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Case Series

Chronic suppurative otitis media (CSOM) Due to Aspergillus nidulans: A case series from a tertiary care centre in Western India

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Abstract

Background: Chronic Suppurative Otitis Media (CSOM) is a major public health problem in India. It is a persistent disease with a great risk of irreversible complications like hearing loss, particularly in the developing world. While bacterial pathogens are often implicated, fungal infections, particularly by *Aspergillus* species, are increasingly recognized as causative agents. *Aspergillus nidulans*, though rarely reported in otomycosis, appears to be emerging as a potential pathogen. This case series highlights the clinical presentation, predisposing factors, and laboratory findings in five patients with Chronic Suppurative Otitis Media due to *Aspergillus nidulans*.

Case Series: Five patients presenting to the ENT outpatient department with chronic ear discharge were clinically evaluated, and samples of otorrhea were subjected to Gram's staining and culture on routine bacteriological media and Sabouraud Dextrose Agar (SDA). Fungal isolates were identified based on macroscopic and microscopic morphology (KOH and LPCB Mount), including the presence of Hülle cells.

Results: All five patients, ranging from children to adults, presented with unilateral or bilateral ear symptoms, including pain, itching, and discharge, with hearing loss and pruritus. History of ear cleaning with foreign objects, use of cotton buds, and co-existing conditions like diabetes or Chronic suppurative otitis media (CSOM), were noted. Fungal culture on SDA revealed growth of *Aspergillus nidulans* with characteristic morphological features. In some cases, growth was delayed, and direct microscopy was inconclusive. Management with topical antifungals and aural toileting led to symptomatic improvement.

Conclusion: These case series emphasize the importance of considering fungal etiology, especially *Aspergillus nidulans*, in recalcitrant CSOM, which is a treatment-resistant middle ear infection characterized by persistent otorrhea through a perforated tympanic membrane despite adequate and appropriate therapeutic interventions. Culture-based confirmation is essential for accurate diagnosis and tailored antifungal management. Increased awareness of non-*fumigatus* Aspergillus species in otitis media is warranted.

Keywords: *Aspergillus nidulans*, Chronic suppurative otitis media (CSOM), Hülle cells, Fungal infections, Risk factors.

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1. Introduction

The World Health Organisation defines Chronic Suppurative Otitis Media (CSOM) as a chronic inflammation of the middle ear cleft, i.e., eustachian tube, middle ear, and mastoid cavity, commonly characterized by recurrent otorrhea through a perforated tympanic membrane for at least 2 weeks or more.[1] Although bacterial pathogens have historically been considered the principal causative agents, there is increasing evidence that fungal organisms play a significant role, particularly in patients with prolonged antibiotic use, malnutrition, overcrowding, recurrent upper respiratory tract infections, poor hygiene, habitual ear cleaning, or comorbidities such as diabetes mellitus, malignancies, steroids and HIV infections.[2,3] Otomycosis**,** a fungal infection of the external and/or middle ear, is most commonly caused by species of Aspergillus and Candida. Among the Aspergillus spp., *A. fumigatus*, *A. niger*, and *A. flavus* are the most frequently implicated organisms. This trend may be attributed, in part, to the orthodox clinical approach—such as

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the overuse of topical antibiotics or steroids—which alters the local ear environment, making it more susceptible to fungal colonization.[3] However, *Aspergillus nidulans*—a rare but emerging pathogen in otomycosis—is infrequently reported in the literature. *Aspergillus nidulans* is a ubiquitous filamentous fungus commonly found in the environment, exclusively in humid and putrefying organic materials such as manure, soil, and plant debris.[4] While typically harmless, it can cause opportunistic infections in immunocompromised individuals.[4] Its involvement in localized infections like CSOM remains underrecognized and underreported, especially in immunocompetent individuals.[4] The identification of *A. nidulans* requires a high index of suspicion, as its slow growth and subtle culture features may be overlooked in routine microbiological workup.[4] The presence of Hülle cells—a defining morphological feature—alongside characteristic colony morphology on Sabouraud Dextrose Agar (SDA), can aid in accurate identification.[4,5] Early detection and mycological confirmation are essential to avoid complications and to guide targeted antifungal therapy. This case series highlights five clinically and microbiologically confirmed cases of CSOM due to *Aspergillus nidulans*, including both immunocompetent and immunocompromised individuals. Through these cases, we aim to underscore the importance of considering rare fungal pathogens in chronic ear infections and the need for robust fungal diagnostics in ENT practice.

1.1. BOX-1: Identification of Aspergillus nidulans

Aspergillus nidulans can be identified through a combination of macroscopic colony characteristics and microscopic morphology**.** On Sabouraud Dextrose Agar (SDA), colonies appear velvety to floccose with a greenish to olive-brown coloration and often develop a purplish to reddish-brown reverse pigment with age. The colony grows moderately rapidly and may show a radial furrowed pattern. Microscopically, LPCB mounts reveal septate hyphae**,** short conidiophores arising from foot cells, and club-shaped vesicles. The conidiophores exhibit a biseriate arrangement, with metulae giving rise to phialides, which in turn produce rough-walled, brownish conidia arranged in chains. A hallmark feature aiding in the definitive identification of *A. nidulans* is the presence of Hülle cells—large, thick-walled, hyaline cells often associated with the fungus's sexual stage.(**Figure 6**, and **Figure 7**).

2. **Case Series**

2.1. Case 1

1. Patient Profile- A 39-year-old male, known case of diabetes mellitus, with a history of chronic smoking, alcohol consumption, and tobacco use for over 11 years, presented to the ENT outpatient department (OPD).
2. Clinical presentation: Recurrent episodes of bilateral ear pain, mucopurulent, foul-smelling discharge (Figure 1), persistent itching, and hearing loss for the last 1 month.
3. Risk factor: He reported using cotton buds and sticks to clean his ears 2–3 times a month.
4. Otoscopic examination revealed inflamed auditory canals with purulent debris bilaterally.
5. Diagnostic Workup [4,5]: Gram stain showed pus cells and fungal hyphae. SDA culture yielded velvety green colonies with tufts of buff and yellow with a white border; the reverse side showed brownish-orange pigment (Figure 3 and Figure 4). Fungal identification was done based on the characteristics explained in BOX 1 (**Figure 6**, and **Figure 7**). Hülle cells were distinctly seen, confirming *Aspergillus nidulans*. (**Figure 5**)
6. Management: Topical antifungal therapy and aural toileting led to clinical improvement.
7. Clinical Significance: The isolate was identified as *Aspergillus nidulans*. The case underscores the importance of suspecting fungal etiology in diabetic individuals with chronic otitis symptoms and a history of ear trauma.

2.2. Case 2

1. Patient Profile: A 10-year-old female child, with no known comorbidities, presented to the ENT outpatient department (OPD).
2. Clinical presentation: The patient complained of bilateral ear pain and intermittent greenish mucoid discharge occurring (2–3 episodes per week) without associated Odor for the last 15 days.(**Figure 2**)
3. Risk Factors: Habit of cleaning her ears 2–3 times per week, increasing the likelihood of external auditory canal microtrauma.
4. Diagnostic Workup[4,5]: Her samples were cultured on a plate of Blood agar and Nutrient agar. After 24 hrs of incubation, there was no growth seen on the plates. Culture showed growth exclusively on SDA, with greenish-yellow velvety colonies of 1–2 cm in diameter. *Aspergillus nidulans* identification was done based on the characteristic and morphological features explained in BOX 1.
5. Management: Antifungal therapy was initiated, and symptoms gradually resolved.
6. Clinical Significance: This case highlights paediatric susceptibility to fungal CSOM and demonstrates the importance of early fungal investigation, especially when bacterial cultures are sterile.

2.3. Case 3

1. Patient Profile: A 26-year-old immunocompetent female housewife with no history of chronic illness or prior ear surgery presented to the ENT OPD.
2. Clinical Presentation: She reported right-sided ear pain, mucoid discharge, hearing loss, temporal headaches, tinnitus, and recurrent nasal congestion.

3. Risk Factors: The patient cleaned her ears approximately 2–3 times per month. No other significant exposures were noted.
4. Diagnostic Workup: Direct microscopy of the discharge showed no organisms or pus cells. However, the clinical suspicion of otomycosis was high. While initial microscopy was inconclusive, SDA culture showed growth consistent with *Aspergillus nidulans*, confirmed by morphological features (BOX 1, **Figure 3**, **Figure 4**).
5. Management: Topical antifungals and mechanical debridement of debris were performed, with symptomatic relief achieved over follow-up.
6. Clinical Significance: This case illustrates that fungal otitis may not always be apparent on direct microscopy, emphasizing the need for culture in suspected cases.

2.4. Case 4

1. Patient profile: A 35-year-old otherwise healthy female with a prior diagnosis of CSOM attended the ENT OPD.
2. Clinical Presentation: She complained of right ear pain, hearing loss, and a sensation of a foreign body or blockage. Discharge was intermittent and whitish, but non-foul-smelling.
3. Risk Factors: The patient used cotton buds for ear cleaning several times a week.
4. Diagnostic Workup: Microscopy revealed very few pus cells and no organisms. Culture on SDA initially showed minimal growth, which became more prominent after one week. The colonies appeared velvety white with internal orange and dark pigmentation. (**Figure 3**, **Figure 4**). The presence of septate hyphae, biseriate phialides, and Hülle cells confirmed *Aspergillus nidulans*. (Box 1, **Figure 5**)
5. Clinical Significance: This case emphasizes the delayed growth potential of *A. nidulans*, reinforcing the need for extended incubation in fungal cultures and caution against premature reporting.
6. Management: The patient was treated with topical clotrimazole ear drops twice daily for two weeks and oral itraconazole (100 mg daily) for 10 days.

Figure 1: Mucopurulent discharge in the middle ear (Case 1)

Figure 2: Greenish mucopurulent discharge (case 2)

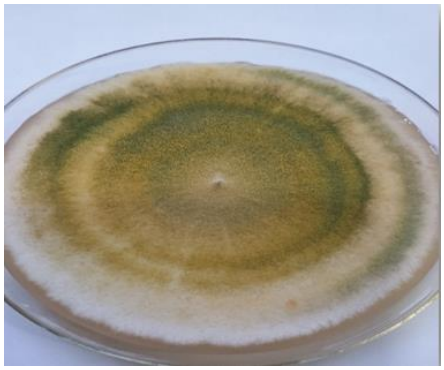

Figure 3: Growth of Aspergillus nidulans on SDA- showing greenish yellow velvety colonies (Obverse view)

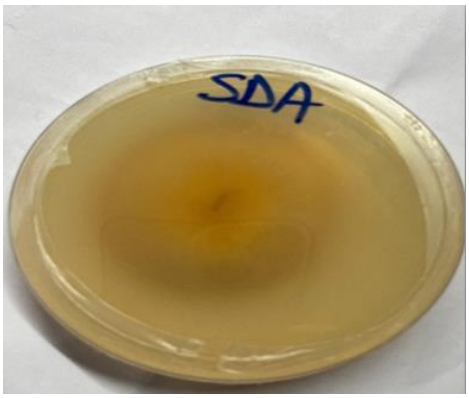

Figure 4: Growth of Aspergillus nidulans on a plate of SDA- - Brown pigment (Reverse view)

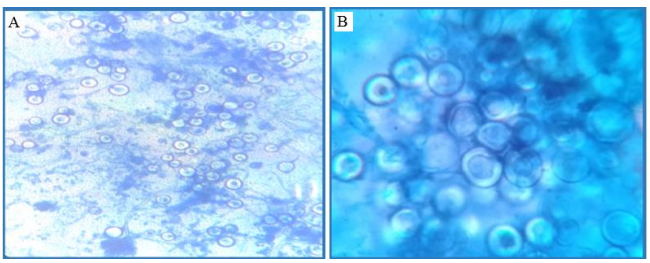

Figure 5: A*:* LPCB mount showing numerous large, thick-walled, spherical Hülle cells of *Aspergillus nidulans.* These hyaline structures, characteristic of the sexual stage of the fungus, typically found surrounding cleistothecia in mature cultures*;* ***B:*** LPCB mount showing abundant thick-walled, spherical Hülle cells (Enlarged view)

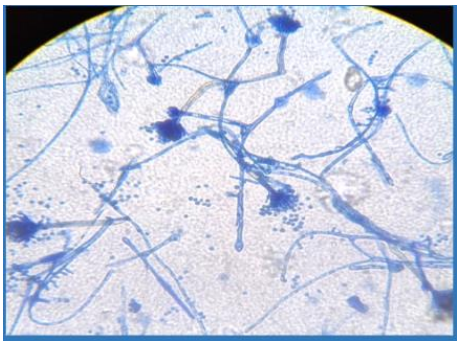

Figure 6: LPCB Mount of Aspergillus nidulans showing septate hyphae, short conidiophore, Biseriate arrangement (40X)

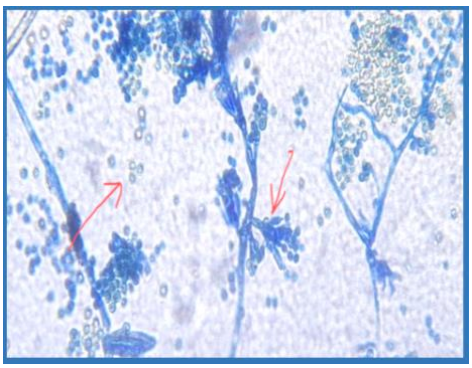

Figure 7: LPCB mount showing classical features of *Aspergillus nidulans:* septate hyphae, short conidiophores terminating in dome-shaped vesicles with biseriate arrangement of metulae and phialides, and chains of rough-walled conidia. Hülle cell is also seen at the lower left corner, supporting identification.

2.5. Case 5

1. Patient Profile: A 25-year-old female, working in a temple, presented with bilateral ear symptoms.
2. Clinical Presentation: She reported right ear pain aggravated by eating, hearing loss, bilateral ear itching, and a sudden onset of intermittent ear discharge.
3. Risk Factors: History included tobacco use, thyroid disorder, and frequent use of foreign objects to clean the ear (4–5 times per month). She had a previous diagnosis of CSOM.
4. Diagnostic Workup: No organisms or pus cells were seen on microscopy. Routine bacteriological cultures were sterile. Fungal culture on SDA was pending at initial reporting but subsequently yielded colonies consistent with *Aspergillus nidulans*.(**Figure 3**, **Figure 4**)
5. Clinical Significance: This case highlights the importance of considering fungal pathogens in CSOM, especially when patients present with recurrent symptoms and sterile bacterial cultures.

3. Discussion

Fungal infections of the ear are an often-overlooked component of CSOM, especially when patients present with nonspecific symptoms or when empirical antibiotic therapy masks or modifies the disease course. In our case series, *Aspergillus nidulans* was isolated from five patients presenting with chronic otologic symptoms, highlighting its potential role as an etiological agent in both paediatric and adult populations. While *A. nidulans* is rarely isolated from ear infections, its identification in multiple cases suggests it may be underdiagnosed. This could be attributed to its relatively slow growth in culture and the subtlety of its macroscopic features, which can mimic other *Aspergillus* species. However, the consistent presence of septate hyphae, long conidiophores with metulae and phialides, and particularly Hülle cells in all our isolates facilitated accurate diagnosis.[4,5] The latter is a hallmark of *A. nidulans* and is seldom found in other *Aspergillus* species, serving as a key diagnostic clue. Several risk factors were recurrent across our cases, including the use of cotton buds or other foreign objects to clean the ears, which likely caused microabrasions in the external auditory canal and predisposed to fungal colonization.[6,7] Notably, one patient was diabetic, a well-established risk factor for fungal infections due to impaired immune response and a favorable glucose-rich microenvironment. Interestingly, most of our patients were otherwise healthy, suggesting that *A. nidulans* can infect immunocompetent hosts given sufficient local predisposing conditions. The diversity of clinical presentations—from foul-smelling mucopurulent discharge to subtle itching and hearing loss—also highlights the diagnostic challenge. In two cases, direct microscopy was non-revealing, but culture yielded the pathogen, underscoring the importance of fungal cultures even when initial smears are inconclusive. Moreover, delayed fungal growth in culture observed in some cases stresses the need for prolonged incubation times, especially when fungal etiology is suspected.

In summary, this case series reaffirms the need for clinicians and microbiologists to maintain a high index of suspicion for *Aspergillus nidulans* in chronic ear infections. Its identification requires careful attention to both clinical and mycological clues. Furthermore, awareness about the ototoxicity of habitual ear-cleaning practices and over-the-counter topical agents should be emphasized in patient education to prevent such infections.[6,7] Unlike more aggressive pathogens, *A. nidulans* tends to present subtly. Its identification demands careful mycological examination. In our cases, direct microscopy using Gram staining revealed fungal hyphae in three out of five patients, but it failed to detect organisms in the remaining two, underscoring the limitations of routine microscopy in low-load infections. Importantly, all five isolates were confirmed by culture on Sabouraud Dextrose Agar, albeit with delayed growth in some cases. The characteristic velvety surface and inner orange pigmentation, along with the presence of septate hyphae and distinctive Hülle cells on microscopy, helped in confidently identifying *A. nidulans.*[8] This slow-growing nature often leads to underdiagnosis if cultures are discarded within 48–72 hours. As seen in our series, at least two cultures showed visible growth only after prolonged

incubation, emphasizing the need for extended culture periods in cases of suspected otomycosis, especially when initial microscopy is negative, but clinical suspicion persists. Interestingly, the spectrum of disease caused by *A. nidulans* is typically limited to superficial infections; however, in immunocompromised hosts, it has been reported to cause deeper tissue infections and even disseminated disease. Fortunately, none of our patients progressed beyond localized infection, and all responded well to topical antifungal therapy combined with regular ear toileting. Agents such as clotrimazole and miconazole, along with mechanical removal of fungal debris, remain the cornerstone of treatment.[4,8] Systemic therapy was not required in any of the presented cases. From a microbiological standpoint, this series reinforces the importance of species-level identification in fungal ear infections.

3.1. Antifungal susceptibility and efficacy[4,9,10]

From a therapeutic standpoint, *Aspergillus nidulans* demonstrates variable susceptibility to antifungal agents. In vitro studies have shown that it is generally susceptible to topical azoles, including clotrimazole, miconazole, and econazole, which are commonly used in the treatment of otomycosis. All five patients in our case series responded well to topical clotrimazole or miconazole, combined with regular aural toileting and removal of fungal debris. Systemic therapy was not required in any case, aligning with the superficial and localized nature of the infections. However, it's important to note that *A. nidulans* is known to exhibit reduced susceptibility to amphotericin B and echinocandins, and in immunocompromised patients or in cases of invasive disease, treatment may require triazoles such as voriconazole or posaconazole. These agents have shown good in vitro activity, although resistance patterns can vary regionally. Therefore, species-level identification, along with antifungal susceptibility testing, remains essential, especially in recurrent or refractory cases. This highlights the role of the microbiology laboratory not only in diagnosis but also in guiding effective treatment strategies.[11]

4. Conclusion

This case series sheds light on the uncommon but clinically relevant role of *Aspergillus nidulans* as an etiological agent in CSOM. Though typically considered a less virulent environmental saprophyte, *Aspergillus nidulans* can act as an opportunistic pathogen in individuals with local or systemic risk factors, such as chronic ear infections, diabetes, or habits that compromise the ear's natural defenses. Our findings highlight the indispensable role of fungal culture, prolonged incubation, and microscopic examination—including identification of Hülle cells—for accurate species-level diagnosis. In conclusion, *A. nidulans* should be considered in the differential diagnosis of otomycosis, particularly in cases with slow-growing colonies or atypical presentations. Awareness among clinicians and microbiologists, along with appropriate diagnostic support, can ensure these infections are not overlooked and are treated promptly and appropriately.

5. Source of Funding

None.

6. Conflict of Interest

None.

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