Article published online: 2023-06-19

Mucormycosis of the Middle Ear—A Report of a Rare Case

Megha Madhu[1] Shrinath D. Kamath P.[1] Vadisha Bhat[1] Teerthanath Srinivas[2]

[1] Department of ENT, KS Hegde Medical Academy, Mangalore, Karnataka, India
[2] Department of Pathology, KS Hegde Medical Academy, Mangalore, Karnataka, India

Address for correspondence Vadisha Bhat, MBBS, Department of ENT, KS Hegde Medical Academy, Nitte (Deemed to be University), Deralakatte, Mangalore- 575018, Karnataka, India (e-mail: vadishbhat@nitte.edu.in).

J Health Allied Sci[NU] 2024;14:290–293.

Abstract

Mucormycosis is an opportunistic fungal infection that often affects the nose and paranasal sinuses. The disease prevalence was very high in India during the coronavirus disease 2019 pandemic, thereby raising public awareness about this disease. The general practitioners were updated about the disease characteristics and the requirement for emergency management. Yet, in some instances, the treatment was inadequate due to delayed presentation and low affordability for treatment. The mucormycosis of the ear, on the other hand, is a rare occurrence that demands meticulous study for early diagnosis and management. Here, we discuss the case of a patient with mucormycosis of the middle ear.

Keywords

- mucormycosis
- middle ear
- diabetic
- facial palsy

Introduction

Mucormycosis is an aggressive, opportunistic, invasive fungal infection accompanying significant immunological dysfunction.[1] It has a very high fatality rate and the available treatment options are only a few. It displays a clear preference for invading endothelial cells in the vascular system, which is significant in the spread of disease from an initial focus of infection.[2]

Infections caused by the members of the order Mucorales are referred to as mucormycosis. Although Rhizopus, Mucor, and Rhizomucor are responsible for many human illnesses, the order Mucorales also includes Actinomucor, Apophysomyces, Cunninghamella, Lichtheimia (formerly known as Absidia), Saksenaea, and Syncephalastrum.[3]

Sinonasal mucormycosis accounts for 40% of mucormycosis that is acquired by airborne transmission. The overall prognosis is poor and largely dependent on early detection and treatment. The rapid extension is often fatal.[1] We present here a rare case of mucormycosis of the middle ear in a nondiabetic patient.

Case Report

A 52-year-old male presented to the ENT outpatient department with complaints of pain, discharge and decreased hearing in the left ear for six months, left-sided facial weakness, and difficulty in closing the left eye for the past 20 days. The earache was dull aching, radiating to the postauricular region and left side of the face. On examination, the external auditory canal was filled with mucopurulent discharge and the tympanic membrane had a subtotal perforation with granulation tissue in middle ear (►**Fig. 1**). Facial nerve examination showed normal symmetry at rest, left lagophthalmos, and incomplete closure with effort. The angle of the mouth was asymmetrical, absent forehead wrinkling (►**Fig. 2**). Nose, throat, and neck examination was normal.

Hematological investigations were within normal limits. His blood sugars were elevated, and he was diagnosed with newly detected diabetic. An audiogram revealed profound mixed hearing loss in the left ear. High-resolution computed tomographic scan of the temporal bone showed nonenhancing mucosal thickening in left middle ear cavity along the

article published online
June 19, 2023

DOI https://doi.org/10.1055/s-0043-1769583.
ISSN 2582-4287.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

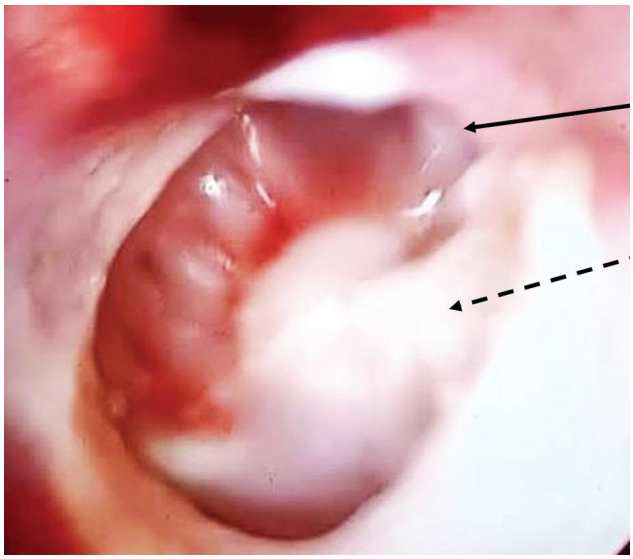

Fig. 1 Otoendoscopy picture with subtotal perforation (solid arrow pointing to the perforation, dotted arrow pointing to the promontory).

Fig. 2 Clinical picture of patient with facial palsy-incomplete closure of left eye, deviation of angle of mouth to right, loss of nasolabial fold on left side.

walls and peri-ossicular region. Soft tissue density was seen with air-fluid levels in the mastoid air cells (►**Fig. 3A**). There were also two well-defined sclerotic lesions measuring 3.5 and 2.6 mm noted within mastoid air cells, suggestive of osteoma (►**Fig. 3B**). The differential diagnosis was atticoantral otitis media, malignant otitis externa, or acute necrotizing otitis media, with left lower motor neuron facial palsy-House-Brackmann grade IV with left severe sensorineural hearing loss.

The ear discharge was sent for culture and sensitivity showed presence of methicillin-resistant coagulase-negative staphylococci. AFB staining did not show any Acid-fast bacillus, and tuberculous otitis media was ruled out. Fungal culture showed growth of Penicillium species.

The granulation tissue from the middle was sent for histopathology, which showed filamentous fungal colonies containing variable wide angle, irregular branching aseptate hyphae in the background of neutrophils, histiocytes, and necrotic debris (►**Fig. 4**). Periodic acid–Schiff stain showed magenta colored mucor fungal colony (►**Fig. 5**). Histological features were suggestive of mucormycosis.

Facial physiotherapy with galvanic stimulation was initiated. The patient was advised amphotericin B infusion followed by surgical clearance. However, the patient was not willing to continue the treatment in our city due to personal reasons, and hence was discharged from the hospital.

Discussion

Mucormycosis is a fungal infection that typically manifests acutely in those with compromised immune systems. Numerous species of common soil saprophytes and filamentous fungi of the zygomycete class of the Mucorales order contribute to its development.[3]

Rhinoorbitocerebral, pulmonary, disseminated, cutaneous, and gastrointestinal are the types of infection caused by mucormycosis. Less common ones are endocarditis, osteomyelitis, peritonitis, and pyelonephritis.[4] Sinonasal or pulmonary are common, because spore inhalation causes contamination more frequently than their intake or transcutaneous injection.[3]

After initial penetration, spores develop into hyphae and cause angioinvasion, which has the potential to affect many organs and spread hematogenously.[5] The high-affinity iron permease (FTR1), which enables pathogen persistence in iron-poor settings, is one of the main virulence factors peculiar to the pathogenesis of Mucorales.[6]

The Mucorales spore surface contains the spore coat (CotH) protein, which weakens host immunological defenses, and the adenosine diphosphate (ADP) -ribosylation factor, which seems to be involved in Mucorales proliferation and shape.[7] Alkaline *Rhizopus* protease enzyme (Arp) has a role in enhancing the coagulation process in patients suffering from mucormycosis.[8] ADP-ribosylation factor (Arf) is a virulence factor that is necessary for growth, fungal dimorphism, and virulence.[9]

Uncontrolled diabetes has been noted as one of the predisposing factors. By encouraging spore germination, ketoacidosis appears to play a more decisive role than hyperglycemia.[10] Drug misuse, immunosuppressive therapy, advanced kidney failure, prolonged corticosteroid therapy, acquired immunodeficiency syndrome, immune insufficiency, malignant hemopathy, and bone marrow or organ grafts are some other reported risk factors.[11] Neutropenia, polynuclear neutrophil chemotactic deficit, and phagocytosis deficit are predisposing

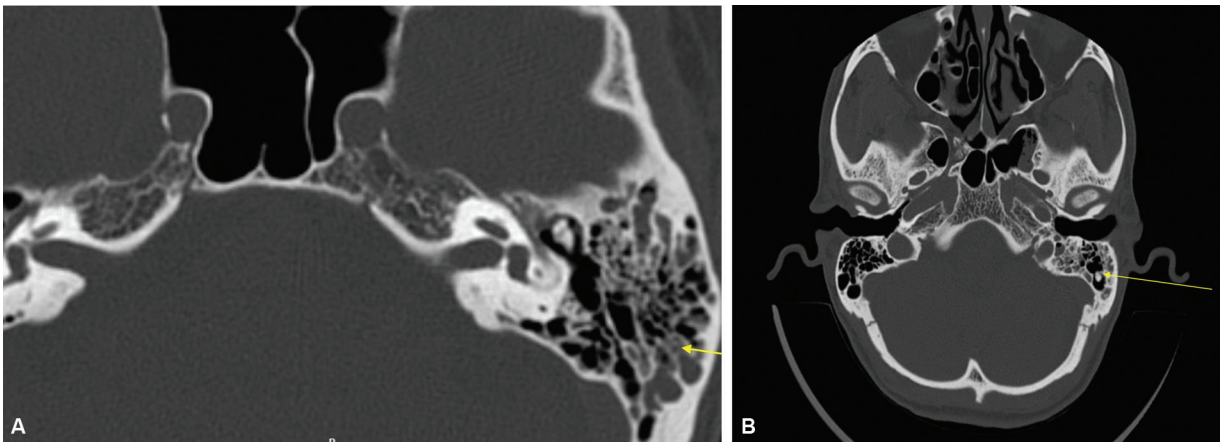

Fig. 3 Computed tomographic (CT) scan images of the temporal bone: (**A**) CT image with arrow pointing to soft tissue density with air-fluid levels in the mastoid air cells. (**B**) CT image with arrow pointing to osteoma within mastoid air cells.

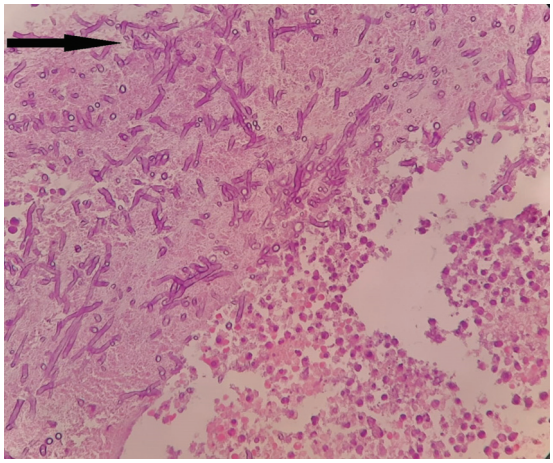

Fig. 4 Histopathology image (40X), arrow pointing to fungal hyphae.

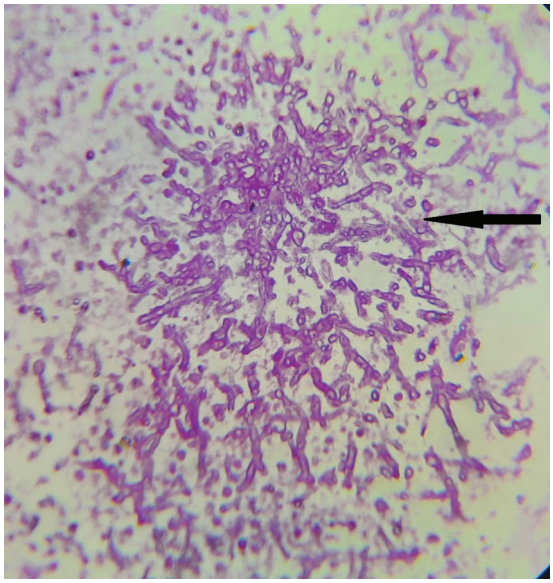

Fig. 5 Periodic acid–Schiff image on microscopy (40X), arrow pointing to fungal hyphae.

factors that are variously implicated in the aforementioned and promote fungal development.[12]

Otologic involvement is one of the unusual ENT presentations that has been reported. The nasopharynx or an existing tympanic perforation is the most likely entry point for otologic mucormycosis.[1]

Diagnosis is based on culture and histopathology. In Sabouraud dextrose agar, the fungus develops into fluffy white, gray, or brownish colonies in 1 to 7 days.[4] Potassium hydroxide (20%), Gomori's methenamine silver staining, hematoxylin and eosin staining, or periodic acid-Schiff staining are all options for direct microscopic investigation. They are typically described as broad ribbon-like aseptate hyphae with right angled branching. Histopathologically, this infection is characterized by angioinvasion and tissue invasion.[4]

Antifungal drugs, debridement to lower fungus burden and improve drug accessibility, and correction of neutropenia or other risk factors in patients with immunological deficiencies are the three components of treatment.[13]

The standard antifungal for mucormycosis is amphotericin B in its traditional desoxycholate form at 1 to 1.5 mg/kg/d or in liposomal form. It accumulates preferentially in macrophages, including those of infected tissue, and exhibits good central nervous system penetration. The liposomal form exhibits reduced nephrotoxicity, allowing higher doses, from 5 to 15 mg/kg/day, for a longer period.[14] Posaconazole, a brand-new triazole, is an option in the event of failure. It has been shown to be effective in vitro and in vivo, is well-tolerated, and has fewer adverse effects.[15]

Due to poor antifungal diffusion inside necrotic tissue and a reduction in fungal burden, surgical debridement must be incorporated into medical treatment. Developing necrosis is a symptom of severity that necessitates urgent surgery. With healthy margins and debridement of all necrotic lesions, resection should be as thorough as feasible.[1]

Granulocyte transfusion and bone marrow transplantation are also included in treatment. Hyperbaric oxygen therapy is another treatment where the increased oxygenation of the

affected tissues distal to the occluded vessel and decreased local acidosis enhance the activity of antifungals. Stem cell bone marrow transplantation was also used successfully.[16]

Otologic mucormycosis reports are limited in number. Kermani et al[1] reported two cases of otologic mucormycosis. Otologic mucormycosis has been reported commonly among diabetic patients.[16,17] Hazarika et al[18] have reported the case of mucormycosis of the middle ear and mastoid in a nondiabetic patient. Mucormycosis that was otherwise not causing any symptoms has been found in the middle ear incidentally in a patient during revision tympanoplasty in a nondiabetic patient.[4]

Conclusion

Mucormycosis of the middle ear in an immune-compromised patient can be aggressive, causing complications like facial palsy. There will be serious or even fatal implications if the diagnosis and treatment are delayed. Treatment is antifungal medication combined with surgical procedures. The prognosis can be improved with appropriate early treatment, including liposomal amphotericin B, necrotic tissue removal, and risk factor control. The higher cost of liposomal amphotericin is a hindrance to an affordable complete treatment. In our case, further follow-up could not be done to incomplete treatment. This case is presented due to its rarity of occurrence.

Conflict of Interest
None.

References

1 Kermani W, Bouttay R, Belcadhi M, Zaghouani H, Ben Ali M, Abdelkéfi M. ENT mucormycosis. Report of 4 cases. Eur Ann Otorhinolaryngol Head Neck Dis 2016;133(02):83–86
2 Riley TT, Muzny CA, Swiatlo E, Legendre DP. Breaking the mold: a review of mucormycosis and current pharmacological treatment options. Ann Pharmacother 2016;50(09):747–757
3 Steinbrink JM, Miceli MH. Mucormycosis. Infect Dis Clin North Am 2021;35(02):435–452
4 Biniyam K, Bhat V, Bhandary SB, Aroor R. Asymptomatic mucormycosis of middle ear: an incidental finding during tympanoplasty. Indian J Otol 2014;20:83–85
5 Hassan MIA, Voigt K. Pathogenicity patterns of mucormycosis: epidemiology, interaction with immune cells and virulence factors. Med Mycol 2019;57(Suppl 2):S245–S256
6 Ibrahim AS, Gebermariam T, Fu Y, et al. The iron chelator deferasirox protects mice from mucormycosis through iron starvation. J Clin Invest 2007;117(09):2649–2657
7 Gebremariam T, Liu M, Luo G, et al. CotH3 mediates fungal invasion of host cells during mucormycosis. J Clin Invest 2014; 124(01):237–250
8 Spreer A, Rüchel R, Reichard U. Characterization of an extracellular subtilisin protease of Rhizopus microsporus and evidence for its expression during invasive rhinoorbital mycosis. Med Mycol 2006;44(08):723–731
9 Patiño-Medina JA, Maldonado-Herrera G, Pérez-Arques C, et al. Control of morphology and virulence by ADP-ribosylation factors (Arf) in Mucor circinelloides. Curr Genet 2018;64(04):853–869
10 Bhansali A, Bhadada S, Sharma A, et al. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J 2004;80(949):670–674
11 Charfi S, Ayadi L, Makni S, et al. Rhinocerebral mucormycosis: anatomoclinical study of seventh cases. J Mycol Med 2008; 18:46–52
12 Spellberg B, Edwards J Jr, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. Clin Microbiol Rev 2005;18(03):556–569
13 Rogers TR. Treatment of zygomycosis: current and new options. J Antimicrob Chemother 2008;61(Suppl 1):i35–i40
14 Kim JG, Park HJ, Park JH, et al. Importance of immediate surgical intervention and antifungal treatment for rhinocerebral mucormycosis: a case report. J Korean Assoc Oral Maxillofac Surg 2013; 39(05):246–250
15 Almannai M, Imran H, Estrada B, Siddiqui AH. Successful treatment of rhino-orbital mucormycosis with posaconazole and hyperbaric oxygen therapy. Pediatr Hematol Oncol 2013;30 (03):184–186
16 Yun MW, Lui CC, Chen WJ. Facial paralysis secondary to tympanic mucormycosis: case report. Am J Otol 1994;15(03):413–414
17 Macdonell RA, Donnan GA, Kalnins RM, Richards MJ, Bladin PF. Otocerebral mucormycosis–a case report. Clin Exp Neurol 1987; 23:225–232
18 Hazarika P, Ravikumar V, Nayak RG, Roa PS, Shivnanda PG. Rhinocerebral mucormycosis. Ear Nose Throat J 1984;63:100–106