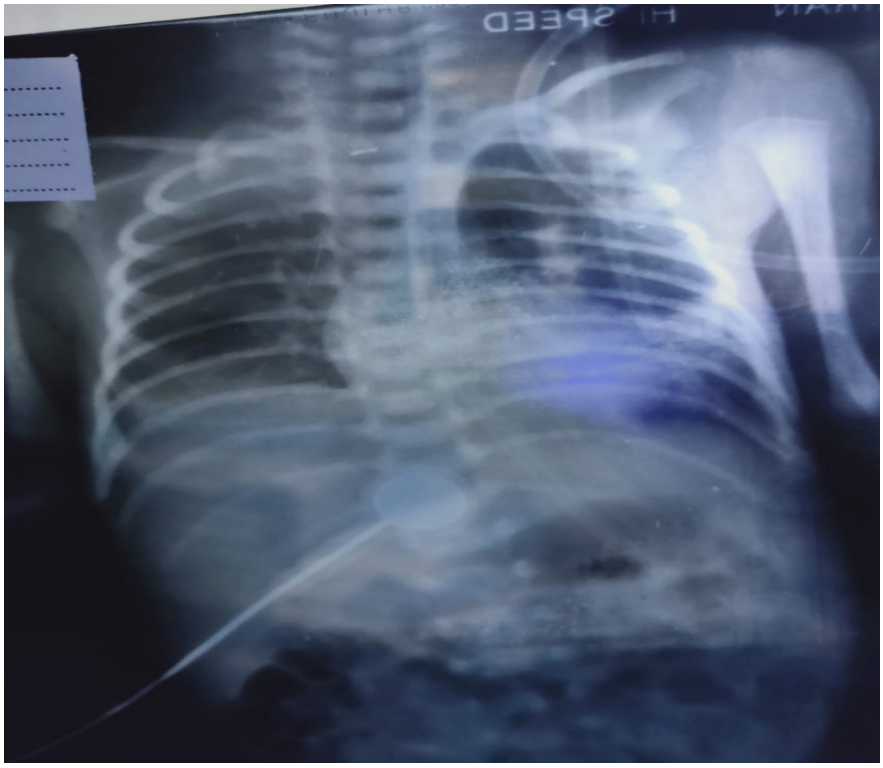

Fig. 2. Chest X-ray showing pneumonia.

(Fig. 4). Ellipsoid, smooth, lightly coloured sporangiospores were seen. The flask shaped apophyses were observed on columella. There was absence of rhizoids.

Thus the child was diagnosed with cutaneous mucormycosis caused by *Lichtheimia ramosa* based on the morphological characteristics and angioinvasion.

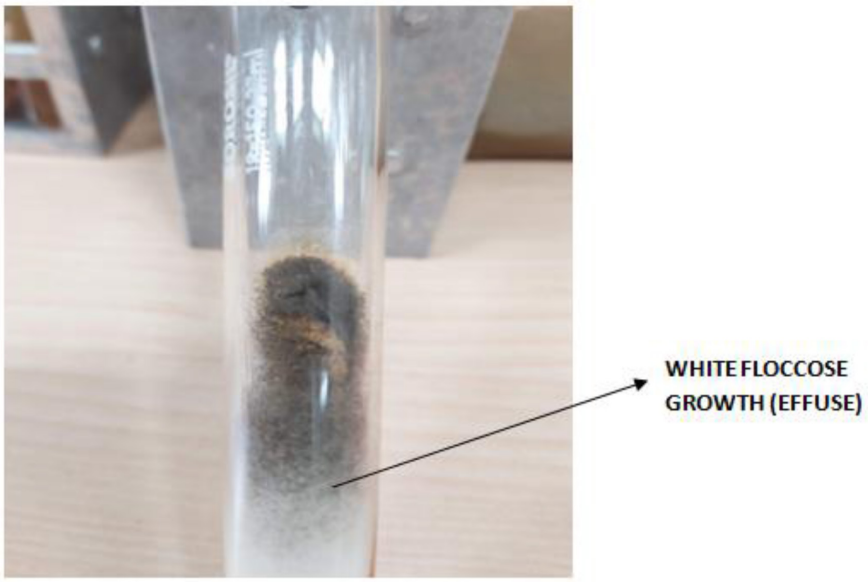

Fig. 3. Growth on Sabouraud dextrose agar.

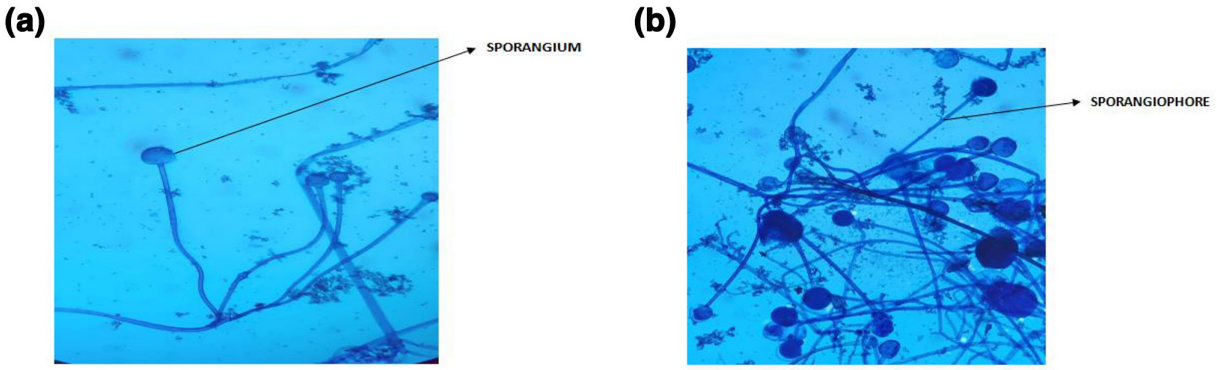

Fig. 4. (a and b): LPCB mount showing *Lichtheimia ramos*a.

The child showed improvement in clinical symptoms. The sloughing of necrotic tissue is decreased significantly followed by formation of healthy granulation tissue (Fig. 5). The child was discharged subsequently after 20 days of admission and was called for regular follow up visits. Therefore the early diagnosis and management had played vital role in saving the life of child.

DISCUSSION

Mucormycosis is an acute, fatal fungal infection which causes necrosis of tissues and high mortality rate [8, 9]. The risk factors in infants are slightly different from adults [8] which include prematurity, low birth weight, and use of broad spectrum antimicrobials for presumed sepsis and corticosteroids for respiratory distress. Damage to the skin from adhesive tapes and invasive catheters are other predisposing factors [10].

The *Lichtheimia* species (*L. corymbifera* and *L. ramosa*) are very similar in morphology but there are some differences that have been observed among them. Macroscopic appearance of compact growth is usually characterstic of *L. corymbifera* but effuse growth is observed in *L. ramosa*. Moreover, microscopic examination from the growth shows smooth, hyaline and ellipsoidal sporangiospores which are smooth, lightly coloured and more ellipsoidal in cases of *L. ramosa* [11]. Similar morphological characterstics of *L. ramosa* have been observed in this case. There had been reports in which globally distributed infections caused by *L. corymbifera* were later found to be *L. ramosa* infections [4]. Woo *et al*. described about the collection and re-characterization

Fig. 5. (a and b): Post debridement formation of healthy granulation tissue.

Table 1. Some similar/related cases of cutaneous mucormycosis

S.NO	AGE	Case study	Risk factors	Species	Treatment	Authors
1.	Pediatric age group	Invasive cutaneous mucormycosis in a preterm neonate presenting as a vesicobullous lesion	1.Predisposing factors include prematurity, low birth weight, and use of corticosteroids for respiratory distress. 2.Skin damage due to usage of adhesive tapes and invasive catheters are additional risk factors	---	Surgical debridement and Amphotericin B	Mishra S *et al.* [10]
2.	Adult age group	Primary cutaneous mucormycosis in a patient with burn wounds due to *Lichtheimia ramosa*	Altered immune function and lost skin protection	*L. ramosa*	Surgical debridement and Amphotericin B	Kaur, R. *et al.* [4]
3.	Adult age group	Necrotising fasciitis due to *Absidia corymbifera* in wounds dressed with non-sterile bandages	Risk factors for cutaneous zygomycosis include diabetes, immunosuppression (neutropenia or steroid-induced neutrophil dysfunction) or traumatic inoculation of sporangiophores through soil or contaminated dressings	*L. corymbifera*	The patient was managed with repeated debridements and intravenous amphotericin	Shakoor S *et al.* [16]
4.	Adult age group	Wound infection caused by *Lichtheimia ramosa* due to a car accident	Trauma had been the most important predisposing factor (in patients with normal immune response)	*L. ramosa*	Surgical debridement and antimycotic solution	Bibashi E *et al.* [17]

of 13 strains of *L. corymbifera* which after identification on the basis of phenotypic and genotypic characterstics had been clearly identified as *L. ramosa* [12].

Since this child was born prematurely with low birth weight of 1.8 kg, he was prone to the fungal infection. The presence of other risk factors like respiratory distress at birth and administration of corticosteroid therapy was also noticed in this case which further led to immunosuppression. He was also given broad spectrum antibiotics due to the presumption of neonatal sepsis. The usage of cutaneous dressings with adhesive tape could also serve as the entry route of pathogen in the skin due to the disruption of integrity of cutaneous tissue. There are some similar/related cases of cutaneous mucormycosis with risk factors/mechanism of inoculation and treatment have been shown in Table 1.

Mouronte-Roibás C *et al.* stated that there was a case of *Lichtheimia ramosa* in which there was development of necrotizing bilateral pneumonia with disseminated mycotic thrombosis [13]. The dissemination of fungal spores in the lungs can be the cause of developing pneumonia. It is also possible that the child in the study had also developed secondary pneumonia with mucormycosis.

The differential diagnosis of ecchymosis in neonates include parasitic infections (toxoplasmosis), viral infections (rubella, cytomegalovirus, herpes virus, varicella virus) and fungal infections caused by *Aspergillus*, *Fusarium*, Zygomycetes (*Rhizopus*, *Mucor* and *Absidia*). Bacterial and mycobacterial cultures are also needed to be included [14]. In this study, the results of cultures and serological tests were negative for bacterial pathogens and viruses while fungal culture came positive for *Lichtheimia ramosa*.

In neonates, the aetiology for ecchymoses at the site of trauma to skin (e.g. adhesive tape, cutaneous trauma) includes the inoculation of infectious pathogens into cutaneous tissue. Moreover the skin barrier is immature in premature infants as they have very thin skin as compared to full term neonates [14]. Therefore it is possible that this infection might have been acquired through nosocomial means of fungal inoculation. There have been various studies done in intensive care and orthopaedic units, which showed the results of nosocomial cross transmission of *Lichtheimia* species (e.g. Absidia/Mycocladus) leading to cutaneous mucormycosis [4].

The usual treatment of mucormycosisis the surgical removal of devitalized tissue by debridement and empirical antifungal therapy [4]. In adult patients, Isavuconazole has been recommended as therapeutic antifungal drug with contraindication to Amphotericin –B. The treatment guidelines have not approved the usage of Isavuconazole in paediatric patients [15]. In

Lichtheimia species infection, the drug of choice is Amphotericin B (geometric mean of 0.07 mg litre^{-1} at 24 h), and among azoles-posaconazole (geometric mean of 0.34 mg litre^{-1} at 24 h) [14].

In conclusion, the present case highlights the risk of mucormycosis in premature low birth weight neonates and emphasizes that a high index of suspicion, early diagnosis and management is essential as a life saving measure against this fulminant infection.

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Conflicts of interest
The authors declare that there are no conflicts of interest.

Consent to publish
The consent to publish has been obtained.

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