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Primary laryngeal cryptococcosis resembling laryngeal carcinoma

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ABSTRACT

A case of an 82-year-old female with primary laryngeal cryptococcosis who had undergone long-term corticosteroid therapy for chronic obstructive pulmonary disease and rheumatoid arthritis is reported. She complained hoarseness with swallowing pain and irritability of the larynx for over a month. Endoscopic examination revealed a white, exudative irregular region on right arytenoid that mimicked a laryngeal carcinoma. Histological examination showed pseudoepitheliomatous hyperplasia and severe submucosal inflammation with ovoid budding yeasts by Grocott's stain. A serological study indicated a high titer of cryptococcal antigen. After treating with oral fluconazole for 3 months, her primary lesion of larynx turned to be clear.

We implicate a long-term use of steroids as the significant risk factor in developing cryptococcosis of the larynx.

1. Introduction

Cryptococcus neoformans is a ubiquitous yeast occurring in soil and pigeon feces. The pathogen generally causes a self-limited subacute pulmonary infection among immunocompromised hosts. About 25–40% of cryptococcal infections in the United States occur in immunocompromised hosts. The incidence of cryptococcal infection in immunocompromised individuals with deficient cellular immunity is increasing with the increasing prevalence of HIV. It is estimated that cryptococcal infections develop in 6–8% of patients with AIDS in the U.S. [1]. Patients undergoing lengthy corticosteroid therapy are exposed to one of the significant risks for developing cryptococcal infections [2].

The most common site of cryptococcal infections is the lung because *C. neoformans* yeast exists in a 2- to 7-μm, encapsulated, air-bone form that is easily inhaled. In contrast, the primary cryptococcal infection of the larynx is very rare [2–7]. In this report, we describe a case of primary laryngeal cryptococcosis in an 82-year-old female with a history of lengthy corticosteroid against COPD and rheumatoid arthritis. Our study of this case indicated that lengthy corticosteroid and exposure to high doses of inhaled forms of *C. neoformans* become a significant contributing factor to the development of cryptococcal infections.

2. Case

An 82-year-old female was seen because of a month of hoarseness with throat pain, dry cough, and irritability of the larynx. Several days of empirical antimicrobial treatment had failed to improve these symptoms. The patient had a long history of treatments for rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), and chronic heart failure. Her current medications were predonizolone (15 mg/day), salazosulfapyridine (500 mg/day), furosemide (20 mg/day), warfarin potassium (0.5 mg/day), and sulfamethoxazole (1600 mg/day). She had no history of smoking or alcohol abuse and had not traveled abroad or had close contact with pigeons.

Endoscopic examination revealed a white, exudative irregular lesion (0.7 cm × 0.7 cm in diameter) on the patient's right arytenoid (Fig. 1A). The mobility of her bilateral vocal cord was not disturbed. The anterior commissure was not involved, and the supraglottic and subglottic lesion were normal. No cervical lymphoadenopathy was evident. Because the malignant tumor was initially suspected, an excisional biopsy was performed under local anesthesia. Histological examination showed pseudoepitheliomatous hyperplasia and severe submucosal inflammation caused by fungal yeast forms (Fig. 2A). Grocott's stain revealed numerous encapsulated ovoid budding yeasts (Fig. 2B). Serological

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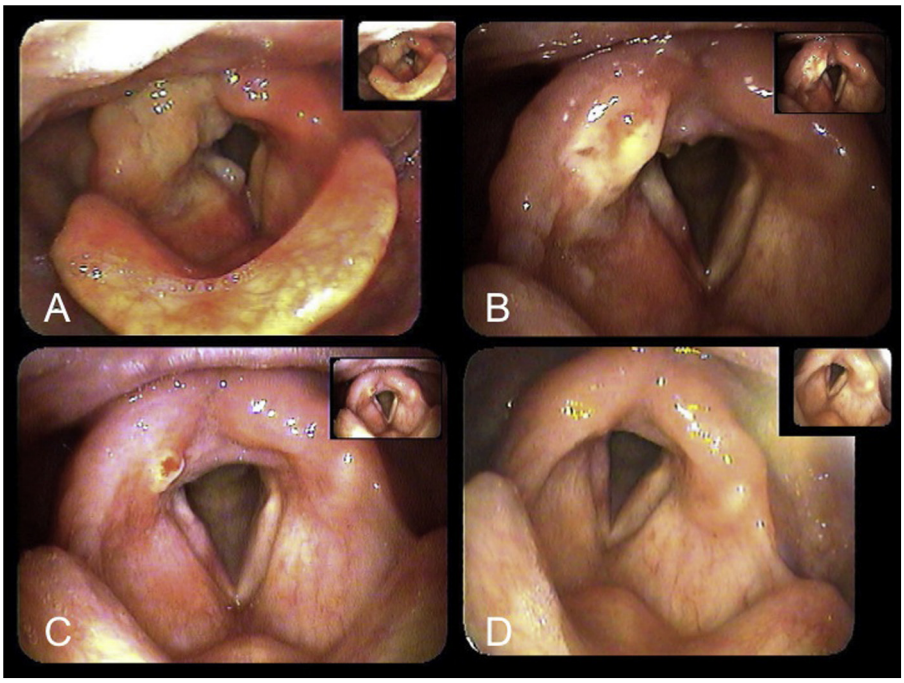

Fig. 1. Endoscopic findings of the larynx. At the first visit, a white and exudative irregular lesion (0.7 cm × 0.7 cm in diameter) was seen on right arytenoid (A). During the treatment course, the primary laryngeal lesion was gradually decreased on day 14 (B), on day 28 (C) and finally turn to be clear on day 42 (D).

evaluation revealed a high titer of cryptococcal antigen at 256 times and normal levels of β-D-glucan in serum. A chest X-ray showed no remarkable focus of infection in the lungs. After considering all of the above, the patient was diagnosed with primary laryngeal cryptococcosis.

She was treated with oral fluconazole (200 mg/day). At a half-year follow-up, she had no symptoms, including no swallowing pain and no irritability of the larynx. We reduced dosage of corticosteroid from 15 mg/day to 9 mg/day over 4 months during the treatment of laryngeal cryptococcosis. The endoscopic examination of the primary lesion on the patient's larynx revealed that it had returned to be clear (Fig. 1B–D). After 182 days of treatment, serological evaluation showed that the patient's cryptococcal antigens had gradually decreased from 256 to 64.

3. Discussion

C. neoformans is a well-documented pathogenic fungus and is rarely implicated in primary laryngitis. To date, there are some reports of primary laryngeal cryptococcosis in English literature from European countries and the United States (Table 1) [1,2,4–10]. However, the fungus is very neurotropic and readily frequent among immunocompromised host [11]. In addition, the increase of COPD cases has become a serious clinical problem in the U.S. and Japan. Although corticosteroid is commonly used for steroid-dependent COPD patients and brings great benefit to COPD patients, it also exposes those patients to a significant risk of developing cryptococcosis. Isaacson et al. have reported that the use of high-dose inhaled corticosteroid also increases patients' risk

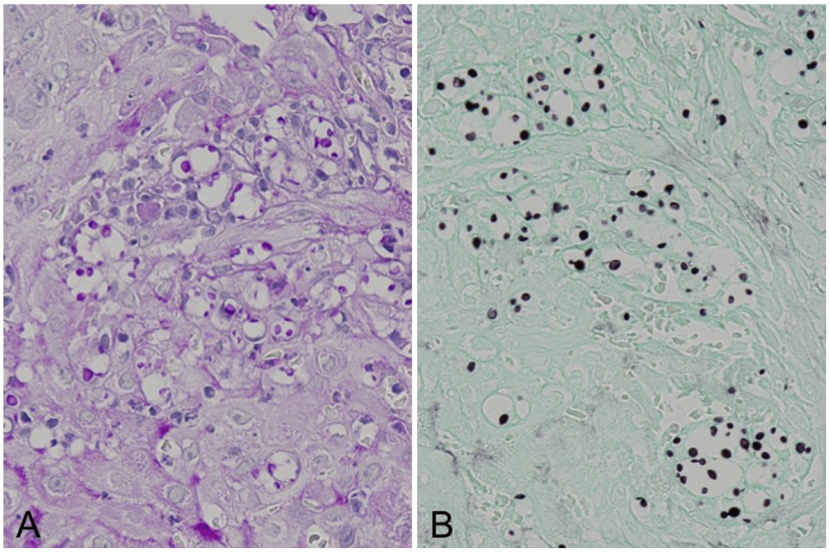

Fig. 2. Histological findings. (A) Pseudoepitheliomatous hyperplasia and severe submucosal inflammation caused by fungal yeast forms were observed (HE stain, 400×). (B) Numerous encapsulated ovoid budding yeast cells were observed (Grocott's stain, 400×).