DOI: https://doi.org/10.4038/gmj.v30i3.8289

Silent invasion: A diagnostic and therapeutic challenge of rhino-cerebral mucormycosis

SMAN De Alwis, CK Bodinayake

Professorial Medical Unit, National Hospital Galle, Sri Lanka.

Correspondence: Dr. Achala De Alwis
e-mail*: animanthika92@gmail.com*
https://orcid.org/0000-0003-3313-7890

Submitted on 22.07.2025 and accepted for publication on 25.08.2025

Introduction

Mucormycosis is caused by fungi of the order Mucorales, predominantly *Rhizopus* species. They are saprophytic molds found in soil, decaying organic material, fruits and vegetables. They are participants of decomposition process but can also act as important opportunistic pathogens in humans. Immuno-compromised subjects are at a greater risk, particularly individuals with uncontrolled diabetes (1,2). Mucormycosis can affect different regions of human body causing rhino-orbito-cerebral, pulmonary, gastrointestinal, cutaneous and disseminated forms. Rhino-cerebral mucormycosis is the most common and well-known entity, often mistaken as sinusitis, delaying the diagnosis and initiation of appropriate treatment. Mucormycosis is extremely aggressive and rapidly invades deep adjacent and vital structures, due to vascular invasion and tissue necrosis (3), rendering curative surgery impossible. This poses a diagnostic and therapeutic challenge, as early subtle signs do not indicate a grave pathology, and once overt signs appear, it is almost too advanced for curative treatment. We report a case of rhino-cerebral mucormycosis in a 64-year-old female with poorly controlled diabetes.

Case presentation

A 64-year-old female with uncontrolled diabetes and rheumatoid arthritis (defaulted follow-up), presented with left-sided frontal headache for one day. Three weeks prior, she has had a similar headache with fever and had been managed as sinusitis, after which her symptoms resolved. Currently, she complained of photophobia and phonophobia, without a fever.

She was confused with a Glasgow Coma Scale of 12/15 (E-3, V-4, M-5) and was hemodynamically stable. There was no facial oedema, sinus tenderness, oral lesions or ocular proptosis. Clinical examinations did not reveal any meningeal signs or focus of infection. Other system examinations were unremarkable.

Her full blood count revealed a neutrophil leukocytosis with a white blood cell count of 13.0 x 10^9 /L. Her inflammatory markers were high with a C-reactive protein value of 39.6 mg/L, and the erythrocyte sedimentation rate was 108 mm/hour. Her urine and blood cultures yielded no bacterial growth. Non-contrast CT (NCCT) scan of the brain and paranasal sinuses were normal. Cerebrospinal fluid analysis showed raised protein (83 mg/dL [15-60]) with normal glucose (110 mg/dL) and lymphocytic pleocytosis. (polymorphs 93 cells/µL and lymphocytes - 138 cells/µL). Cerebrospinal fluid pyogenic culture and polymerase chain reaction (PCR) test for *Mycobacterium tuberculosis* were negative.

Despite broad-spectrum antibiotics, her headache worsened, and she developed neck pain and vomiting. A subsequent NCCT brain which was done 5 days after the admission revealed a suspicious hypodense area in the brain. Contrast

enhanced CT scan confirmed the presence of cerebral abscess and pansinusitis (Figure 1). Functional Endoscopic Sinus Surgery (FESS) showed highly invasive infection with distortion and erosions in nasal cavity and cribriform plate with necrotic debris which were removed during the procedure (Figure 2). Direct intraoperative smears revealed ribbon like aseptate fungal hyphae, which was strongly suggest mucormycosis, which was later confirmed by histopathological evaluation. Culture was not done.

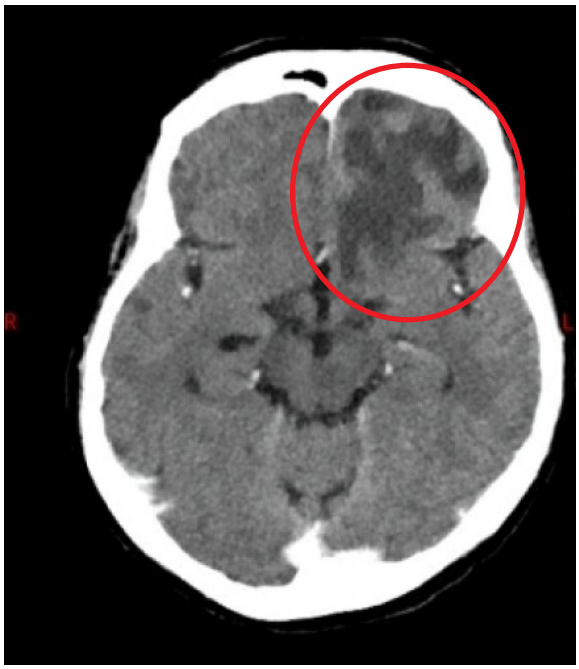

Figure 1: CECT scan of the brain shows hypodense lesion involving the frontal region (circled in red)

Intravenous amphotericin B 10mg/kg once daily was commenced after omission of all antibiotics as advised by the mycology team.

The neurosurgical team advised on conservative management due to the high operative risk associated with manipulation of sinus cavities in the presence of invasive cerebral disease. She developed diarrhoea, pruritus, erratic blood sugar control, hypokalemia and cholestatic liver injury which could be due to amphotericin B therapy. Repeated Contrast CT on day 10 of amphotericin B, failed to demonstrate an interval reduction of the brain lesion. Despite antifungal therapy and supportive measures, she succumbed to her illness.

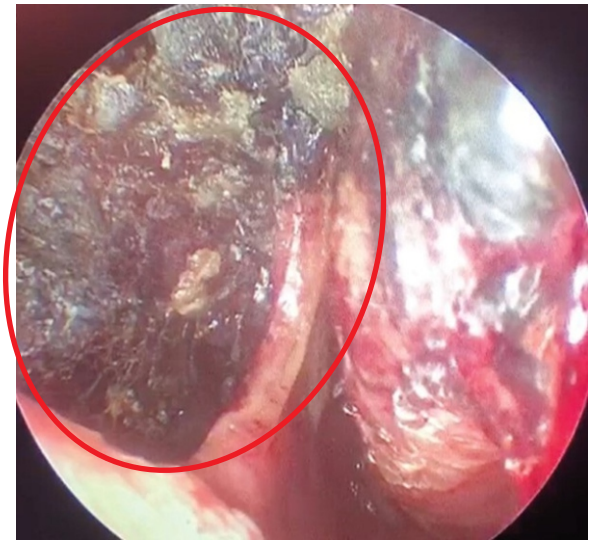

Figure 2: FESS image showing of invasive fungal infection with distortion and erosions in nasal cavity.

Discussion

Rhino-cerebral mucormycosis is a rare but highly aggressive fungal infection with a high mortality and morbidity, predominantly affecting the immuno-compromised population.

Multiple factors contributed to the diagnostic dilemma observed in this patient. This patient with poorly controlled diabetes presented with an acute headache and an altered sensorium. She lacked features of meningism or fever. CSF analysis was nonspecific with elevated protein, normal glucose and lymphocytic pleocytosis. The initial non-contrast CT scan of the brain was normal. Subtle clinical signs and symptoms with initial inconclusive investigations gave a false reassurance, masking aggressive underlying disease.

In this context, several differential diagnoses were considered. History of presumptive sinusitis, headache with altered sensorium and neutrophil leukocytosis favoured pyogenic meningitis. Lymphocytic pleocytosis with subacute progression raised the suspicion of tuberculosis, which was discouraged by negative *Mycobacterium tuber--culosis* nucleic acid amplification test (NAAT) in CSF, and a non-reactive Mantoux test. Viral meningitis was considered less likely due to the subacute nature of her illness. She was commenced

on broad-spectrum antibiotics, considering the high likelihood of partially treated bacterial meningitis and absence of definitive evidence for an alternative diagnosis. Deterioration despite antibiotics raised the suspicion of atypical or resistant infections. FESS suggested rhino-cerebral mucormycosis. Diagnosis was histopathologically confirmed as mucormycosis by direct visualisation in the nasal smear.

Fungal culture or histopathological confirmation is the gold standard for diagnosis of mucormycosis. Although *Mucorale* grow rapidly, culture yield is poor due to fragility, difficulty in handling and inability to sporulate in infected tissue.

The management includes source control with early initiation of targeted antifungals (4). Neurosurgical options are limited due to involvement of vital structures as exemplified by cerebral invasion in this case. Thus, early administration of antifungals with optimising other comorbidities is the cornerstone of management. Mucormycosis can worsen treatment outcome by causing vascular thrombosis and tissue necrosis, hindering tissue penetration of antifungals (3). Liposomal amphotericin B is the first-line antifungal treatment in mucormycosis. Ensuring a continuous supply is challenging due to high cost and prolonged treatment duration. Conventional amphotericin B was best avoided due to its significant toxicity, notably nephrotoxicity. Newer agents like posaconazole and isavuconazole have shown promise as salvage therapy or step-down options (5), although their availability is limited.

Adverse effects of amphotericin B therapy include electrolyte disturbances such as hypocalcaemia, hypokalemia, hypomagnesemia, and hyponatremia that may result in cardiac arrhythmia and rhabdomyolysis. Nephrotoxicity and hyper-sensitivity reactions are well-known associations that require close monitoring. These adverse effects limit the efficacy and effectiveness of treatment.

Restoration of euglycaemia remained as a pillar in management to limit the ongoing infection, as hyperglycemia promotes fungal growth by impairing neutrophil chemotaxis and phagocytosis, and by providing acidic glucose-rich growth media (1,2).

Caregiver counselling regarding disease, treatment and treatment related adverse effects is of utmost importance to sustain prolonged treatment.

The prognosis of mucormycosis depends on the anatomical site involved and the extent of the disease. Therefore, early diagnosis and timely initiation of targeted antifungal treatment with surgical débridement are vital for a favourable outcome.

Conclusions

This patient's case illustrates the significant diagnostic and therapeutic challenges inherent in the management of mucormycosis. The non-specific presentation, aggressive progression, and treatment-related complications contribute to high mortality. Clinicians should be vigilant with a high index of suspicion to promptly diagnose and treat rhino-cerebral mucormycosis.

Informed consent has been obtained to publish this case report.

References

1. Welagedara PGRIS, Jayasekera PI. Rhinocerebral Mucormycosis in Sri Lanka - Aetiology and Antifungal Susceptibility. *Ceylon J Otolaryngol*. 2025; **14**(1): 19-24

2. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, *et al.* Global guideline for the diagnosis and management of mucormycosis: an initiative of ECMM and Mycoses Study Group. *Lancet Infect Dis.* 2019; **19**(12): e405-21.

3. Safiia J, Díaz MA, Alshaker H, Atallah CJ, Sakr P, Moshovitis DG, *et al.* Recent advances in diagnostic approaches for mucormycosis. *J Fungi (Basel).* 2024; **10**(10): 727.

4. Brazilian Task Force for the Management of Mucormycosis. Brazilian task force for the management of mucormycosis. *Braz J Infect Dis.* 2025; **29**(1): e00080

5. Bhandari, Jenish, Pawan K. Thada, and Shivaraj Nagalli. 2023. *Rhino cerebral Mucormycosis*. Last updated September 15, 2023.