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# Challenges in the management of severe cutaneous mucormycosis: A case of rapid progression in uncontrolled diabetes mellitus with polymicrobial implications

Sara Harrar [a,*], Nidae Mimouni [a], Rabie Kharchi [b], Imad Abkari [b], Awatif El Hakkouni [a]

[a] Parasitology-Mycology Laboratory Department, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, 40000, Morocco

[b] Traumatology-Orthopedy B Department, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, 40000, Morocco

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ABSTRACT

Mucormycosis, a rare but life-threatening fungal infection, poses significant challenges in clinical management, particularly in patients with uncontrolled diabetes mellitus. This case report presents the clinical journey of a 44-year-old woman who developed a rapidly progressing Mucorales infection following a domestic knife injury. Her condition, complicated by diabetic ketoacidosis and co-infection with *Candida albicans*, led to severe hand phlegm and sepsis. Despite aggressive intervention, the infection continued to advance, ultimately resulting in the patient's demise.

## 1. Introduction

Mucormycosis is a serious and complex medical issue that can be life-threatening. Mucorales are ubiquitous in the environment and primarily soil-borne. They can be spread easily through spores in the air, ingestion, or through breaches in the skin. While they can infect various anatomical sites, cutaneous localization accounts for a notable portion [1,2].

Individuals with weakened immune systems are particularly vulnerable to Mucorales infections. Type 2 diabetes is a significant risk factor for this type of infection [3].

Mucorales infections can quickly become severe, and in the case of co-infection with other microorganisms, they can be even more dangerous [4].

In this case, we present a patient with type 2 diabetes, who had a hand injury from a knife accident. The wound became infected with Mucorales, leading to a hand phlegmon. Despite aggressive medical and surgical interventions, the infection continued to spread, resulting in the patient's death. This case highlights the critical role of early diagnosis and emphasizes the contribution of biologists in identifying the infecting pathogens.

## 2. Case

A 44-year-old woman arrived at the emergency department (Day 0) due to cellulitis in her right hand which had developed five days prior (Day −5). The cellulitis was a result of a domestic knife injury to her third finger, which she had left untreated for a month (Day −32). The patient had no prior history of steroid intake.

Upon initial examination on Day 0, the patient had a Glasgow score of 14/15, was dehydrated, hypertensive (blood pressure: 160/70 mmHg), tachycardic at 160 beats per minute, and had a SpO2 reading of 96%. The patient also exhibited signs of diabetic ketoacidosis, with hyperglycemia at 4.5 g/l, low bicarbonate at 6 mmol/l, as well as glycosuria and ketonuria. Examination of the patient's upper right limb revealed generalized edema of the hand, necrosis of the third finger, and cyanosis of the second finger. There was also an extensive necrotic lesion on the dorsal side of the hand with secretion of pus and serous fluid (Figs. 1 and 2).

The patient reported feeling pain when actively extending her hand. Further examination did not reveal any issues with blood vessels or nerves, and radiology did not show any signs of osteitis.

After stabilization of diabetic ketoacidosis, the patient was transferred to the traumatology department for further management (Day 0).

* Corresponding author.
*E-mail address:* Harrarsara4@gmail.com (S. Harrar).

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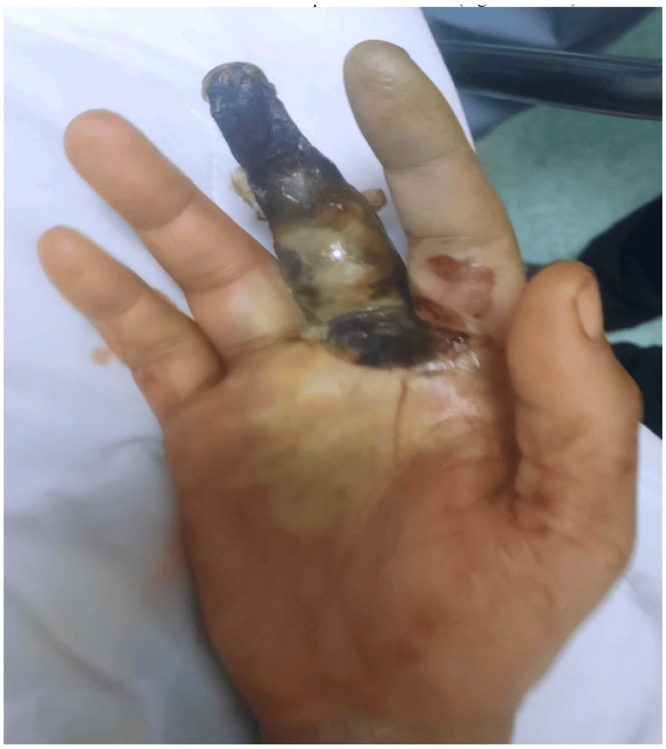

**Fig. 1.** Generalized edema of the hand with necrosis of the third finger (Palmar side).

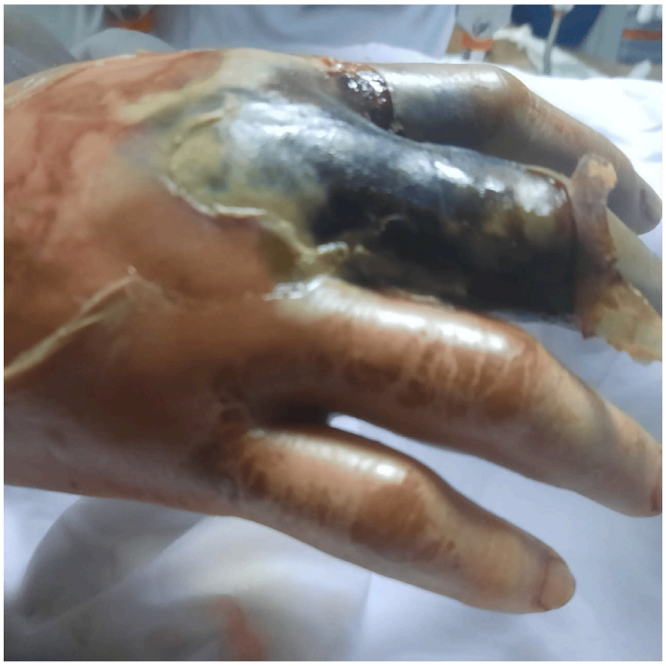

**Fig. 2.** Extensive necrotic patch of the hand (Dorsal side).

The biological workup showed an infectious syndrome with elevated white blood cells (48,000 elements/mm3), normochromic normocytic anemia (Hemoglobin at 9 g/dL), with a C-reactive protein at 220 mg/l, lactate dehydrogenase at 380 U/l, Creatinine level at 3.4 mg/dl and negative serological tests for Hepatitis (B and C) and HIV (1 and 2).

Following surgical excision, cleaning, and amputation of the third metacarpal bone on Day +1 (Fig. 3), the patient was prescribed bi-antibiotic therapy administered via intravenous injection. This therapy

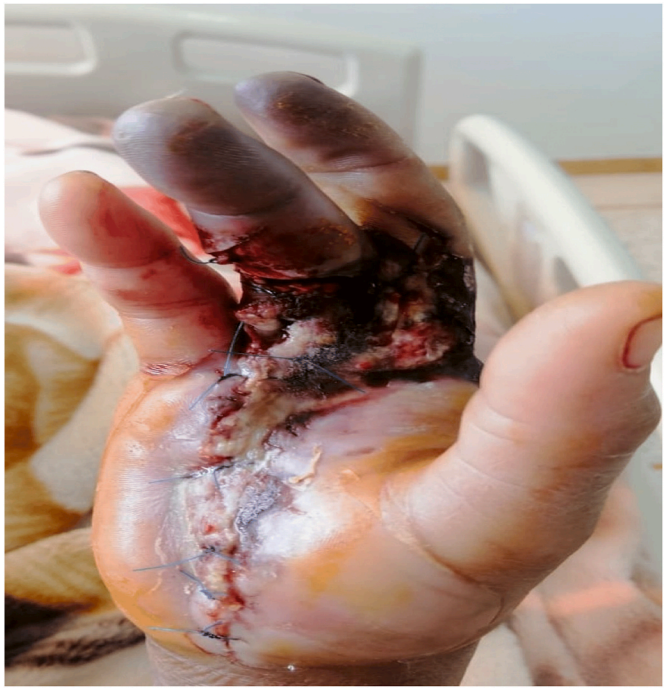

**Fig. 3.** Post-operative picture showing amputation of the 3rd finger.

involved administering 4g of Piperacillin-Tazobactam every 6 hours and 1.5g of Amikacin daily for three days. To manage pain, antalgics like Paracetamol and Néfopam were also utilized.

The evolution was marked by the extension of the necrosis, two days later, to the second and fourth fingers, which were amputated the same day (Day+3) (Fig. 4).

Swabs and biopsy tissue were taken per-operatively during both

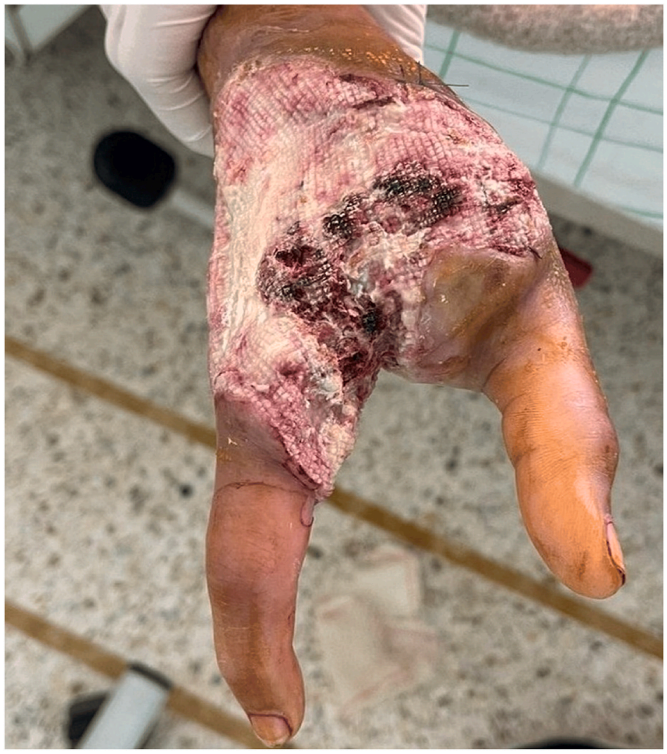

**Fig. 4.** Post-operative picture showing amputation of the second and fourth fingers.

interventions (Day+1 and Day+3) and sent to the mycology laboratory.

Direct microscopic examination of the samples in a 10% potassium hydroxide (KOH) mount and then May Grunwald Giemsa (MGG) and lactophenol blue staining found filamentous Fungi associated with the presence of hyaline mycelial filaments, large, with irregular contours, thin-walled, and sparsely septate, consistent with Mucorales infection.

The fungal culture was performed using two plates of Sabouraud Dextrose Agar (SDA) additioned with Chloramphenicol, and incubated at 25 °C and 37 °C for each of the two samples. Two days after receiving the first sample (Day+3), there was a growth of round whitish and mucous colonies and white turning to grey molds. The second sample showed the same aspect after 24 hours (Day+4) (Fig. 5).

The mucosal colonies were identified as *Candida albicans* using automated identification by the VITEK® 2 Yeast identification card (YST). The slide culture findings consisted of the presence of ellipsoidal columella, with short funnel-shaped apophysis, and hyaline to slightly pigmented sporangiophores, corresponding to the aspect of *Lichtheimia* spp. (Fig. 6). The minimum inhibitory concentrations and molecular identification were not available.

The Patient was put on liposomal amphotericin B (lAMB) (5mg/kg/24H) on Day+5. Her condition deteriorated, and despite initial treatment and surgical interventions, she died a few days later (Day+13) due to multiple organ failure and underlying diabetes which was hard to stabilize.

## 3. Discussion

*Lichtheimia* spp., previously classified as *Absidia* spp., has a propensity to cause severe, invasive infections, often with a poor prognosis. It is known to infect various anatomical sites, including the sino-pulmonary tract, rhino-orbito-cerebral localization, and cutaneous tissue which is considered a significant clinical presentation in Mucorales infections [5,6].

Hyperglycemia, immune dysregulation, and diabetes are risk factors for developing opportunistic infections [2]. The suppression of innate and adaptive immunity in diabetic patients is well-documented, making them more susceptible to Mucorales infections. Additionally, other immunological backgrounds, such as neutropenia resulting from hematological malignancies or immunosuppressive therapies, can also increase susceptibility to severe fungal infections [3].


**Fig. 5.** Culture showing white to grey molds (1) and round mucous colonies (2).

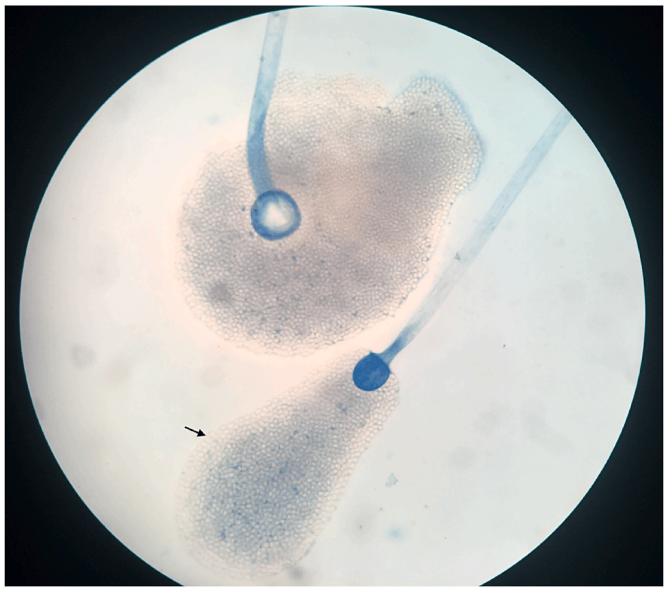

**Fig. 6.** Microscopic examination using lactophenol blue stain showing small and dark spores inside pear-shaped sporangia (x400).

The pathophysiology of Mucorales cutaneous infections is rooted in the unique biology of these fungal pathogens and the host's immune response. These fungi enter the host through breaches in the skin, often caused by minor traumas or injuries. Once introduced, Mucorales spores germinate and invade the surrounding tissue. They are characterized by their capacity to produce angioinvasive hyphae that infiltrate and damage blood vessels, causing thrombosis and subsequent tissue ischemia. Moreover, the fungi induce an inflammatory response that can lead to tissue necrosis and thereby the characteristic black eschar formation, as observed in cutaneous infections[1,2].

While *Candida albicans* is a well-recognized opportunistic fungal pathogen, its co-infection with *Lichtheimia* spp. is less common but not unheard of in clinical practice. The interplay between these pathogens may lead to an exacerbation of symptoms and more rapid disease progression. These co-infections are associated with higher mortality rates [5,6].

In the presented case, the occurrence of a co-infection in the context of diabetic ketoacidosis favored the onset of bacterial sepsis. This amplified the polymicrobial damage, ultimately causing the patient's death.

Direct microscopic examination of clinical samples is a critical step in the diagnosis of Mucorales infections, the characteristic features observed may include hyaline mycelial filaments with irregular contours, thin-walled, banded, and branching at ninety-degree angles [10]. These hyphae are often non-septate, although some species may have occasional septations [9].

The aspects of fungal colonies can vary depending on the culture medium, incubation conditions, and the specific species of Mucorales. Typically, Mucorales colonies grown on appropriate fungal culture media, like Sabouraud Dextrose Agar (SDA), exhibit distinctive characteristics. They often appear pale white turning grey with age, which was the case for the cultures we performed [10].

Under the microscope, the *Lichtheimia* spp. genus is characterized by the arrangement of sporangiophores, either isolated or grouped, attached to stolons, and branched in clusters, the funnel-shaped expansion of the sporangiophore at its end, forming a broad conical apophysis, the pear-shaped sporangia with a hemispherical columella protruding into the sporangia, and the presence of rhizoids, generally few, located on the stolons, away from the nodes [11].

The identification of the *Lichtheimia* genus and its primary species (*Lichtheimia corymbifera, L. ramosa, L. ornata*) can be more specific using PCR techniques that target different regions of ribosomal DNA (18S, 28S, or ITS regions for Internal Transcribed Spacer), or through MALDI-TOF mass spectrometry [12,13]. The detection of circulating DNA by quantitative PCR allows for an estimated early diagnosis within nine days [14].

The treatment of Mucorales infections represents a critical component of patient care. The cornerstone of therapy for mucormycosis involves surgical debridement or amputation and the prompt initiation of antifungal agents, primarily liposomal amphotericin B, which has demonstrated efficacy against Mucorales fungi. The use of lAMB formulations over conventional ones (cAMB) is preferred because they allow the administration of higher doses with fewer side effects and better tolerability [5–15].

The recent past has also seen the introduction of newer antifungals and other modalities of treatment for invasive and systemic forms of mucormycosis. Among triazoles, posaconazole has emerged as an important antifungal agent [16]. Isavuconazole also showed activity against mucormycosis with efficacy similar to amphotericin B [17].

Mucormycosis represents a challenge in the realm of fungal infections, especially when occurring in the context of uncontrolled diabetes mellitus. This case report illuminates the intricate interplay of factors that contribute to the rapid and often devastating progression of Mucorales infections. The patient's journey, from an initial domestic knife injury to a life-threatening infection, serves as a stark reminder of the importance of early recognition, prompt diagnosis, and multidisciplinary management. It emphasizes the crucial role of mycologists and biologists in recognizing the infecting pathogens and guiding treatment decisions.

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There are none.

## Consent

Written informed consent was obtained from the patient or legal guardian(s) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## CRediT authorship contribution statement

**Sara Harrar:** designed the study, Formal analysis, interpreted the patient data, Writing – original draft. **Nidae Mimouni:** contributed to data collection, Formal analysis. **Rabie Kharchi:** performed data collection and revision. **Imad Abkari:** contributed to data collection and revision. **Awatif El Hakkouni:** designed the study, Formal analysis, interpreted the patient data, Writing – original draft, Writing – review & editing, All authors read and approved the final manuscript.

## Declaration of competing interest

There are none.

## Acknowledgements

There are none.

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