Cryptococcal Laryngitis: A Case Report

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Infections caused by Cryptococcus neoformans range from those in an asymptomatic state to systemic disease, especially in immunocompromised hosts. Laryngeal cryptococcal infections are extremely rare - only 7 cases have been reported in the literature. We present a case of cryptococcal laryngitis in an 83-year-old male with chronic obstructive pulmonary disease (COPD) and long-term corticosteroid use. The patient was admitted with a 14-day history of dysphagia, hoarseness, respiratory distress, and upper airway obstruction that necessitated tracheostomy. After intensive respiratory care and fluconazole treatment, his symptoms improved. (Thorac Med 2006; 21: 33-39)

Key words: cryptococcal laryngitis, cryptococcosis, laryngitis

Introduction

Cryptococcosis of the larynx was first described in 1975 by Reese [1]; 6 additional cases have been reported since then [2-7]. Cryptococcus neoformans is an encapsulated and well-documented pathogenic yeast [8-9]. The organism resides in soil and avian excrement, especially that of pigeons. Those who work with pigeons are at an increased risk of exposure, but most infected individuals do not have significant exposure to pigeons. Exposure generally causes a self-limiting subacute pulmonary infection in immunocompetent hosts, or spreads hematogenously, resulting in invasion of the central nervous system (CNS). Once it has invaded the CNS, the infection is fatal if not treated appropriately. One of the most important features of cryptococcal infections in patients with human immunodeficiency virus (HIV) infection, compared to those without, is that the former has a very high rate of relapse after treatment (30~50%) [10]. Cryptococcal infections occur predominantly in patients with T-cell-mediated immune defects, especially those with acquired immunodeficiency syndrome (AIDS) and those with transplant-related immunosuppression [11]. Acute epiglottitis is most common among children, and is a serious disease because of its potential for sudden fatal airway obstruction in previously healthy persons. Fatal airway obstruction can occur without warning, indicating a need for early protection of the airway in adults as well as in children [12]. However, cryptococcal infections rarely present as fungal laryngitis. Cryptococcus can infect the larynx in both immunocompromised and immu-
nocompetent hosts.

**Case Report**

An 83-year-old man presented with hoarseness, sore throat, and dysphagia for 2 weeks. He had a 25-year history of pipe smoking, but had quit after being diagnosed with chronic obstructive pulmonary disease (COPD) in 1987. He had been receiving high doses of oral corticosteroids at another institution to control his symptoms during the past 10 years. We tried a high dose of Seretide (salmeterol/fluticasone propionate) combination therapy to taper his oral corticosteroids. Later, his COPD was brought under control with a lower dose of glucocorticosteroids (predisolone, 5 mg a day) and Seretide 2-puff inhalation twice a day (salmeterol 200 mcg/fluticasone propionate 1000 mcg) for the following 2 years at our hospital. He had had no foreign travel history for more than 1 year and no exposure to pigeons in his neighborhood. Physical examination was unremarkable, although it revealed dyspnea and diffuse wheezing in both lung fields. The chest radiograph disclosed bilateral pulmonary emphysema without notable change compared to previous films. Laboratory studies showed LDH 527 IU/L, cholesterol 260 mg/dL, C-reactive protein 18.4 mg/dL (normal range, 0-0.8 mg/dL), and positive urine cryptococcal antigen. The patient refused a lumbar puncture for cerebrospinal fluid (CSF) studies after laryngeal biopsy proved cryptococcal infection. His arterial blood gas showed pH: 7.459, PCO₂: 45.3 mmHg, PO₂: 112.9 mmHg, HCO₃: 30.5 mmol/L, and O₂ saturation: 98.3% with nasal oxygen at 3 liters per minute.

The fibrobronchoscopic examination revealed a bilaterally edematous and erythematous epiglottis with nearly 85% obstruction of the airway. The false and true vocal cords were mobile. There were multiple, white, exudative papules

![Fig. 1. (A, B) Bronchoscopy reveals bilaterally edematous and erythematous epiglottis with nearly 85% obstruction. There were multiple, white, exudative papules on the vocal cords and epiglottis mucosa. (C, D) Follow-up bronchoscopy demonstrates that the white exudative lesions on the vocal cords and epiglottis had disappeared.](image-url)
over the vocal cords and epiglottis mucosa (Figures 1A & 1B). The patient had severe dyspnea after admission. The otorhinolaryngist was consulted for the upper airway obstruction, and tracheostomy was performed. Biopsy of the lesion gathered 4 tissue fragments up to 0.2 x 0.1 x 0.1 cm in size. The pathology showed chronic granulomatous inflammation-expressing inflammatory cells and a few giant cells. Gomori’s methenamine silver (GMS) and mucicarmine stains demonstrated microorganisms that ranged in size from approximately 4–6 µm in diameter, and were consistent with Cryptococcus organisms (Figures 2 & 3). Fungus culture of the supraglottic post commissure biopsies was negative. The patient improved after tracheostomy and intravenous fluconazole 200 mg twice a day for 5 weeks. A fibrobronchoscopic follow-up was done and the white exudative lesions on the vocal cords and epiglottis had disappeared (Figures 1C & 1D).

**Discussion**

Acute epiglottitis is a serious disease because of its potential for sudden fatal airway obstruction in previously healthy persons. It may be caused by infective organisms including *Haemophilus parainfluenzae*, *Streptococcus pneumoniae*, and group A streptococci. The less common etiologies include *Staphylococcus aureus*, mycobacteria, *Herpes simplex virus*, Candida, thermal causes (including those associated with crack cocaine smoking), and caustic insults. Rapid swelling of the epiglottis results in airway obstruction and asphyxia [13]. The risk of death is high due to sudden airway obstruction and the difficulty in intubating patients with extensive swelling of the supraglottic structure. Tracheostomy may be necessary for any patient with epiglottitis. The patient may deteriorate precipitously, and airway equipment, including that for cricothyrotomy, should be available at bedside [12].

*Cryptococcus neoformans* is an encapsulated fungus, measuring 4–6 µm, and is surrounded by a polysaccharide capsule. It is globally distributed, and commonly found in soil, avian feces, fruit, wood, and vegetables [14]. Airborne transmission is thought to occur, with subsequent respiratory infection and dissemination in HIV-infected patients in the absence of a cell-mediated response. About 5% of HIV-infected patients develop disseminated cryptococcosis, and most
cases are seen in patients with a CD4+ cell count lower than 50/mm³ [11].

Cryptococcal infections occur predominantly in patients with T-cell-mediated immune defects, especially those with AIDS and transplant-related immunosuppression [11, 15]. Corticosteroid therapy and cancer chemotherapy are also predisposing factors for the development of cryptococcal infections. The incidence of cryptococcosis is increased in subjects with hematologic malignancies, sarcoidosis, and diabetes mellitus [15-16].

The most common presentation of cryptococcal infection is meningitis. Pneumonia is described in 10~30% of patients. Patients with lung involvement usually have disseminated infection. The demonstration of the organism in respiratory secretions is an indication for a thorough evaluation of cryptococcal meningitis [17]. The best option for disease diagnosis in terms of high sensitivity and quick results is the detection of cryptococcal polysaccharide antigens by latex particle agglutination in body fluids, such as CSF, serum and urine. The direct examination, the histological analysis, and the culture can have discordant results. The drugs of choice for cryptococcal infection are amphotericin B, 5-fluorocytosine, itraconazole and fluconazole [18].

A Medline search revealed only 7 cases of Cryptococcus infection of the larynx, reported from 1975 to 2004, and our patient would be the eighth (Table 1) [1-7]. All reported patients were adults between the ages of 31 and 87 years, and included 7 males and 1 female. Presenting symptoms included hoarseness (8/8), dyspnea (2/8), and cough (2/8). There were 2 cases, including ours, with severe respiratory distress and upper airway obstruction that necessitated tracheostomy. Their underlying diseases included AIDS, diabetes mellitus, COPD, asthma, cryptococcal pneumonia history, smoking, and alcohol abuse (Table 1). One patient had been exposed to soil rich in chicken manure [1]. Six patients were immunocompromised, including 1 with HIV infection [3] and 2 with diabetes mellitus [4-5]. Those patients with COPD or asthma had a history of long-term oral (2/8) or inhaled corticosteroid use (2/8). Our patient had COPD and used both oral and inhaled corticosteroids.

Serologic cryptococcal antigen tests of the CSF, blood, and urine are usually negative in cryptococcal laryngitis. Only in Kerschner’s patient [5] was the serum cryptococcal antigen positive. In our patient, the cryptococcal antigen was positive in the urine. No diagnostic method has 100% sensitivity and specificity for cryptococcosis—a combination of several methods is recommended. A diagnosis based on combined culture and tissue results is the gold standard method, with greater specificity and almost 100% sensitivity for cryptococcosis diagnosis [19]. Both the bronchial washing in Reese’s patient [1] and laryngeal biopsy specimen in Nadrous’s patient [7] grew Cryptococcus neoformans. In other cases, the blood, CSF, and urine fungal cultures were all negative. All of these cases, including ours, had tissue biopsies and positive special fungal stains proving cryptococcal infection. Two cases [2, 4] received only endoscopic polypectomy without medical treatment. Six other cases, including ours, were treated with antifungal chemotherapy (amphotericin B, itraconazole and/or fluconazole). In all 8 cases, the symptoms improved or the disease was successfully cured during a period of 1 to 17 months. In our case, fibrobronchoscopic follow-up revealed resolution of the white exudative lesions on the vocal cords and epiglottis (Figures 1C & 1D), but residual mild swelling of the epiglottis. The patient’s pulmonary function test was worse 1 year before...
Table 1. Summary of 8 reported cases of cryptococcal laryngitis

<table>
<thead>
<tr>
<th>Author</th>
<th>Patient (Age, sex)</th>
<th>Symptoms</th>
<th>Underlying disease</th>
<th>Steroid dependent</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reese [1] 1975</td>
<td>47, M</td>
<td>hoarseness, dyspnea</td>
<td>hypertension, CAD</td>
<td>no</td>
<td>biopsy, bronchial washing*</td>
<td>tracheostomy, amphotericin B</td>
</tr>
<tr>
<td>Smallma [2] 1989</td>
<td>31, F</td>
<td>hoarseness</td>
<td>unknown</td>
<td>no</td>
<td>biopsy</td>
<td>endoscopic polypectomy</td>
</tr>
<tr>
<td>Frisch [4] 1995</td>
<td>73, M</td>
<td>hoarseness</td>
<td>DM, smoking</td>
<td>no</td>
<td>biopsy</td>
<td>endoscopic polypectomy</td>
</tr>
<tr>
<td>Kerschne [5] 1995</td>
<td>61, M</td>
<td>hoarseness</td>
<td>COPD, DM, smoking, alcohol abuse</td>
<td>predisolone 60 mg/day</td>
<td>biopsy, blood antigen(+)</td>
<td>fluconazole</td>
</tr>
<tr>
<td>Isacoson [6] 1996</td>
<td>87, M</td>
<td>hoarseness, dry cough</td>
<td>COPD, smoking</td>
<td>dependent before, without steroid for years</td>
<td>biopsy</td>
<td>fluconazole</td>
</tr>
<tr>
<td>Nadrous [7] 2004</td>
<td>55, M</td>
<td>hoarseness, cough</td>
<td>asthma</td>
<td>high dose inhaled steroid</td>
<td>biopsy, culture;†</td>
<td>itraconazole, fluconazole</td>
</tr>
<tr>
<td>Current case</td>
<td>83, M</td>
<td>hoarseness, dyspnea</td>
<td>COPD, smoking</td>
<td>predisolone 5 mg/day</td>
<td>biopsy, urine antigen(+)</td>
<td>tracheostomy, fluconazole</td>
</tr>
</tbody>
</table>

M: male, F: female, DM: diabetes mellitus, CAD: coronary artery disease
COPD: chronic obstructive pulmonary disease
AIDS: acquired immunodeficiency syndrome
*: Bronchial washing cultured Cryptococcus neoformans
†: Biopsy fungal cultures grew Cryptococcus neoformans
(FEV1: 1.07 L/min, FEV1/FVC: 54%). Because of concern due to his poor pulmonary function and episodic dyspneic symptoms, we decided not to remove his tracheostomy tube until his upper airway obstruction had reached complete remission. He has been undergoing oral fluconazole treatment and outpatient follow-up.

Conclusion

Cryptococcal laryngeal infection is rare, but it should be included in the differential diagnosis of laryngitis in immunocompromised patients, including patients who have inhaled and/or who are oral steroid-dependent.

References

新型隱球菌性咽喉炎：一病例報告及文獻回顧

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新型隱球菌性咽喉炎，相當的罕見—目前僅有七例病例報告。新型隱球菌的感染程度，由沒有症狀至全身性感染皆可見，特別在免疫不全的病人身上。我們將報告一位 83 歲男性，長期使用類固醇控制慢性阻塞性肺疾病，他因為喉嚨痛及吞嚥困難約 14 天，至門診求助，住院後因呼吸窘迫及上呼吸道阻塞，需接受氣切來維持呼吸道暢通，在接受積極照護及 Fluconazole 治療後，症狀有明顯改善。(胸腔醫學 2006; 21: 33-39)

關鍵詞：新型隱球菌性咽喉炎，新型隱球菌症，咽喉炎

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