

Laryngeal aspergilloma: a complication of inhaled fluticasone therapy for asthma

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Abstract

Primary laryngeal aspergillosis in immunocompetent patients is rare. We describe a case of a 59-year-old woman with laryngeal aspergillosis thought to be secondary to long-term inhaled fluticasone therapy. Laryngeal aspergillosis may be an underrecognized complication of inhaled corticosteroid therapy.

Introduction

The topical complications of inhaled corticosteroid therapy are well known. Oral candidiasis has been reported in up to 3–4% percent of patients receiving fluticasone treatment on doses of 1 mg/day and 2 mg/day respectively. Other relatively common adverse effects include throat pain, glossitis, and a mild laryngeal myopathy resulting in hoarseness [1]. We report a serious complication of fluticasone therapy for asthma – primary laryngeal aspergillosis.

Case Report

A 59-year-old woman presented for evaluation of hoarseness which had persisted for 1 month. She was diagnosed with asthma at the age of 28 and fluticasone propionate had been administered in a daily dose of 500 mcg for many years via the use of a large volume spacer device. She previously experienced two to three asthma exacerbations annually which responded to pulse doses of oral corticosteroids. Ten years prior to the development of hoarseness, immunoglobulin E (IgE) specific antibodies to aspergillus and aspergillus precipitins were negative and a serum IgE level

was 135. Previous attempts at discontinuation of inhaled corticosteroids resulted in more frequent exacerbations of her asthma symptoms and a methacholine challenge test had demonstrated significant bronchial hyperresponsiveness. At the age of 51, she was diagnosed with focal bronchiectasis in the right middle lobe which had been associated with recurrent *Pseudomonas aeruginosa* infection treated with courses of anti-Pseudomonas antibiotics. Her medical history also included cigarette smoking, 15 sticks/day for 7 years until the age of 26. There was no history of immunodeficiency, malignancy, or diabetes mellitus. Lung function testing at the time of presentation was normal with a forced expiratory volume in one second of 2.72 L (111% predicted). A referral was made for an ear, nose, and throat opinion and she underwent microlaryngoscopy which demonstrated a cystic lesion of the left vocal cord (Fig. 1). This was excised and the histopathology demonstrated a laryngoma with fungal colonies containing branching hyphae, consistent with aspergillus (Fig. 2). Unfortunately, the excised tissue was not sent for culture or polymerase chain reaction analysis. Recent measurements of aspergillus precipitins were negative and a serum IgE level was normal. She was treated with itraconazole as the treatment of choice, and inhaled



Figure 1. Images of the vocal cords at microlaryngoscopy pre- (left) and post- (right) excision of the vocal cord cyst.

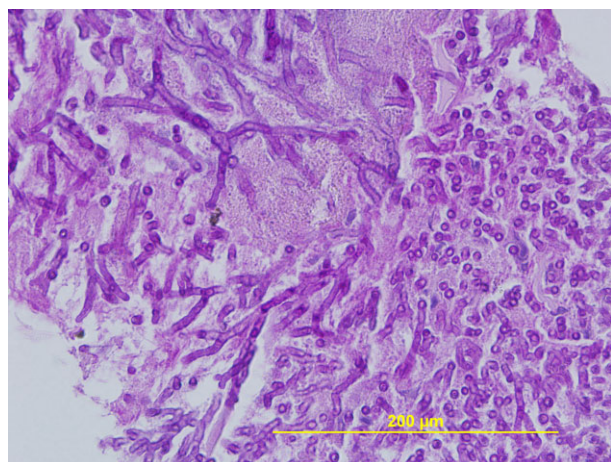


Figure 2. Necrotic material and numerous septated fungal hyphae branching at 45 degree angles. The appearances are consistent with that of aspergillus.

corticosteroids were ceased. She remained on inhaled salbutamol as required, and her asthma symptoms were infrequent. Repeat laryngoscopy at 3 months demonstrated complete resolution of the lesion. Fiberoptic bronchoscopy and bronchial washings after the diagnosis of laryngoma did not demonstrate fungal elements on cytologic examination and fungal cultures were negative. Investigations for underlying B or T cell-associated immunodeficiency were normal. The patient has been followed for 18 months since the onset of vocal cord aspergillosis and there has been no recurrence of the fungal infection.

Discussion

Aspergilli are ubiquitous airborne saprophytes that commonly grow on decaying plant material. Although they lack sophisticated virulence traits, they may cause a wide spectrum of clinical disease in humans from localized hypersensitivity reactions to invasive infections with significant associated mortality. *Aspergillus fumigatus* is the most

common species recovered from cases of invasive aspergillosis. The upper airways are normally resistant to colonization with aspergillus. The majority of cases of laryngeal aspergillosis have been in the context of an immunocompromised host, such as patients with acquired immunodeficiency syndrome or hematologic malignancy. The finding of laryngeal aspergillosis in an immunocompetent patient, however, is rare. A literature search of over 40 years revealed only 24 cases of primary laryngeal aspergillosis in immunocompetent patients [2]. Predisposing aetiological factors in these cases included previous laryngeal radiotherapy and laser treatment, broad-spectrum antibiotics, vocal cord cysts, vocal abuse and one case possibly related to oral sex [3].

There have been two published case reports of laryngeal aspergillosis that were attributable to long-term inhaled corticosteroids. The first was from Stafford (UK) in 1997 and described a patient on fluticasone at a daily dose of 2 mg [4]. The second was from Lancashire (UK) in 2011 and described a patient on fluticasone at a daily dose of 1 mg [5]. The doses of inhaled fluticasone in these cases were considerably higher than that administered to our patient (500 mcg daily).

A significant proportion of inhaled corticosteroid administered in either chlorofluorocarbons containing metered-dose inhalers or dry powder inhalers is deposited in the upper airways including the larynx. A meta-analysis published in 2007 reported that adverse oropharyngeal events may be reduced by post-dose mouth rinsing or the use of a spacer device [6].

Asthma is a highly prevalent condition in Australia for which long-term inhaled corticosteroids are the mainstay of treatment. Laryngeal aspergillosis may be an underrecognized aetiology of progressive hoarseness in this patient group. We recommend that cessation of inhaled steroids be considered if clinically safe to do so, when patients develop hoarseness. If the hoarseness persists, we recommend laryngoscopy and, if required, biopsy specimens be taken for histopathology and fungal cultures. Our

paper has shown that this condition can occur at doses of fluticasone as low as 500 mcg daily.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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