Case Report

Laryngeal Cryptococcoma Resulting in Airway Compromise in an Immunocompetent Patient: A Case Report

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**Cryptococcus neoformans** is a yeast that can result in isolated or disseminated infections. This case report describes an immunocompetent patient presenting with airway obstruction secondary to laryngeal cryptococcoma, mimicking a laryngeal malignancy, and describes associated management. A 68-year-old immunocompetent female with a new positron emission tomography–avid laryngeal lesion was intubated after acute respiratory decompensation. Airway evaluation revealed diffuse mucosal changes throughout the endolarynx with significant loss of normal native tissue architecture. Operative biopsy confirmed infection of *C. neoformans*. The patient was treated with extended-course fluconazole. This case reinforces characteristic physical and histologic findings described for laryngeal cryptococcal infection.

**Key Words:** Laryngitis, *Cryptococcus neoformans*, fungal laryngitis, *Cryptococcus*, fluconazole, laryngeal diseases, airway compromise.

**INTRODUCTION**

Cryptococcal infection is a rare fungal infection that may present as disseminated or localized disease. Most commonly, *Cryptococcus* is diagnosed as a primary lower respiratory condition but may also be encountered as a secondary disseminated disease. Diagnosis of cryptococcal infections involves sampling of blood, urine, and cerebrospinal fluid for a cryptococcal-specific antigen, whereas localized infection is classically diagnosed with tissue biopsy and fungal staining.

Localized laryngeal cryptococcal infection is a rare entity that is sparsely described in the literature. It has most commonly been described in immunocompromised conditions including human immunodeficiency virus (HIV)/acquired immune deficiency syndrome or posttransplant patients. More recently, multiple reports have demonstrated disease in immunocompetent hosts, most commonly associated with inhaled corticosteroid use. Diagnosis is typically delayed, as specific laryngeal findings are many times nonspecific, even at times being mistaken for laryngeal carcinoma. Furthermore, given the rarity of presentation and diagnosis, treatment guidelines are variable, with patients being treated with weeks to months of fluconazole therapy.

We describe a case of laryngeal cryptococcal infection with subglottic involvement in an immunocompetent patient contributing to airway compromise, its associated management and outcomes, along with a review of the recent literature.

**CASE REPORT**

A 68-year-old immunocompetent female, with chronic obstructive pulmonary disease, history of colon cancer, and a new positron emission tomography (PET)–avid laryngeal lesion, was transferred from a referring institution and intubated after acute respiratory decompensation reported from a subglottic mass. A detailed history revealed that the patient had experienced chronic cough for greater than 2 years and a 1-year history of dysphonia, dysphagia, and 20-pound weight loss. Ultimately, a PET scan revealed a PET-positive laryngeal mass extending into the subglottis (Fig. 1A–C). At an outside institution she underwent direct laryngoscopy and bronchoscopy with a biopsy of a reported fungating subglottic mass and bronchoalveolar lavage. Immediately postoperatively she developed cough, confusion, respiratory acidosis, and a pCO2 of 86. She was intubated, started on Decadron, and transferred to a tertiary care center for further evaluation. Pathologic findings of her laryngeal biopsy showed squamous epithelial cells with candidalike lesions superficially. Submucosal tissue further demonstrated extensive encapsulated yeast infection concerning for cryptococcal infection.
The patient was taken to the operating room for repeat direct laryngoscopy and bronchoscopy revealing diffuse mucosal changes in the supraglottis with irregular waxy-appearing bilateral true vocal folds with significant loss of normal native tissue architecture (Fig. 1D,E). The subglottis demonstrated mucosal inflammation and exudative change throughout (Fig. 1F). The patient was successfully extubated. Histopathology from operative biopsy confirmed submucosal laryngeal subglottic infection of Cryptococcus neoformans (Fig. 2A–D). Serum cryptococcal antigen was positive. HIV testing was negative. The patient was treated with extended-course fluconazole of 400 mg orally daily for 12 months. Voice complaints resolved within 6 months. Hoarseness improved after 1 month of treatment with increased phonation time and attainable volume. Dysphagia improved 2 weeks after beginning treatment. No further airway complaints developed. Although the patient had complete symptom resolution within 6 months of treatment, the patient’s treatment course with fluconazole was dictated through infectious disease specialists. Treatment was deemed sufficient after normalization of serum cryptococcal antigen at 12 months of treatment.

DISCUSSION

C neoformans is an encapsulated yeast most commonly associated with soil contaminated by feces from birds, particularly pigeons. As a systemic pathogen, the route of infection remains mysterious, but is theorized to be secondary to aerosolized particles that infect and disseminate in the alveoli of the lungs, ultimately diffusing systemically. Interestingly, however, there is an increasing number of localized infections reported in immunocompetent hosts. Immunocompetent patients tend to have localized disease without systemic manifestations. Recent published case reports allude to the role of localized immunosuppression, particularly associated with inhaled corticosteroids, as the most significant risk for infection.

Localized cryptococcal laryngitis is an uncommon infection of the larynx, with less than 25 cases reported in the current literature. Laryngeal Cryptococcus, particularly in immunocompetent hosts, consistently presents with nonspecific symptomatology, lack of specific exposures, and variable endoscopic findings, making this diagnosis difficult to obtain. Furthermore, tissue biopsy with specific staining is required for diagnosis. Many times this diagnosis can be mistaken for malignancy. Interestingly, this patient demonstrated a PET-positive lesion of the larynx (Fig. 1A–C). To our knowledge this is the first demonstrated case of a PET-positive laryngeal lesion subsequently found to be isolated laryngeal cryptococcal infection. However, the correlation between increased inflammation, particularly with macrophage involvement, and false-positive PET lesions including Cryptococcus, has been previously demonstrated. Isolated laryngeal disease in an immunocompetent host is theorized to be secondary to the role of localized immunosuppression and disruption of the laryngeal mucosal barrier.

Local immunosuppression from inhaled high-dose corticosteroids (ICSs) has increasingly been found to contribute as a risk factor for laryngeal cryptococcal disease. ICSs have long been known to have a direct effect on the upper airway. The predisposition for deposition of steroids along laryngeal subsites is only recently begun to be elucidated as steroids with greater particle size,
such as fluticasone, are known to have greater glottic deposition.\textsuperscript{13} Given the rarity of this disease, no current evidence has correlated a specific ICS with increased risk of infection. However, a known correlation between increased dosing and frequency of ICSs has been demonstrated to increase laryngeal irritation.\textsuperscript{14} The history of this patient along with other reported cases is suggestive of an indolent course occurring over months secondary to repeated localized toxicity from ICSs. Additionally, there is clearly a predominance of glottic infection when compared to other laryngeal subsites, likely related to the fact this is the narrowest aspect of the adult airway and most susceptible to localized irritation from ICSs and subsequently most susceptible to mycotic infection including \textit{Cryptococcus}.\textsuperscript{15,16}

The above patient’s long-standing dysphonia is consistent with the pathogenesis of steroid inhaler–related dysphonia. Most commonly, this is associated with candidiasis, and interestingly, the above-reported case demonstrated simultaneous superficial laryngeal candidiasis further supporting the likely relationship to ICSs. Interestingly, only a single other case report demonstrates any subglottic mucosal changes as found in the above patient.\textsuperscript{9} Our patient’s long-term dysphonia suggests long-standing infection, which is consistent with other reported cases of isolated laryngeal infection. Although the subglottic aspect of this infection is grossly different from other reported cases, our patient did not show any specific symptoms that would easily differentiate this from reported glottic infections in the literature. Our patient reported improvement of phonation after 1 month and resolution of vocal complaints after 6 months of treatment. This aligns closely with reported symptom resolution in the literature of laryngeal \textit{Cryptococcus} in immunocompetent patients, with an average time to resolution of approximately 5 months.\textsuperscript{2}

Treatment of primary laryngeal \textit{Cryptococcus} is inherently variable and without evidence-based guidelines. The single reported case of subglottic involvement was treated for 10 months similar to the treatment course of our patient. Treatment of isolated laryngeal \textit{Cryptococcus} in immunocompetent patients ranges from 1.5 months to 10 months, with symptom and pathologic resolution closely aligned to treatment time.\textsuperscript{4,9} Treatment of patients with only glottic infection range from 1 to 8 months, suggesting that subglottic involvement may represent a higher infectious burden and or longer standing disease requiring longer treatment.\textsuperscript{2} The involvement of infectious disease specialists cannot be overstated. To our knowledge, this is the first case to report subglottic laryngeal \textit{Cryptococcus} as a contributor to subsequent airway compromise. Although, the patient’s airway compromise is likely multifactorial in nature, we suspect the chronic inflammation secondary to cryptococcal infection of all laryngeal subsites further lowered this patient’s tolerance to airway manipulation, ultimately leading to the need for intubation.

**CONCLUSION**

Isolated laryngeal cryptococcal infection in the immunocompetent patient is rare. \textit{Cryptococcus} can infect
all laryngeal subsites and may result in false-positive imaging findings that mimic malignancy. ICSs appear to play a significant role as risk factors for development of this disease particularly among immunocompetent patients. Close postoperative observation is necessary after laryngeal biopsy in patients with signs of significant laryngeal inflammation, as acute airway compromise is possible. Subglottic infection likely represents a longer-standing and higher infectious burden and may require longer treatment. Fluconazole is an effective treatment for isolated laryngeal infection with Cryptococcus.

BIBLIOGRAPHY