



# Deafness in the Elderly – an Atypical Presentation of Cryptococcal Meningitis

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## Abstract

*Cryptococcus neoformans* is the most common cause of fungal meningitis in both immunocompromised and immunocompetent hosts. Elderly patients account for one-third of cases and presentations are usually atypical. Sensorineural deafness is a common sign of aging but is also one of the complications of cryptococcal meningitis, occurring in more than a quarter of patients. Most of the deafness is bilateral and irreversible, hence devastating for the patient. Visual disturbance is not associated with sensorineural deafness in cryptococcal meningitis. Cryptococcal meningitis should be one of the differential diagnoses in patients with sudden onset of deafness with neurologic symptoms. A prompt diagnosis and directed treatment may prevent further complications of the disease. (J Intern Med Taiwan 2015; 26: 319-323)

**Key Words:** Cryptococcus, Meningitis, Elderly, Deafness

## Introduction

Deafness is one of the more commonly known sequelae of bacterial meningitis. Hearing loss has also been described in meningitis of other infectious or non-infectious causes<sup>1</sup>. Infectious causes of meningitis reported to have caused deafness includes tuberculosis, leptospirosis, mumps, syphilis, *Salmonella*, viruses and *Cryptococcus neoformans*<sup>2-8</sup>.

*Cryptococcus meningitis* is known to be a disease of the immunocompromised. Risk factors for acquisition of this disease includes HIV infection, sarcoidosis, leukemia, lymphoma, sickle cell disease, organ transplant recipients, liver cirrhosis, diabetes mellitus, lung cancer, chronic obstructive

pulmonary disease, innate immunologic and hematological disorders, usage of immunosuppressive agents such as glucocorticoids, cytotoxic chemotherapy and TNF- $\alpha$  inhibitors<sup>9-14</sup>. The proportion of cryptococcosis in the elderly has increased markedly in the late 20th century<sup>15</sup>. Atypical presentations of cryptococcal meningitis such as mania, postural headache and non-syncopal fall have been reported in this age group<sup>16-19</sup>. Here, we present a 98 year-old immunocompetent woman who presented with bilateral sensorineural hearing loss as the initial manifestation of cryptococcal meningitis and review the literature regarding the features of cryptococcal meningitis associated deafness.

## Case

A 98 year-old female presented to our hospital with fever, rhinorrhea, dizziness, nausea, vomiting and chest discomfort that were associated with transient confusion. She was conscious at presentation and was treated with moxifloxacin due to a nodular lesion in the right lung field. She denied having any systemic illnesses other than being treated for pulmonary tuberculosis 3 years ago. Her fever subsided and she was lost to follow up until 2 months later when she developed deterioration of her auditory function in both ears along with persistent right chest pain with dizziness. Another chest X-ray showed enlargement of the previous lung nodule in the right lower lung field. A computed tomography of the lung was done and revealed a 2.2 cm nodule in the right middle lung with visceral pleural invasion. Based on the imaging, she was diagnosed to have lung cancer, right lower lung field, stage IV:T2/N0/M1a, with sensorineural hearing loss and was referred to hospice care.

Serum cryptococcus antigen level was tested due to recurrence of low-grade fever and the titer was  $\geq 1:1024$ . She was released from hospice care and started on liposomal amphotericin B therapy on the presumptive diagnosis of cryptococcosis of the lung. A lumbar tap was done and the opening pressure was 28 cm H<sub>2</sub>O. Cerebrospinal fluid (CSF) analysis found a white blood cell (WBC) count 38 cells/cumm, all lymphocytes. The CSF protein, glucose and lactate level were 89.8mg/dL, 2mg/dL and 5.82 mg/dL, respectively. *Cryptococcus neoformans* were isolated from both her CSF and blood. The pulmonary nodule regressed gradually after treatment. No improvement in her deafness was observed after 3 months of treatment.

## Methods

The Medline database for English language literature was searched for the terms “cryptococ-

cus” “meningitis,” “hearing” and “deafness”. Titles, abstracts, full texts and references were reviewed by one of the authors.

An article was included if the clinical details of individual patients were described. Information recorded included age, sex, underlying medical conditions, CSF protein and glucose level, opening pressure during lumbar tap, otologic signs and symptoms including vestibular involvement, reversibility of deafness, and side of deafness during course of the disease.

## Results

The search yielded 24 relevant articles<sup>20-43</sup>. A total of 33 patients, including our patient, are included in this review. The mean age was 43.97 (SD 19.06, range 16-98) years. Our patient was the oldest in the group. Twenty-one (63.6%) of the patients were male. Eight (24%) had HIV, 2 (6%) had DM, 1 (3%) had liver cirrhosis, 1 (3%) had chronic lymphocytic leukemia and 1 (3%) had idiopathic CD4+ lymphopenia. Twenty (60.6%) had no recorded underlying diseases. The mean CSF opening pressure in 16 patients was 37.6 (SD 13.6, range 19-60) cm H<sub>2</sub>O. The mean CSF glucose and CSF protein level (N=12) was, 30.1 (range 2-101) mg/dL and 124.8 (range 24-380) mg/dL, respectively. Forty-two percent (14/33) of the patients had visual signs and symptoms. Thirty-three percent of patients had blurred vision and 21.2% became blind during the course of the disease. Hearing loss was bilateral in 78% (17 out of 22) of patients. Most (92.6%) of the 27 patients with documented hearing loss had sensorineural hearing loss and 7.4% had a mixed type of deafness. Eleven out of the 32 (34.4%) patients died during the course of the meningitis. The otologic outcome of 18 of the 21 surviving patients was documented, among which 10 (55.6%) had irreversible deafness. Six patients had recovered partially and 2 recovered fully.

## Discussion

The clinical presentation of cryptococcal meningitis may be non-specific and diagnosis may be difficult. The age of our patient and the absence of underlying risk factors render the diagnosis of cryptococcus meningitis more difficult. Fever, headache, and altered mental status are seen in less than 50% of patients<sup>35,44,45</sup>. Diagnosis is particularly difficult in the elderly since patients may present with unusual clinical manifestations of the disease. Common clinical findings in an elderly such as falling during ambulation, postural headache, tinnitus, even in the absence of meningeal signs and altered mental status may be the only signs and symptoms of cryptococcus meningitis.<sup>16,17,26</sup> Deafness has been reported in 27 to 43% of patients with cryptococcal meningitis<sup>35,45,46</sup>, but only 37.5% of these patients were symptomatic. Hearing loss was documented in the rest of the patients only through audiometric testing<sup>35</sup>. Audiometry may show mild unilateral or severe, bilateral, sensorineural hearing loss with a predominantly retrocochlear involvement<sup>24</sup>. The more obvious signs and symptoms of meningitis such as headache and fever may dominate the symptoms of hearing loss, particularly in its mild form. The deafness can be fluctuating, sudden, or progressive during presentation<sup>21,26</sup>. It can progress from mild, unilateral to profound, bilateral hearing impairment<sup>26</sup>. Involvement of the vestibular system may or may not be observed<sup>23,24,31</sup>. Restoration of vestibular function was seen in some patients after treatment<sup>33</sup>. The pathogenic mechanism of hearing loss may be due to direct invasion of the temporal bone, destruction of the spiral ganglion and cochlear nerve or meningeal irritation<sup>35</sup>. Histologic studies of patients with cryptococcal meningitis demonstrate different extents of auditory involvement. Loss of cochlear neurons with disruption of the saccular macula, vestibular nerves, epithelium of the utricle, saccule and ampullae of the semicircular canals, has

been reported in different studies<sup>21,22,32,34</sup>. Harada, et al<sup>31</sup>, however reported the sparing of the vestibular nerves and end organs.

Persistence or progression of the sensorineural hearing loss could probably be due to direct invasion of the neural tissue and sensory end organs<sup>32,33</sup>, or persistence of cryptococcal infection. Cryptococcus was seen in the histopathology of temporal bones of a patient 7 years after being receiving a 2-month regimen for amphotericin B for cryptococcal meningitis<sup>31</sup>. Though one patient functioned well after being given an assisted hearing device<sup>26</sup>, the evidence of cochlear implantation is not sufficient. Patients with post bacterial meningitic deafness benefit significantly from cochlear implantation<sup>47</sup>, because bacterial meningitis, unlike cryptococcal meningitis, often spares the retrocochlear pathways. It is therefore expected that cochlear implantation are not helpful in cryptococcal meningitis associated deafness<sup>23</sup>. Post-implantation complications have been reported<sup>48</sup>, and procedure-associated morbidities should be considered before the decision to utilize these implants.

Visual disturbance was reported to be one of the risk factors for sensorineural hearing loss in cryptococcal meningitis<sup>35</sup>. Visual involvement may be due to direct cryptococcal invasion of the optic nerve, optic nerve infarction, or compression due to increased intracranial pressure<sup>20,36</sup>. Wang, et al<sup>35</sup> reported that visual disturbance was a predictive factor of hearing impairment in cryptococcal meningitis. However, only 42% of patients had either blindness or blurred vision in this review. This could be due to variability of the severity and invasion of the cryptococcal infection. Other reported cases of visual disturbance included 3 cases of diplopia in patients with cryptococcal meningitis related sensorineural hearing loss<sup>20,25,42</sup>.

The incidence of deafness associated with cryptococcus meningitis may be underestimated. The duration of treatment for this complication is

not known. Clinical manifestations and CSF findings of cryptococcus meningitis in the elderly have not been well studied. This disease should be considered in both immunocompromised and immunocompetent hosts with sudden onset of deafness, especially when accompanied by neurologic signs and symptoms. Empiric systemic steroids for idiopathic sensory loss may cause grave consequences and unmask a fulminant form of this infection. Early diagnosis and timely treatment may halt the progression of the deafness and prevent further complications of the disease.

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## 老年人的聽障是隱球菌腦膜炎的非典型表現：文獻回顧

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### 摘要

新型隱球菌為免疫功能不全和正常宿主最常見的真菌性腦膜炎。高達三分之一的患者為老年人，且通常以非典型症狀表現。神經性聽覺障礙常見於年紀老化的退化，但也是隱球菌腦膜炎的併發症之一，且高達四分之一的病患可以發生。大部分聽覺障礙為雙側且不可逆，故對病患的重大影響。通常隱球菌腦膜炎的聽覺障礙不會合併有視覺障礙。隱球菌腦膜炎為突發性耳聾伴有中樞神經症狀的鑑別診斷之一。早期診斷和即時治療可預防發生相關併發症。