# Primary Cryptococcal Infection of the Larynx in a Patient with AIDS : A Case Report

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**Abstract**

Primary laryngeal cryptococcosis was reported in a 42-year-old man with AIDS. The patient also had pulmonary tuberculosis and hydropneumothorax as a complication. Serological tests and/or cultures from blood, CSF, urine and pleural fluid were all negative for cryptococcus. He was succesfully treated with oral fluconazole for 8 weeks to clear the infection and remained clear in the follow-up period 9 months after treatment.

Cryptococcal neoformans is an opportunistic fungus, it usually affects immunocompromised hosts especially patients with AIDS(1). Patients present with either disseminated infection such as meningoencephalitis or septicemia or localized infection such as pneumonitis or lymphadenitis.

To date, only 6 cases(2-7) of laryngeal cryptococcal infection have been reported in the English literature. The first one was described in 1975. One of these patients was healthy(3) and another had AIDS(4).

## CASE REPORT

A 42-year-old man presented with hoarseness at the Department of Otolaryngology, Siriraj Hospital, Thailand in December 1996. His voice had become gradually hoarse for one month until he was unable to teach at school. There was no history of intubation, allergy or cold symptoms before the voice change. He did not have dysphagia or weight loss at that time.

Five months previously, he had presented to another hospital with prolonged fever, weight loss and non-productive cough. The diagnosis of pulmonary tuberculosis was made from chest roentgenography and positive acid-fast bacilli (AFB) on sputum examination. He was initially treated with rifampicin, isoniazid, ethambuthol and pyrazinamide for 2 months and followed by rifampicin and isoniazid. His last sputum examination

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showed no AFB and he had had no cough for 2 months.

He contacted syphilis 20 years ago and was treated and followed-up properly.

Physical examination revealed a healthy man. General physical examination was unremarkable. He had no cervical lymphadenopathy. His otolaryngologic examinations were normal except indirect laryngoscopy which demonstrated redness and irregularity of the anterior part of the right vocal fold and the entire left vocal fold including the vocal process (Fig. 1). Both vocal cords were mobile. Videostroboscopy revealed decreased amplitude and absence of mucosal wave on the left vocal cord. Squamous cell carcinoma and laryngeal tuberculosis were initially suspected and biopsy under direct laryngoscopy was planned. Preoperative blood examination revealed seropositive test for HIV antibody by western blot and ELISA, others were not remarkable.

Direct laryngoscopy and biopsy of vocal cord lesions were done. Pathological report of the biopsy specimen indicated pseudoepitheliomatous hyperplasia of the epithelium (Fig. 2). A small amount of organism surrounded by clear space was found, some of which contained unequal budding. Mucicarmine stain showed thick red mucopolysaccarride capsules around the organism (Fig. 3). The

**Fig. 1. The patient's larynx on the first examination showed swelling and irregularity of both vocal cords, more prominent on the left.**

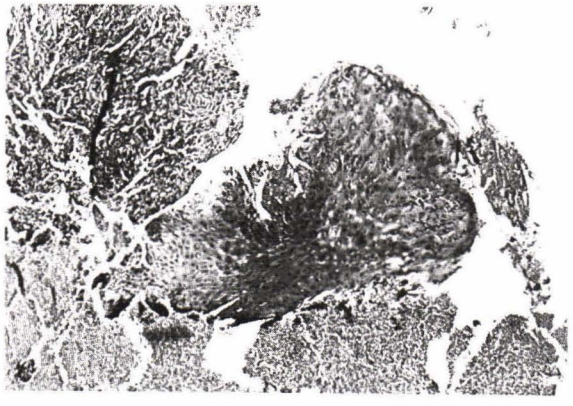
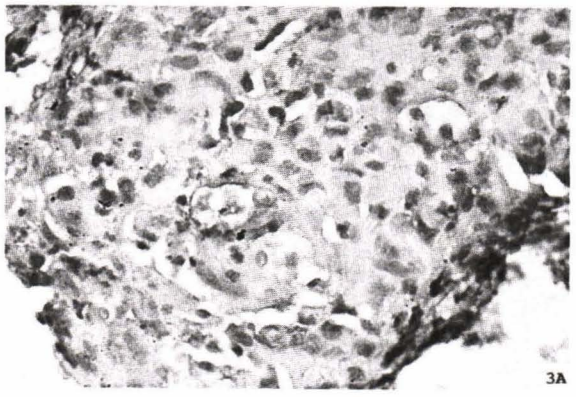


**Fig. 2. The characteristic pseudoepitheliomatous hyperplasia of vocal cord (Hematoxylin & Eosin, X 40).**



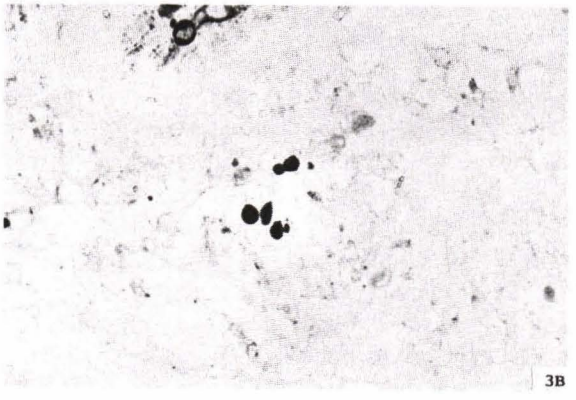




**Fig. 3. Histologic staining revealing, A: a few encapsulated cryptococcal organisms (mucicarmine stain, X 400) and B: budding yeast cells (Gomori's methenamine silver stain, X 400)**

diagnosis was cryptococcal laryngitis which was confirmed by positive culture for Cryptococcus neoformans.

The patient did not believe in the positive result of HIV serological test and sought a repeated blood test and second opinion from another hospital which also confirmed the previous diagnosis.

Five weeks later the patient came back, suffering from spontaneous right hydropneumothorax and was treated with intercostal drainage. The CD4 count=80, CD8=943, CD4/CD8 ratio= 20.08. Bacterial, AFB and fungal culture were negative from pleural fluid as was cryptococcal antibody. Cryptococcal culture and antibody from blood, urine and cerebrospinal fluid were also negative. The pleural cavity became infected later with non-fermentative gram negative rod and was successfully treated with proper antibiotics. The chest tube was removed on the fourth week and he had no further chest problems.

The patient was treated with oral fluconazle (400 mg/day) for 8 weeks. Repeated CD4 count was 34. He also completed a course of antituberculous drugs for 6 months. Laryngeal examination on the 6th week of fluconazole treatment showed a marked decrease in the size of the irregular mass on both vocal cords. Four weeks after completing the course of fluconazole, the vocal cord became smooth but still hyperremic. His voice was much improved. The patient has been followed-up closely with videostroboscopy for 9 months since completion of fluconazole therapy and has shown no sign of relapse.

## DISCUSSION

Cryptococcus is a ubiquitous yeast commonly found in soil worldwide especially in areas contaminated by pigeon droppings. The fungus can be pathogenic to both immunocompromised and immunocompetent hosts. Before the AIDS era, the incidence of cryptococcal infection was uncommon, it usually occured in patients with immunosuppressive conditions such as: long-term steroid use, hematologic malignancy, post renal transplantation and diabetes. Now cryptococcosis is one of the most common life-threatening infections among patients with AIDS[8,9].

The most common form of infection is pulmonary from inhalation of the air-borne yeast. These infections are generally self-limited. The involvement of the central nervous system due to defect in host-defense mechanism is both significant and fatal. Relapse is common and the mortality is as high as 25-30 per cent[8].

The search for systemic involvement especially CNS, urinary, pulmonary and cutaneous involvement by culture of CSF, urine, sputum and suspicious skin lesions respectively are recommended for AIDS patients even though there is no clinical evidence. The search for systemic involvement was all negative in this patient.

There are 6 reported cases of laryngeal cryptococcosis in the English literature which are reviewed in Table 1. Only one of the patients was perfectly healthy[3], another was a debilitated patient[2], although not immunosuppressed. The rest were immunocompromised patients[4-7].

Four patients had only laryngeal involvement[3,5-7]. One patient had cryptococcal ulcers involving the entire tracheobronchial tree. Another patient, who also had AIDS, had had pulmonary cryptococcosis and was treated with ketoconazole for one year[4].

The disease was confined to one or both true vocal cords in 3 patients[4,6,7] as it was in our patient. The rest had supraglottic lesions with or without glottic involvement. One patient had a subglottic mass only[3]. All patients presented with hoarseness, only one patient had upper airway obstruction from edema of true and false vocal cords requiring tracheostomy[2]. Laryngeal videostroboscopy revealed abnormal mucosal wave in one patient[5]. This sign referred infiltration from vocal fold mucosa causing stiffiness to the superficial layer of the lamina propria or deeper infiltration into the vocal ligament which is also found in invasive carcinoma and tuberculosis of the vocal fold.

The diagnosis of laryngeal cryptococcosis in the 6 reported cases was made by characteristic histopathology of budding yeast cells with thick capsules that were positive to staining with Mucicarmine or Alcian blue[2-7]. Our patient and three of the six in previous reports[2,3,7] had pseudoepitheliomatous hyperplasia of mucosa.

Treatment of cryptococcal infection depends on affected sites and the immune status of patients. Cryptococcal meningitis among AIDS patients is associated with a high relapse rate and can be fatal. The primary aggressive treatment is amphotericin B combined with flucytocine or fluconazole until the CSF culture is negative, followed by supression with oral triazole groups[9]. Regi-

Table 1. Summary of clinical presentation, pathology, treatment and its' results of the six reported cases of laryngeal cryptococcosis.

| Author | sex age | Underlying conditions | Signs & symptoms | Sites | Gross pathology | Histology | Surgical treatment | Medical treatment | Result & follow up |
|---|---|---|---|---|---|---|---|---|---|
| Reese & Colclasure 1975 | M 47y | obesity, hypertension, heart disease | Hoarseness, upper airway obstruction | TVC, FVC | edema | pseudoepitheliomatous hyperplasia | tracheos-tomy | Amphotericin B 30 days | no recurrence at 14 months |
| Smallman 1989 | F 31y | healthy | Hoarseness 7 weeks | subglottis | warty like | pseudoepitheliomatous hyperplasia | excision | none (refused further treatment) | edema at 1 month |
| Browing et al 1992 | F 46y | AIDS | Hoarseness 3-4 months | right TVC | erythema , edema | submucosal edema | | Amphtericin B 4 days, Fluconazole unknown duration | normal larynx at 1 month |
| Kercher et al,1995 | M 61y | COPD, steroid dependent, IDDM, alcohol abuse | Hoarseness several months | FVC, arytenoid, posterior comissure | oxophytic mass | granulomatous inflammation | | Fluconazole 6 weeks | no recurrence several months |
| Firsch et al 1995 | M 73y | IDDM, cigaratte 40packs/year | Hoarseness 3 months | left FVC | hyperemic fusiform mass | submucosal mass, granulation | excision | none | neg. biopsy at 5 months |
| Isaacson et al 1996 | M 87y | COPD, steroid inhalant | Hoarseness, dry cough 6 months | both TVC | edema, exudative lesion | pseudoepitheliomatous hyperplasia, marked submucosal inflammation | | Fluconazole 2 months | no recurrence at 1 year |

COPD = chronic obstructive pulmonary diseases
IDDM = insulin-dependent diabetes mellitus
TVC = true vocal cord
FVC = false vocal cord

mens of treatment for other sites of the infection vary.

Amphotericin B is available only through parenteral form and carries a significant risk for nephrotoxicity. Flucytocine, although available as an oral preparation, can cause marked myelosuppression. Oral Fluconazole has been effective in certain cases of non-CNS cryptococcosis in immunocompromised patients[10] and is less toxic than amphotericin B. Two patients with laryngeal cryptococcosis were treated with fluconazole for 6 and 8 weeks[5,7]. We treated our patient with fluconazole for 8 weeks. Repeated biopsy after treatment in our patient was not necessary because the lesion had regressed very well.

Complete surgical excision *via* direct laryngoscopy was the only treatment in two reported patients[3,6]. This may be adequate for an exophytic lesion but close follow-up and rebiopsies are recommended.

## SUMMARY

Cryptococcus neoformans can infect the larynx in both immunocompromised and immunocompetent hosts. A case of primary cryptococcosis of the larynx is reported. Diagnosis was made by biopsy and staining of its mucopolysaccharide capsule as well as culture. Treatment with an eight-week course of oral fluconazole was successful.

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# รายงานผู้ป่วย : เชื้อราคริปโตคอกโคสิส ของกล่องเสียงในผู้ป่วยภาวะภูมิคุ้มกันเสื่อม (เอดส์)

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รายงานผู้ป่วย 1 ราย เป็นเชื้อราคริปโตคอกโคสิสของสายเสียง ในผู้ป่วยชายไทยอายุ 42 ปี ซึ่งมีภาวะภูมิคุ้มกันเสื่อมจากโรคเอดส์ ผู้ป่วยเป็นวัณโรคปอดและมีภาวะแทรกซ้อนคือมีน้ำและลมในช่องเยื่อหุ้มปอด การตรวจหาเชื้อราคริปโตคอกคัสที่อื่น ๆ โดยตรวจปฏิกิริยาภูมิคุ้มกันและเพาะเชื้อจากเลือด, น้ำไขสันหลัง, ปัสสาวะ และน้ำในช่องเยื่อหุ้มปอด ให้ผลลบ ผู้ป่วยได้รับการรักษาโดยรับประทานยา Fluconazole นาน 8 สัปดาห์ และติดตามผลนาน 9 เดือนหลังการรักษา

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