

## ***Cryptococcus neoformans* – A Causative Agent of Meningitis, in a case of Chronic Suppurative Otitis Media**

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**Cryptococcal ear infection is an uncommon but often an undiagnosed fatal complication associated with the ear. This study was undertaken due to the enormous childhood morbidity and health care costs associated with otological infections, together with the increasing prevalence of antibiotic resistant middle ear bacterial pathogens. The aims of this study were to isolate and identify micro-organisms responsible for ear infections and determine their antibiotic susceptibility pattern.**

**Keywords:** *Cryptococcus neoformans*, Otological infections, Chronic Suppurative Otitis Media.

Fungal infection is one of the common causes of otitis externa (Pahwa *et. al.*, 1983). Fungal infections of the ear have increased in incidence over the past few decades. Otomycosis is a chronic condition that is found predominantly in tropical and subtropical regions and is rare in infants and children. A perusal of literature on ear infections in India shows that *Aspergillus niger* and *Candida* spp were the most frequently isolated fungal species (Pahwa *et. al.*, 1983 and Jaisawal 1990). Most infections are due to *A. niger* or, less commonly, *A. fumigatus*; coinfection with *Staphylococcus aureus* or *Pseudomonas* species. Otomycosis prevails in India during the rainy season. Antifungal resistance has become a clinically relevant problem. The frequency of fungal infections is on the rise due to increase in the number of immuno-compromised patients (Joy *et. al.*, 1980). We report a rare case of *Cryptococcus neoformans* in chronic suppurative otitis media.

### **MATERIAL AND METHODS**

A forty year old woman was referred in July 2005 for moderate hearing loss in the left ear. The patient complained of constant headache and nausea with an inconsistent increase in body temperature. Case records of the patient were checked for diabetic history. The ear aspirate was processed for aerobic, anaerobic and fungal growth. CSF and urine cultures were also analysed for microbial growth.

Samples taken from patient were checked for the values of Serum creatinine, haemoglobin, granulocytes and bilirubin and the results were compared with the standard values for inclusion. Antifungal Susceptibility Testing of *Cryptococcus neoformans* was carried out as per NCCLS standards (NCCLS, 1995), against Amphotericin-B, Fluconazole and Ketoconazole by employing the more effective Antibiotic Medium 3. These tests were done in triplicates to confirm the results.

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## RESULTS

On examination, chronic otorrhoea with cholesteatoma, with pus in middle ear cleft and otoblenorrhoea was observed in the patient after ear infection. Case records of the patient showed a family history of being diabetic with an increased glucose level of 212mg/dL. She also had a bout of meningitis in April 2005. A clear watery discharge was seen in this case from middle ear. The ear aspirate that was processed for aerobic, anaerobic and fungal growth yielded no aerobic and anaerobic growth but the Fungus *Cryptococcus neoformans* produced mucoid colonies when inoculated onto Sabouraud's agar.

The yeast cell was found to be large and round on wet preparation.

The first episode of cryptococcal infection in middle ear was included, as the following criteria regarding aspirate was satisfied<sup>4</sup>

- a) A culture positive for *Cryptococcus neoformans*
- b) A positive India Ink Preparation
- c) A positive urease test.

Laboratory criteria for inclusion included the standard values provided by Graybill (1996). The results obtained for the parameters tested are suggestive of Cryptococcal infection. (Table 1).

Antifungal Susceptibility Testing of *C. neoformans* against Amphotericin-B,

**Table 1.** Comparison of the patient sample with the standard values

S. No.	Parameters tested	Standard values	Values shown by patient	Inference
1.	Serum creatinine	> 2.0mg/dL	4.0mg/dL	Serum value was observed to be more than the required.
2.	Hemoglobin	< 8.0 g/ dL	5.0 g/ dL	Abnormal Hemoglobin levels
3.	Granulocytes	< 700/mm <sup>3</sup>	600/mm <sup>3</sup>	Low granulocyte count
4.	Bilirubin	> 2 times normal.	6 mg/ml.	High bilirubin content

Fluconazole and Ketoconazole confirmed that it was sensitive to all. Amphotericin B deoxycholate (a cumulative dose of 0.5 mg) for 6 weeks was given to the patient. The clinical response was observed to be good. Then, Amphotericin-B treatment was continued for four months. No relapse was seen after 5-month follow-up.

## DISCUSSION

Otitis media is a potentially serious disease mainly because of its complications. Avicenna, An Arabian Physician in 930 A.D showed the co-relation between ear discharge and discharge of brain disease. Later, in 1682, Morgagni identified that persistent ear infection led to brain abscess.

Cerebellar abscess is one of the most serious forms considered to be secondary to otitis media (Set, et. al., 2001). Brain abscess was the

first complication of Otitis media to be recognized and it was the first one successfully treated by operation. Analysis of cerebrospinal fluid (CSF) usually reveals a poor white blood cell (WBC) count, inflammatory response, with a normal or low-CSF glucose levels (Subramanian and Mathai 2005) but in this case infection persisted in presence of high glucose level. A watery discharge is indicative of skull trauma, which is caused due to leakage to cerebro-spinal fluid. When granulocytes are fewer than 1000 are detected in the aspirate, the patient could have a partially treated meningitis or meningitis of fungal origin (Glasscock and Shambaugh 1998). Otitis media was far more the frequent cause of meningitis not due to meningococcus. Standard therapy for acute cryptococcal meningitis consists of administration of Amphotericin-B alone or in combination with flucytosine (Bennett et. al., 1979 and Dismukes et al., 1987).

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