



Fungal Suppurative Otitis Media (Histopathology) Among Patients in North India

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Abstract

Chronic suppurative otitis media (CSOM) has a substantial worldwide prevalence and is a major cause of hearing impairment. In cases of CSOM unresponsive to local antibiotics, superimposed fungal infection should be suspected. The aim of the present study was to study the spectrum of cases with fungal otitis media. The study was conducted over a period of 12 years (2006–2017). Fifteen cases of CSOM clinically not suspected to be of fungal etiology that underwent surgery with identification of fungal organisms on histopathology were included in the study. Age of the patients ranged from 12 to 75 years (mean age: 37.1 ± 22.7 years). Of 15 cases, 9 (60.0%) were males and 6 (40.0%) were females. It was a unilateral presentation in all. The complaints observed were ear discharge in all followed by itching (86.7%), pain (46.7%), decreased hearing (26.7%) and blocking sensation (13.3%). Histomorphologic typing of fungus was possible in 13/15 patients. Isolated aspergillus was identified in eight patients while mucor alone was seen in three patients. Mixed infection with Aspergillus + Candida and Aspergillus + Mucor was seen in one patient each. Categorization of fungus could not be done in rest of the two patients due to paucity of fungal profiles. Histopathological identification of fungal organisms in otomycosis provides a quick and fairly reliable diagnosis. Culture is considered the gold standard but it may not always be available or fruitful. Less turnaround time and accurate diagnosis facilitates prompt and optimal therapy in fungal otitis media thus preventing adverse outcomes.

Keywords Fungal · Chronic suppurative · Otitis media · Histopathology

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Introduction

Chronic suppurative otitis media (CSOM) is defined as infection of the middle ear that lasts for > 3 months and is accompanied by tympanic membrane perforation [1]. Worldwide prevalence of CSOM is 65–330 million people and about half of these suffer from hearing impairment [2, 3]. In cases of CSOM, which do not respond to local antibiotics, superimposed fungal infection should be suspected [4]. Though culture studies are considered the gold standard for identification of etiologic agents, they may not always be available or turn positive.

Histopathologic examination remains one of the major diagnostic tools in mycology because it permits rapid, presumptive and fairly reliable identification of fungal infections [5]. Further it helps to delineate whether culture positivity denotes contamination, colonization or true infection. Tissue and vascular invasion, and the host reaction in form of inflammation, necrosis or hemorrhage indicate true fungal infection. Preliminary identification of infectious fungal organisms on histopathology in cases of otitis media is often

the only diagnostic clue when material is not submitted for culture.

The aim of the present study was to study the spectrum of cases with fungal otitis media and type the fungal structures wherever possible.

Materials and Methods

The study was conducted in a tertiary care teaching hospital in the Department of Pathology in collaboration with departments of Otorhinolaryngology and Microbiology over a period of 12 years (2006–2017). 7426 patients visiting Otorhinolaryngology outpatient department were clinically diagnosed as CSOM. Fifteen cases of CSOM clinically not suspected to be of fungal etiology that underwent surgery with material available for histopathology were included in the study. Informed consent was taken from all the patients. Clinical and radiological details were obtained from the patients' file records. Fungal etiology was not suspected clinically and hence the material was not submitted for culture. The biopsy material was received in 10% neutral buffered formalin. Routine hematoxylin and eosin (H&E) stained sections were studied for histopathology. Special stains i.e. periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) were evaluated before rendering the final histopathologic diagnosis. Furthermore, attempt was made to sub-classify the fungi on histopathology.

Results

Age of the patients ranged from 12 to 75 years with mean age of 37.1 ± 22.7 years (Table 1). Out of 15 patients, 9 (60.0%) were males and 6 (40.0%) were females. Male to female ratio was 1.5:1. It was a unilateral presentation in all the cases. The complaints observed were ear discharge in all the patients followed by itching (86.7%), pain (46.7%), decreased hearing (26.7%) and blocking sensation in the ear (13.3%). The duration of symptoms ranged from 6 months to 10 years. High resolution computed tomography (HRCT) scan temporal bone was available in nine cases (Fig. 1). Associated systemic disease, diabetes was present in one case. All the patients had sought medical attention elsewhere before reporting to our facility. Histomorphologic typing of fungus was possible in 13/15 patients. Isolated *Aspergillus* was identified in eight patients while *Mucor* alone was seen in three patients (Fig. 2). Mixed infection with *Aspergillus* + *Candida* and *Aspergillus* + *Mucor* was seen in one patient each. Categorization of fungus could not be done in rest of the two patients due to paucity of fungal structures. The histological findings in addition to identification of fungus were consistent with cholesteatoma in nine patients and inflammatory polyp in two while non descript findings were observed in four patients.

Table 1 Clinical and histopathology findings in fungal otitis media (n = 15)

Case no.	Age/sex	Ear involved	Complaints	Duration	Histopathology
1	25 years/M	Right	Itching, ear discharge	10 years	<i>Aspergillus</i>
2	15 years/M	Left	Pain, itching, ear discharge	4 years	Typing not done
3	49 years/M	Right	Ear discharge	6 months	<i>Mucor</i>
4	23 years/F	Left	Pain, itching, ear discharge	6 months	<i>Aspergillus</i>
5	15 years/M	Right	Itching, ear discharge	6 years	<i>Aspergillus</i> with candida
6	72 years/M	Right	Pain, itching, ear discharge, decreased hearing, blocking	2 years	<i>Aspergillus</i>
7	50 years/F	Right	Pain, ear discharge, decreased hearing	6 months	<i>Aspergillus</i>
8	75 years/F	Left	Itching, ear discharge	5 years	<i>Mucor</i>
9	58 years/M	Right	Pain, itching, ear discharge	1 year	<i>Mucor</i> with <i>aspergillus</i>
10	29 years/F	Left	Itching, ear discharge, decreased hearing	3 years	Typing not done
11	15 years/M	Left	Itching, ear discharge	10 years	<i>Aspergillus</i>
12	19 years/F	Right	Pain, itching, ear discharge, blocking	1 year	<i>Aspergillus</i>
13	70 years/M	Right	Itching, ear discharge	6 months	<i>Mucor</i>
14	29 years/F	Left	Pain, itching, ear discharge	3 years	<i>Aspergillus</i>
15	12 years/M	Right	Itching, ear discharge, decreased hearing	10 years	<i>Aspergillus</i>

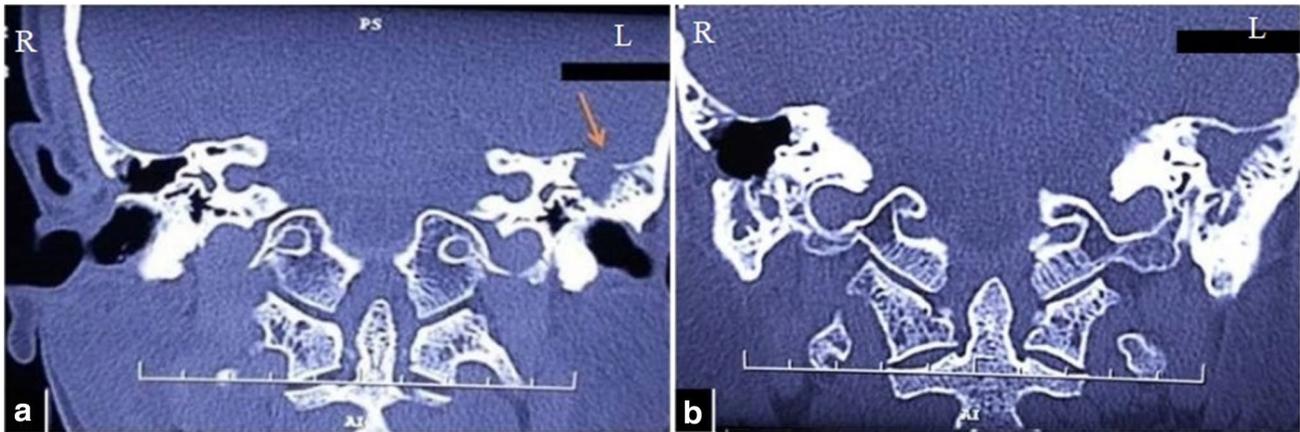


Fig. 1 **a, b** HRCT scan temporal bone, coronal sections showing soft tissue density in the left mastoid antrum and mastoid air cells with destruction of tegmen tympani (arrow) in a case of fungal otitis media with cholesteatoma

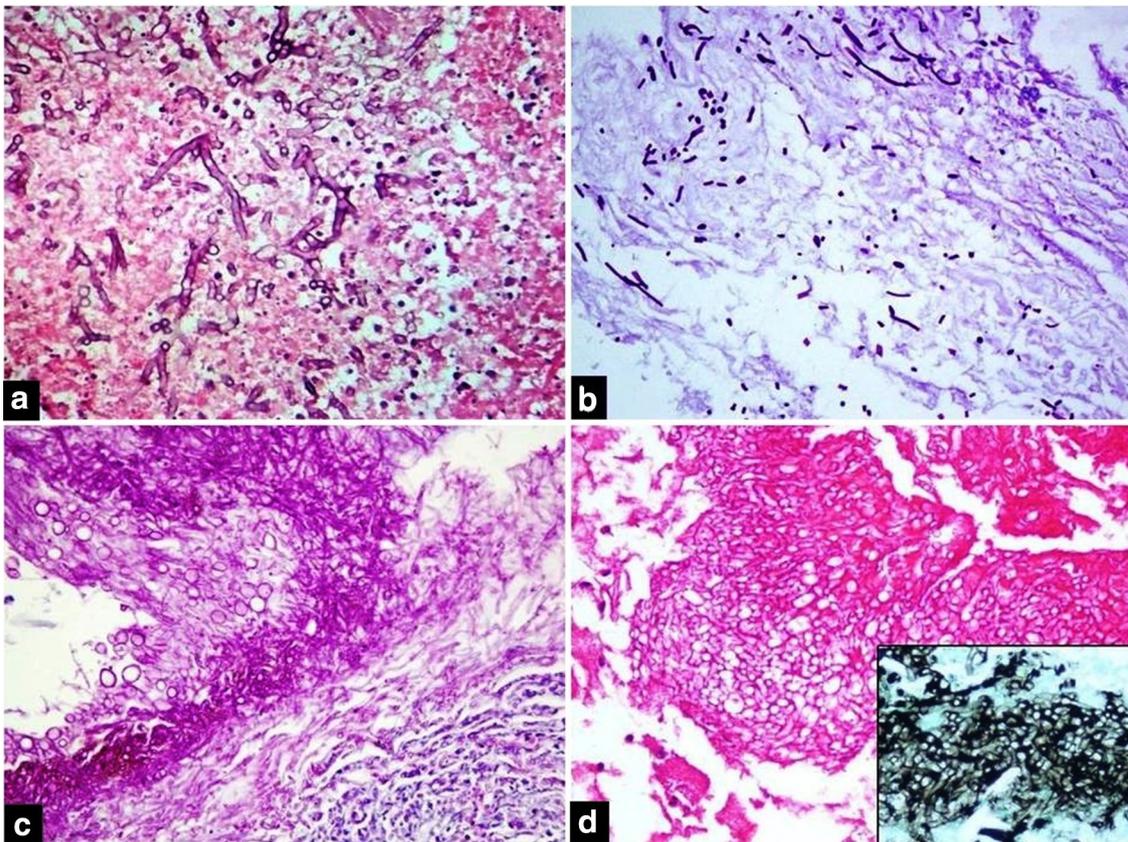


Fig. 2 Fungal otitis media: **a** section showing thin septate fungal hyphae conforming to morphology of aspergillus in a necrotic background (H&E×400) **b** Periodic acid Schiff stained section showing budding yeasts and pseudohyphae of candida (PAS×200) **c** Fungal

elements from aspergillus and mucor (PAS×200) **d** Necrotic debris rich in broad aseptate fungal hyphae of mucor (H&E×400). Inset shows fungal profiles highlighted on Gomori methenamine silver special stain (GMS×400)

Discussion

Chronically draining ear in CSOM is often associated with significant hearing loss and can be difficult to treat [6]. Suppuration can occur with or without cholesteatoma, and the clinical history of both the conditions can be very similar [7]. Prevalence of fungal infections of the ear during moist and humid conditions is high in tropical countries [8, 9]. Coexistent conditions such as diabetes, chemotherapy, malignancy, steroid administration, HIV infection, and prolonged antibiotic use (topical or systemic) render an individual more susceptible to fungal infections of the middle ear [10–12].

Patients with mycotic ear infections have one or more clinical symptoms which include otorrhoea, pruritus, otalgia, tinnitus, fullness, hearing loss, and blocking sensation [13, 14]. In the present study ear discharge was seen in all the patients followed by itching (86.7%), pain (46.7%), decreased hearing (26.7%) and blocking sensation in the ear (13.3%). Otomycosis can occur at any age and has a slight male predilection [9, 15]. Male to female ratio was 1.5:1 in our study. Unilateral ear involvement is seen in vast majority of the patients with right ear being affected more frequently [13, 16]. Bilateral ear involvement is uncommon and seen mostly in immunocompromised patients [15, 17]. None of the cases in our study had bilateral ear involvement and right ear was involved in 9 of the 15 cases.

Information on the exact prevalence of CSOM cases with secondary fungal infections is conspicuously lacking. Otomycosis or ear fungus is usually misdiagnosed as a bacterial infection instead of fungal infection due to which the patient is prescribed antibiotic ear drops in the initial stages [18, 19]. It is only when the antibiotics do not improve the patient's condition that the ear fungus is suspected. Fungal agents commonly implicated in otomycosis are *Aspergillus*, *Candida* and *Penicillium* [7]. In the current study, *Aspergillus* was the most common fungal agent seen in 9 cases out of total 15 cases. Mixed fungal infections are rare and are caused by fungal species from different genera [9]. Two such cases (*Aspergillus* + *Candida* and *Aspergillus* + *Mucor*) were seen in our study. Fungal structures can be picked up on routine H&E stain. Structures bearing resemblance with fungi include Russell bodies, elastic fibres and tiny blood vessels [20]. Diligent scrutiny of histopathologic section by the pathologist prevents overcalling these as fungal structures. Gomori methenamine silver and periodic acid-Schiff are the two most common special stains employed to highlight fungi in tissues and cytology specimens in daily pathology practice.

Pathologists need to give as much information as possible to the treating clinician. Nevertheless, despite best

of the efforts misclassifications do occur on histopathologic examination in at least 20% of the cases [21]. Culture is the gold standard for diagnosis of fungal infection but when the entire specimen is placed in formalin; histopathology, immunohistochemistry (IHC) [22], and molecular profiling [in situ hybridization, and polymerase chain reaction (PCR) with formalin fixed paraffin embedded material] [23] are the only means available to detect specific fungi for diagnosis and research. IHC is commercially available to detect *Aspergillus* spp. and mucormycetes in tissue though a large number of antibodies cross-react with multiple fungi [5]. Automated platforms are available for in situ hybridization which has good specificity compared to histochemistry and immunohistochemistry. Long turnaround time and exorbitant cost are common constraints in a resource poor set up. PCR assays can also be done using various DNA extraction methods. Sequences specific to a particular organism can be targeted or amplification of panfungal gene followed by sequencing the fungal DNA can be done.

When microbiologists, pathologists and clinicians communicate effectively and timely, correct diagnosis of many difficult-to-diagnose cases of otomycosis can often be made [5]. Topical antimycotic agents like clotrimazole, miconazole, fluconazole, tolnaftate, naftifine, bifonazole, econazole, etc are effective in treatment of otomycosis [24]. Fluconazole, itraconazole, posaconazole and voriconazole are systemic antifungals for patients with mastoiditis and cerebral mycosis. Combined use of systemic and topical antimycotic agents is often necessary in immunocompromised patients.

Conclusions

Chronic ear discharge unresponsive to antibacterial therapy warrants suspicion for mycotic otitis media. Histopathologic evaluation is a quick and easy way to identify fungal organisms. ENT specialists should necessarily be aware of the leading causal agent depending on different geographical locales in order to prescribe antifungal drugs appropriately.

Author Contributions RSP conceptualized the study. RSP, SKS, AD, JC did the data interpretation. RSP, SKS and RK did collection and analysis of data, literature search and prepared the manuscript. RSP, SKS, JC and AD revised the final manuscript critically for important intellectual content.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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