Fungal Laryngitis in Immunocompetent Patients

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Received: 1 February 2011 / Accepted: 27 October 2011 / Published online: 10 November 2011
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Abstract The diagnosis of fungal laryngitis is often overlooked in immunocompetent patients because it is commonly considered a disease of the immunocompromised. Further confusion is caused by clinical and histological similarity to more common conditions like Leukoplakia. Demonstration of hyperkeratosis particularly if associated with intraepithelial neutrophils on biopsy should trigger a search for fungus using specialized stains. These patients usually present with hoarseness of voice. Pain is present inconsistently along with dysphagia and odynophagia. We present three cases of fungal laryngitis in immunocompetent patients out of which one underwent microlaryngeal surgery with excision biopsy. All these patients responded well with oral antifungal therapy.

Keywords Laryngitis · Fungal · Immunocompetence

Introduction

Fungal laryngitis in immunocompetent patients is an uncommon condition. Unless a diagnosis of fungal laryngitis is considered proactively, it may be missed resulting in inappropriate treatment, prolonged disability and sometimes associated with unwarranted surgical intervention [1]. A high index of suspicion is required to make a diagnosis and should be considered in any immunocompetent patient with

persistent or refractory laryngitis and with risk factors predisposing to local mucosal barrier impairment e.g. Gastropharyngeal reflux, smoking or inhaled steroid use [2]. The presence of fungal infection of the larynx can mimic gastroesophageal reflux disease, granulomatous diseases, and carcinoma [3]. Conditions such as laryngopharyngeal reflux, antibiotic use, inhaled steroids can predispose to fungal laryngitis.

Case Report

Case I

A 34 year old female patient presented with complaints of hoarseness of voice and cough for 2 months. Video laryngoscopy showed keratotic patches on both vocal cords. Stroboscopy revealed irregularity of both vocal cords and a patch on superior surface of middle one-third of both vocal cords (Fig 1). Both the cords were mobile. She was thoroughly investigated to check for any co morbid conditions like diabetes, immunodeficiency status and Tuberculosis which were negative. Microlaryngeal surgery with biopsy was done. Intraoperatively, both vocal cords were found to be oedematous and irregular with whitish patches seen at the junction of anterior and middle third of both vocal cords extending into the ventricles which bled on touch. The patches were stripped and sent for histopathological examination.

Histopathological examination revealed keratosis with nonspecific inflammatory changes from the lesion on right vocal cord and aspergillus ball with evidence of inflammation from the lesion on left vocal cord (Fig 2). Postoperatively patient was administered oral Itraconazole 100 mg twice daily for 3 weeks with dramatic improvement in

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Fig. 1 Stroboscopic picture showing white patches over the junction of anterior and middle third of bilateral vocal cord

Fig. 3 Stroboscopy picture, 2 weeks after the start of antifungal therapy showing well healed vocal cords with improved symptoms and phonation

Fig. 2 HPE showing stratified squamous epithelium with subepithelial region showing acute on chronic inflammation. Also seen are fungal balls consisting of thin septate hyphae with acute angle branching suggestive of aspergillosis

Fig. 4 White patch on both tonsils with congested uvula and posterior pharyngeal wall

symptoms. Evaluation of the larynx at 2 weeks post operatively showed complete resolution of symptoms and signs with normal vocal cord movements (Fig 3).

Case II

A 52 year old female presented with chief complaints of hoarseness of voice, burning sensation in the throat, difficulty in swallowing and cough for 7 days. Clinical examination revealed a white patch on both tonsils with congested uvula and posterior pharyngeal wall (Fig 4). Video laryngoscopy showed congested epiglottis and arytenoids with congested edematous vocal cords (Fig 5). Initial treatment with antibiotics was not effective. Throat swab from the white patch in the posterior pharyngeal wall

was sent for fungal culture and a diagnosis of fungal pharyngitis with laryngitis was made based on presence of aseptate hyphae on KOH staining. She was started on oral Itraconazole 100 mg twice a day for 3 weeks. Within 3 days the patient showed dramatic improvement in her symptoms and complete resolution of signs and symptoms at 3 weeks.

Case III

A 38 year old male presented with hoarseness and vocal fatigue for past 4 months he had been treated elsewhere for acute bacterial laryngitis, Gastroesophageal reflux disorder with no relief of symptoms, he was not a known diabetic or hypertensive, no other comorbid condition, stroboscopy showed a raised irregular white patch with erythematous

Fig. 5 Videolaryngoscopic picture of case 2 showing congested arytenoids and congested edematous vocal cords

Fig. 6 Stroboscopic picture of the vocal cords showing irregular white patch with erythematous surrounding in the middle 1/3rd of vocal cords typical of fungal laryngitis

surrounding in the middle 1/3rd of both vocal cords (Fig 6). Since there were loose white flakes over the vocal cords and he had already been treated with various antibiotic, a provisional diagnosis of fungal laryngitis was made and the patient was empirically started on antifungal. We had counseled the patient the need for further investigation if there was no resolution of symptoms. We started him on antifungal Itraconazole 100 mg twice daily for 3 weeks. He showed dramatic improvement within 5 days. Post treatment stroboscopy showed complete resolution with normal voice (Fig 7).

Fig. 7 Post treatment with antifungal of the same patient shown in Fig 6 showing complete resolution of signs

Discussion

Fungal laryngitis has often been described in immunocompromised patients [1], but it is rarely reported in immunocompetent hosts. May be because of its perceived rarity or because the microscopic appearances are similar to and often confused with that of a smoker's dysplasia. The three cases presented above typify the presentation of fungal laryngitis in immunocompetent hosts. Various predisposing factors for fungal laryngitis are [2]:

- Factors altering immune response: Diabetes, immunodeficiency status, immunosuppressive medication.
(e.g. chemotherapy, corticosteroids), nutritional deficiency, etc.
- Factors altering mucosal barrier: previous radiotherapy, inhaled corticosteroids, Gastroesophageal reflux disorder,
- Trauma (e.g. Intubation), smoking, etc.

The usual mode of presentation in an immunocompromised patient is with the change of voice, dysphagia, odynophagia, dyspnoea. The presence of fungal laryngeal infections can mimic gastroesophageal reflux disease, granulomatous diseases, leukoplakia, and carcinoma [3, 4]. Although mycotic infections of the larynx are typically considered to be associated with immunocompromise, such infections can occur in immunocompetent hosts in whom there are alterations in the mucosal barrier. The three patients reported were immunocompetent. Examination in both these cases showed white patches adherent to mucosa with mucosal edema, erythema.

The most common fungi causing laryngitis is *Candida* [2]. Other fungal infections like Aspergillosis, Cryptococcal

[5], Blastomycosis [6], Histoplasmosis and candidiasis [7] are implicated. Infection is almost always secondary to pulmonary or oropharyngeal infection. Thus making this diagnosis requires a high index of suspicion.

Definitive diagnosis is made by the demonstration of fungal spores, hyphae or pseudohyphae either by tissue biopsy or fungal KOH smear and culture. Hematoxylin and eosin (H&E) stains show epithelial hyperplasia with hyperkeratosis, neutrophils within the upper epithelial layers, lymphocytes, plasma cells and scarring in the sub-mucosal stroma. The characteristic histopathological features are termed 'pseudoepitheliomatous hyperplasia' [2]. Whilst most authors advocate biopsy of the lesion to establish the diagnosis, some reserve this for the refractory cases or for cases that are highly suspicious of malignancy.

Reports in the literature differ regarding the first line antifungal agent and the mode of initial treatment (local or systemic). In immunocompetent patients with no evidence of spreading disease, topical nystatin (as a suspension or pastille) for 3 weeks is recommended. Excision of the lesion with application of gentian violet has also been reported to be successful. If the condition does not resolve, the patient is treated with systemic oral antifungal agent like Fluconazole or Itraconazole daily for 3 or 4 weeks. Oral antifungal agent is the first line of treatment, especially for the immunocompromised patient with non-invasive disease. Intravenous Amphotericin B is used for refractory cases or in patients with significant tissue invasion. The three cases reported here were administered Itraconazole 100 mg twice a day for 3 weeks and showed significant improvement with complete resolution of signs and symptoms.

Conclusion

A high index of suspicion is required to make a diagnosis of fungal laryngitis in immunocompetent patients. A demonstration of hyperkeratosis on biopsy should trigger a search for fungal elements. Fungal laryngitis in immunocompetent patient is a rare diagnosis but should be kept in mind in cases of refractory laryngitis. Patients should be counseled for treatment with systemic antifungal together with the elimination of predisposing factors such as GERD, smoking and inhaled steroids.

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