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REVIEW: CUTANEOUS MUCORMYCOSIS

Mayur D. Dorle*, Ashwini Bhivasane and Dr. Gajanan S. Sanap

Late Bhagirathi Yashwantrao Pathrikar College of D Pharmacy (D Pharm & B Pharm), Pathri,Aurangabad – 431111, Maharashtra, India.

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***Corresponding Author**
Mayur D. Dorle
Late Bhagirathi Yashwantrao Pathrikar College of D Pharmacy (D Pharm & B Pharm), Pathri, Aurangabad – 431111, Maharashtra, India.

ABSTRACT

Diabetes Mallitus, burn patients, iron overload, extra use of corticosteroids etc. The signs and symptoms vary widely, and it is important to make the diagnosis as early as possible in order to achieve a better outcome. early diagnosis and multidisciplinary treatment should be offered to increase Survival A significant percentage of patients are at risk for cutaneous mucormycosis due to serious burns. The treatment is the chronic fungal infection caused by order of mucorals called as mucomycets. Is also called as black fungas. Mucormycosis is classified into five Types, a) Rhinocerebral (sinus and brain) mucormycosis, b**)** Pulmonary (lung) mucormycosis c) Gastrointestinal Mucormycosis mucormycosis, d), e) Disseminated mucormycosis. Cutaneous mucormycosis is the third most common clinical type of mucormycosis. Cutaneous mucormycosis Spreading of infection to skin, and various part of the skin such as face, upper extremities, lower extremities etc. Risk factors for the development of mucormycosis include, ofchoice is amphotericin B, but new azoles, such as posaconazole and isavuconazole, must be considered.

KEYWORD: Cutaneous Mucormycosis, Black Fungus, Amphotericin B, Diabetes Mallitus.

INTRODUCTION

Saksenaea An emerging fungal infection known as mucormycosis, or "black fungus," is brought on by fungi belonging to the order Mucorales. The most prevalent underlying disease in the world is diabetes mellitus.[1,2] Skin and subcutaneous tissue are considered to be localised mucormycosis, muscle, tendons, and bone are considered to be deep extensions, and other noncontiguous organs are considered to be disseminated.[13] The use of illicit intravenous drugs, iron overload, haematological and other malignancies, transplantation,

neutropenia, corticosteroids, trauma, burns, and neonatal prematurity are additional risk factors.[3] The incidence of mucormycosis has increased due to the rising prevalence of diabetes, particularly in low- and middle-income countries.[4] After rhinocerebral and pulmonary mucormycosis, cutaneous mucormycosis is the third most prevalent clinical type of this infection.[3] India was hit by a massive (disastrous) second wave in April and May 2021, with the highest number of cases occurring on May 7, 2021, at about 4 lakh.[1] During the second wave of COVID-19, India emerged as one of the centres for the coronavirus disease-associated mucormycosis (CAM), which had only been occasionally reported during the first wave.[5] Its epidemiology is changing as previously uncommon species, like erythrospora[46] and Apophysomyces mexicanus.[47] Infection from trauma occurs in a large percentage of patients with cutaneous mucormycosis who have no underlying disease. A better outcome can be attained by making the diagnosis as soon as possible because the signs and symptoms can vary greatly. Because of this, we conducted a systematic review of the epidemiology, clinical manifestation, diagnosis, and treatment of cutaneous mucormycosis by looking at case reports and case series published between 2006 and 2022.

METHODOLOGY

A] Warning signs

Warning signs include pain and redness around the eyes or nose, with fever, headache, coughing, shortness of breath, bloody vomits, and altered mental status. According to the advisory, infection with mucormycetes should be suspected when there is.

(1) Sinusitis - nasal blockade or congestion, nasal discharge (blackish/bloody);
(2) Local pain on the cheekbone, one-sided facial pain, numbness or swelling;
(3) Blackish discoloration over bridge of nose/ palate;
(4) Loosening of teeth, jaw involvement;
(5) Blurred or double vision with pain;
(6) Thrombosis, necrosis, skin lesion; Chest pain, pleural effusion, worsening ofrespiratory symptoms.

B] Risk factors

Mucormycosis is rarely reported in healthy people; it is predisposed by comorbidities like diabetes mellitus, organ transplantation, cancer (especially haematological cancer), immunosuppressive therapy, such as corticosteroids, prolonged neutropenia, iron overload, chronic antibiotic use, severe burns, intravenous drug abuse, and malnutrition, which causes

immunocompromise.[6]

This infection ranks third among opportunistic fungal infections in immunosuppressed hosts and accounts for 5–15% of all invasive fungal infections, especially in its rhinocerebral, pulmonary, and gastro-intestinal forms. In addition, the loss of the skin barrier due to an insectbite[45], car accident, burn injury, invasive catheter, or intramuscular injection is a risk factorfor developing cutaneous mucormycosis, the rarest type of mucormycosis.

C] Diabetes Mallitus

With 77 million adult patients, India is regarded as the diabetes capital of the world.[7] Due to its impact on the immune system of the host, poorly controlled DM significantly raises the mortality and hospitalisation rates.[8] According to reports, mucormycosis is more common in patients with severe COVID-19 infection, and both are made more likely by DM. Increased COVID-19 infection severity and higher mortality were both linked to the presence of DM.[9,10] Reduced cell-mediated immune responses (phagocytic activity), which are both brought on by corticosteroids and a hyperglycemic state, make ketoacidosis an ideal environment for the germination of fungal spores.[11,12] This worsens the situation and leads to invasive mucormycosis.

D] Clinicle Presentation

Cutaneous mucormycosis is classified as localised when it only affects the skin and subcutaneous tissue, as having deep extension when the infection spreads to underlying muscle, tendons, or bone, and as disseminated when it impacts additional, non-contiguous organs. The most frequent locations for cutaneous mucormycosis were the upper and lower extremities, but it could affect any part of the skin (figure 1).

Different clinical signs and symptoms of cutaneous mucormycosis exist. In the current review,70 (10%) cases lacked a detailed description of the signs and symptoms, so 623 cases had theiranalysis completed. A black eschar is the typical clinical symptom of mucormycosis.

However, not every case presents the same way, and the initial presentation differs quite frequently. The cutaneous lesions were described as "necrosis," "necrotic," or "necrotizing" in 346 (55%) of the cases. Eschar was mentioned 59 times (9%) and "blackish discoloration" of the skin, the wound, or the ulcer was mentioned 10 times. In 20 cases, the infection was labelled as "cellulitis," and in 7, "abscess." Prior to the emergence of the full picture of

necrosis, in many cases, the initial presentation was a small nodule[20], erythematous nodules[21], ulcerative, nodular wounds[22], vesicles grouped in a circular fashion[23], an ulcer with a white mold-like growth after a spider bite[24], a cottony growth[25], a small blister[26], tender, purpuric macules with peripheral erythema[27], a 1-cm hard papule[28], a vesicular eruption[29], an indurated mass[30], or an indurated, woody, and hard swelling.[31] In two cases, the infection presented as a "purple bull's-eye lesion"[32] or "bull's-eye infarct".[33] In another three, the lesions were described as ecthyma gangrenosum.[34]

"erythema nodosum-like rash"[35], or "pyoderma gangrenosum-like".[36] Pain severity varied. The lesions were completely painless in some cases, and painful or very painful in others. The patients could also have signs and symptoms of sepsis, depending on the underlying disease and the extent of the infection.In the majority of cases, the infection progressed rapidly, sometimes leading to gangrene and hematogenous dissemination. However, there are several case reports, mainly from China, presenting cases of mucormycosis due to Mucor irregularis, where the infection progressed very slowly.[37] In addition to M. irregularis, cases due to Saksenaea vasiformis have been reported to progress over months.[38,39] There have also been reports of slowly progressing lesions due to Mucor hiemalis[40,41], Syncephalastrum sp.[42], and Rhizopus microspores.[43,44]

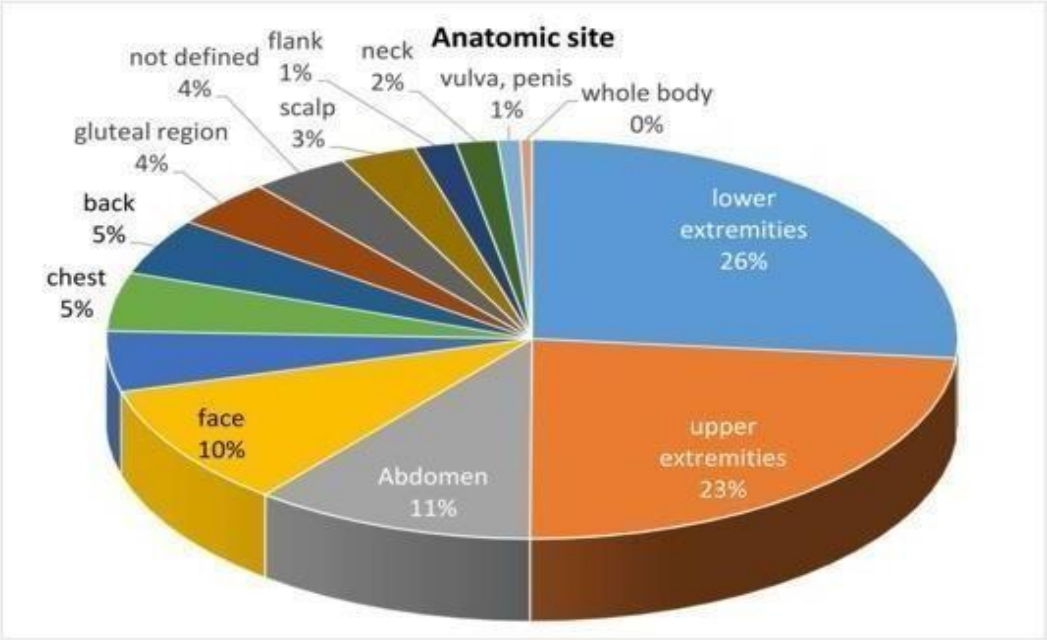


Figure 1: Anatomic site of infections.

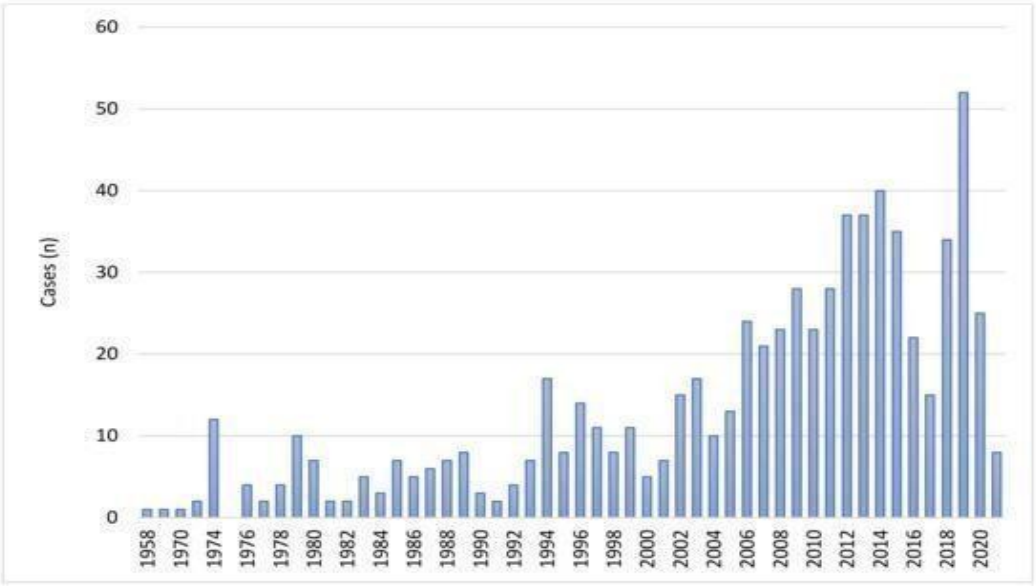
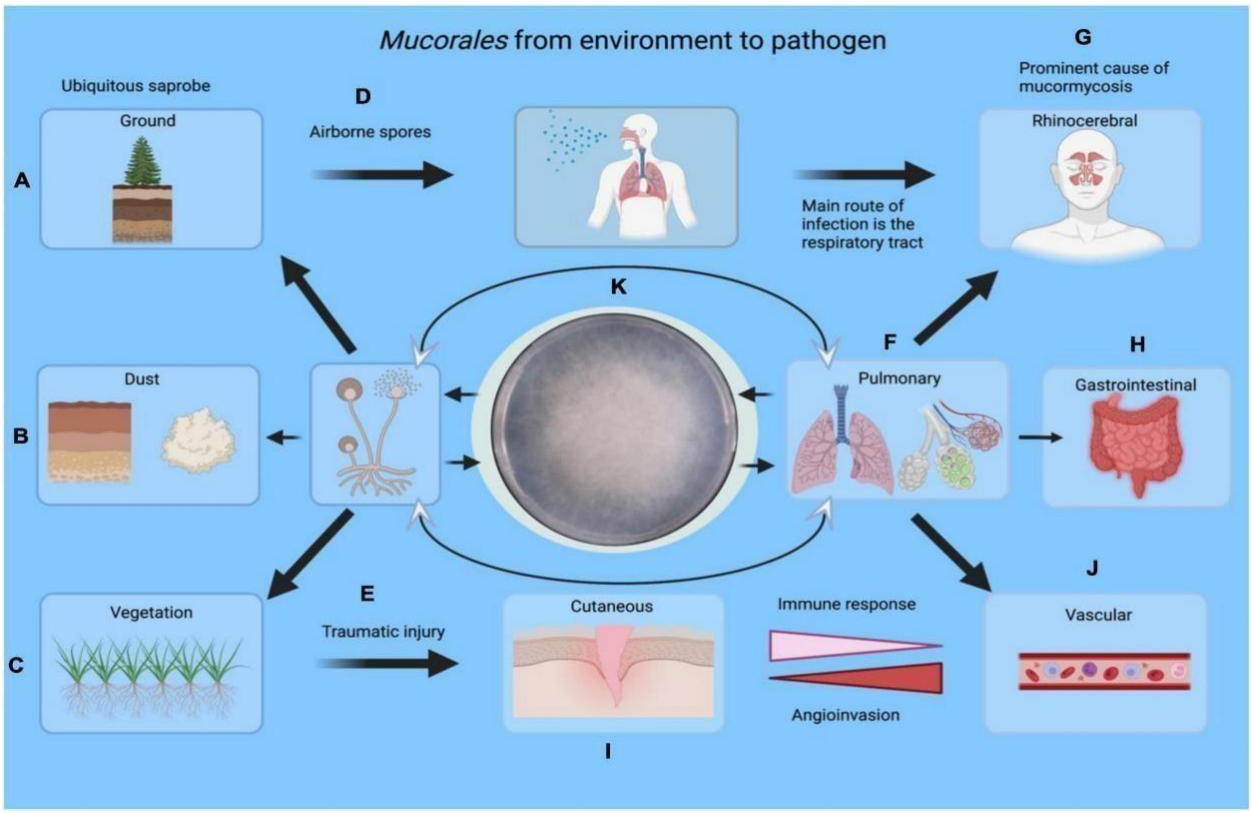


Figure 2: Cases of cutaneous mucormycosis per year from 1958 to 30 June 2020.

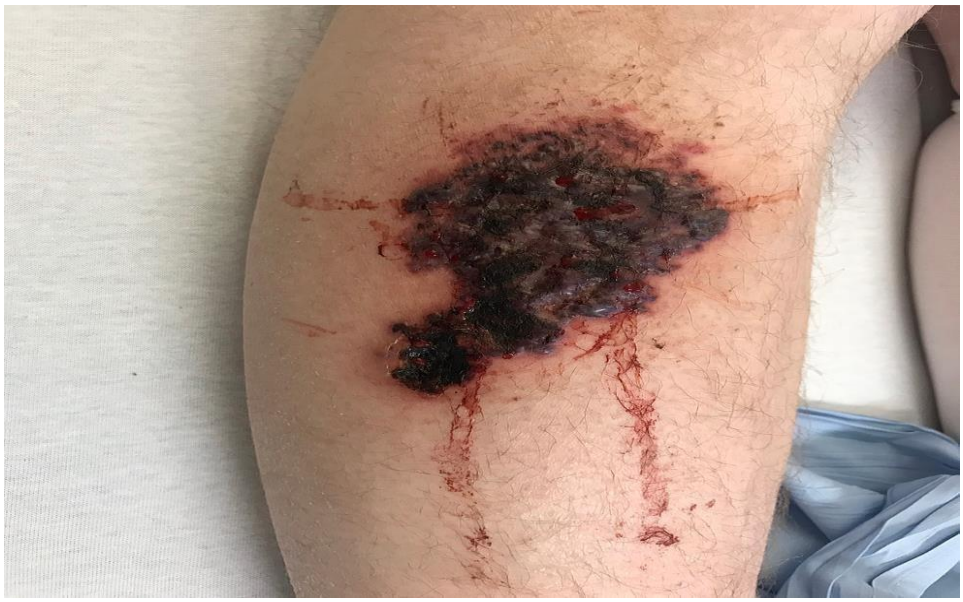


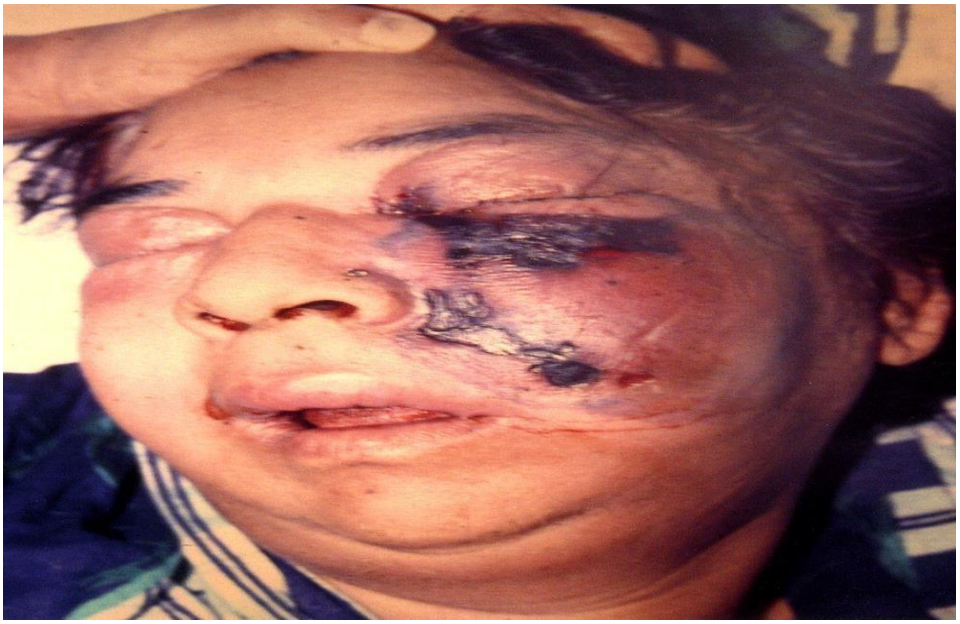
Mucorales From environment to pathogen

An overview of infection routes of Mucorales from the environment toward the development as pathogens. Mucorales can be found in soil **(A)**, dust **(B)**, and vegetation **(C)**. The spores can infect humans through the respiratory tract *via* airborne spores **(D)**, injuries **(E)**, pulmonary **(F)** rhinocerebral **(G)** or the gastrointestinal tract **(H)**. Cutaneous cases, on the

other hand, are associated with vegetal trauma or motor vehicle accidents **(I)**. Any of these local infections can cause vascular spread leading to thrombosis **(J)**. Specimens **(F–I)** can be obtained for laboratory diagnosis by culture **(K)**

Following images are infected patients in mucormycosis.





E] Diagnosis

Cutaneous mucormycosis has non-specific clinical signs. Establishing prompt antifungal treatment required early fungus identification. Direct KOH microscopic examination can be used to detect the presence of non-septated, hyaline hyphae that are 5 mm wide and 20 mm to 50 mm long, with irregular branching at right angles, mostly at the lesionsEdge. Smears made from the wounds may also be helpful.[55]

A biopsy and molecular diagnostic teste should be taken from the center of the lesion, includin Subcutaneous fat. Histalogy is more useful in primary cutaneous mucormycosis. Common findings are edema, thrombosis, infarction, necrosis and an inflammatory reaction that includes polymorphonuclear cells, plasma cells, and eosinophils. Real-time PCR provides identification of mucorales in tissue samples and clinical isolates with high specificity. Nevertheless, more sensitivity has been reported in formalin-fixed paraffin-embendded tissues.[56]

F] Treatment

The management of cutaneous mucormycosis is not supported by any clinical guidelines. Grossly necrotic tissue must always be surgically removed. Antifungal medications should also be given. Both superficial and gangrenous forms of the disease are indicated for amphotericin B chemotherapy at a daily dosage of 1-1.5 mg kg-1.[14] Amphotericin B's liposomal formulation is less nephrotoxic than its conventional formulation, but higher doses are still necessary.[15] Mohs micrographic surgery's position regarding the preservation of healthy tissue is still unclear.[16,17] In this procedures,the PAS or GMS staining require several hours. The so-called rapid GMS stain, with increased temperature of methenamine silver solution and increased percentage of chromic solution is preferred because it requires only about 30 min.[18]

Interferon and hyperbaric oxygen may be helpful as supplemental therapies.[18] Overall, a key component of treatment is enhancing general health in immunocompromised patients, for instance by managing diabetes mellitus, stopping corticosteroids[19], and attending to hydro-electrolytic disorders in burn patients. Second-line therapy for mucormycosis has been described as posaconazole.[48,49] Retrospective studies using this antifungal medication have shown promising outcomes. This triazole was primarily used in patients who had failed or developed an intolerance to AmB. The oral formulation has the advantages of enabling earlier patient discharge and reducing relapse with continued administration.[50,51]

Posaconazole was found to have a good response in a single prospective study of 21 patients who were refractory or intolerant to AmB, with the exception of those with disseminated disease.[52] For patients with refractory disease, intolerance to AmB, or those who require prolonged treatment maintenance, posaconazole is advised as a second-line treatment. The recommended dose is 400 mg bid, and treatment is typically given for several months, according to reported cases.[53]

First-line therapy involves amphotericin monotherapy. There are reports and preclinical data on the use of antifungal combinations, but there aren't any clinical studies to back up this assertion. If necessary, caspofungin or posaconazole should be used in addition to a lipid formulation of AmB as the main antifungal.[54]

In the United States, a brand-new azole called isavuconazole has just been approved for the treatment of invasive mucormycosis.[60] With IV and oral formulations readily available, it has a safety profile that is comparable to fluconazole.[61] There are three reported cases of immunocompromised patients with pulmonary, rhinocerebral, and disseminated mucormycosis refractory to AmB and posaconazole but treated successfully with isavuconazole.[62,63]

CONCLUSION

Mucormycosis, including its cutaneous form, is a devastating disease. It is important to clearly distinguish a contamination from a real invasive infection. Where available, new molecular tests should be used to expedite diagnosis.

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