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CASE REPORT

Fungal Laryngitis in Immunocompetent Individuals: Not so Uncommon

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ABSTRACT

Fungal laryngitis (FL) in immunocompetent individuals has been described as a rare entity. Management of 11 cases of suspected isolated FL in immunocompetent patients is discussed. Fungal laryngitis was suspected if white smooth plaques with surrounding inflammation were seen on the larynx. Suspected patients were given 200 mg OD oral fluconazole for 3 to 4 weeks. In those who showed no improvement at 2 weeks, complete excision of the lesion was performed (five patients). Eight patients gave history of having received a course of oral steroids, one of inhaled steroids. The average erythrocyte sedimentation rate (ESR) of the patients was 42.

Keywords: Fungal, Hoarseness, Laryngitis.

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INTRODUCTION

Fungi are organisms of low pathogenicity, manifesting as opportunistic infections, typically in an immunocompromised host.[1] Fungal laryngitis historically has been labeled as quite uncommon in immunocompetent patients.[2] Fungal laryngitis is usually seen as a part of a generalized fungal infection of the oropharyngeal and respiratory tract, and isolated fungal infection of the larynx is less common, especially in healthy patients.

The commonest type of fungus to infect the larynx is *Candida albicans* seen most commonly in immunocompromised patients and patients using inhaled corticosteroids.[3] The clinical hallmark of FL (especially Candida infection) is bilateral white plaque on a bed of severe erythema. 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, for example, gastropharyngeal reflux, smoking, or inhaled steroid use.[4]

We performed an audit of all our FL patients over a period of 2 years from October 2014 to September 2016 with an analysis of the predisposing factors in our patient group, diagnostic pointers, and our rate of surgical intervention and outcomes.

CASE DISCUSSIONS

Patients visiting our voice clinic from October 2014 to September 2016, who were suspected of having FL on clinical examination, were included in this study (11 patients). Suspicion was based upon laryngostroboscopy revealing white smooth plaques with surrounding erythema on the vocal fold, typically bilateral (Fig. 1). A narrow band imaging (NBI) revealed absence of type IV and type V (Ngi classification) vascular patterns at the periphery of the white plaques in all patients (Fig. 2). In two patients (18.18%), extensive lesions involving the false vocal folds with severe congestion and edema were observed (Fig. 3).

A detailed history was elicited from each patient, especially pertaining to previous use of oral or inhaled steroids, antibiotics, smoking, and history of tuberculosis. All 11 suspected FL patients were then prescribed oral antifungal therapy consisting of fluconazole 200 mg OD

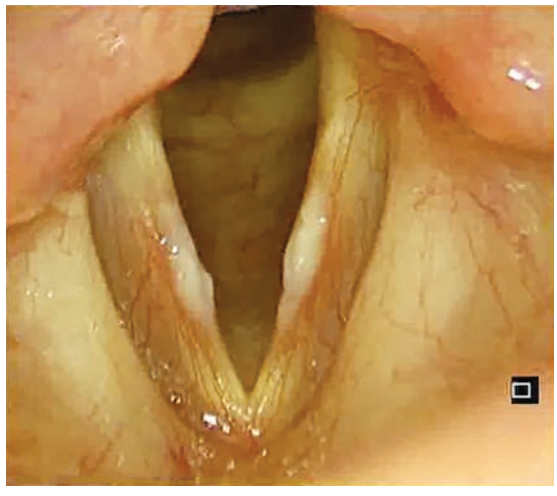

Fig. 1: Typical appearance of bilateral FL of the true vocal folds showing white flaky smooth deposits and surrounding inflammation (*Reprinted with permission from the Atlas of Phonomicrosurgery*)

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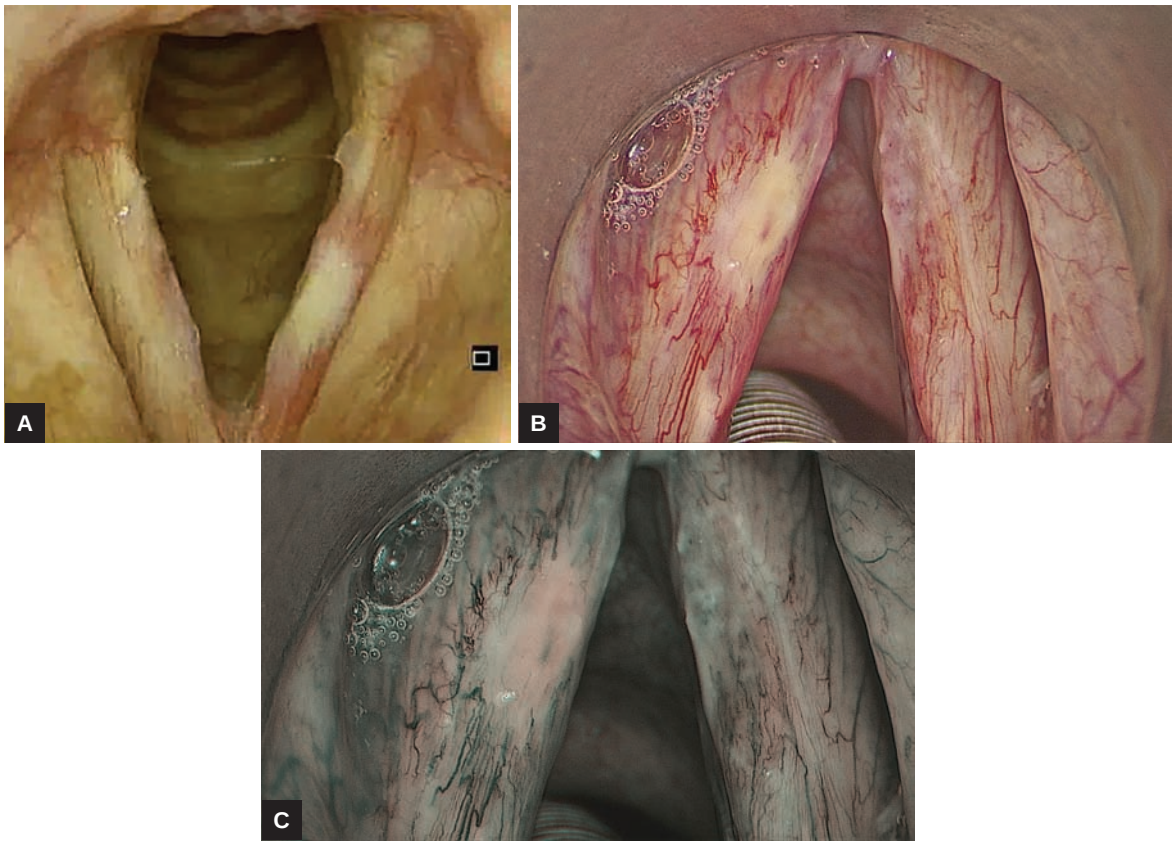


Figs 2A to C: Left vocal fold FL images seen (A) On white light; (B) On Clara-chroma mode; and (C) On Spectra A mode of SPIES (*Figures 2B and C are reprinted with permission from the Atlas of Phonomicrosurgery*)

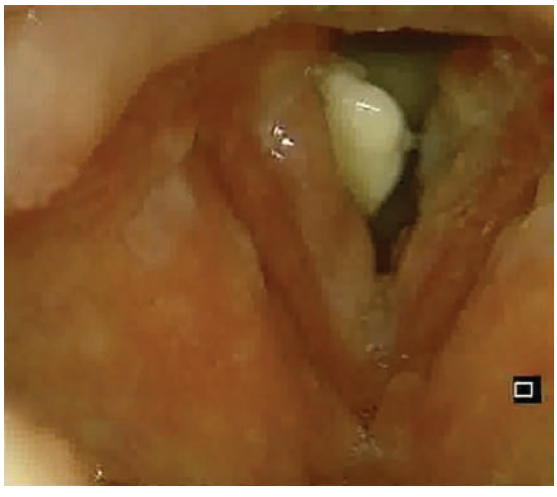


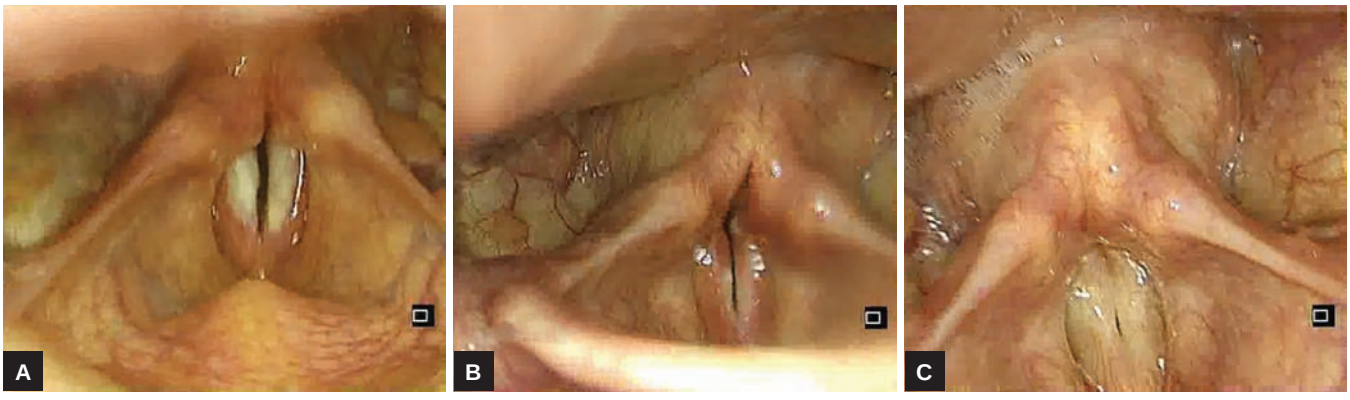
Fig. 3: Rigid laryngoscopy of concurrent fungal laryngitis with tuberculous laryngitis (*Figure 3 reprinted with permission from the Atlas of Phonomicrosurgery*)

for a period of 2 weeks. All patients were advised adequate hydration, proton pump inhibitors twice a day, and were asked to follow-up weekly. A complete hemogram including ESR was performed at the initial visit.

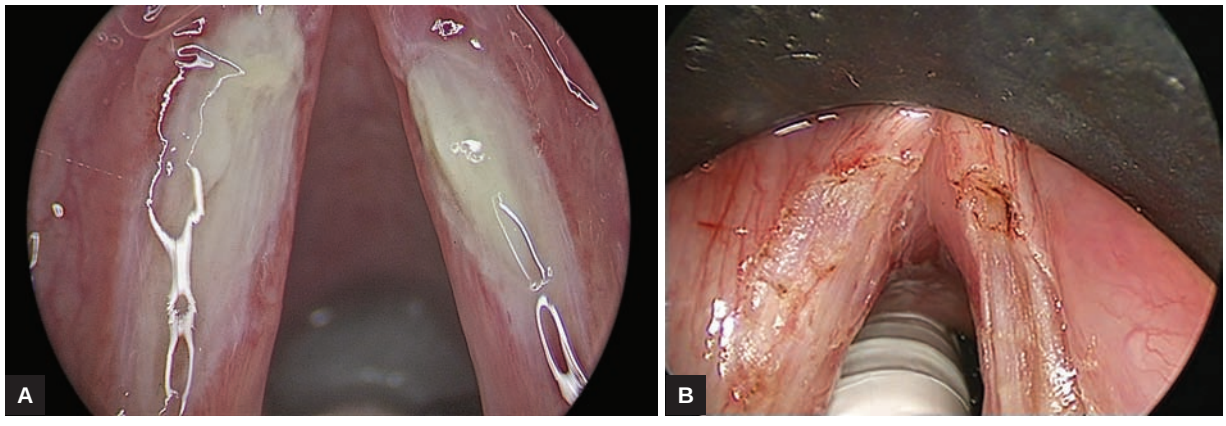
Patients who at 2 weeks showed complete resolution of lesions were asked to stop the antifungals at 3 weeks (total antifungal duration) and those who showed considerable regression but not complete resolution in the size of the lesions were asked to continue the oral antifungal treatment for an additional 2 weeks (Fig. 4). Patients who did not show any regression of their lesion were advised microlaryngeal surgery with excision of the lesions (Fig. 5). The specimen was sent for a potassium hydroxide (KOH) preparation examination, fungal culture, mycobacterium culture, and histopathology. At the seventh post-operative day, depending on the results of the fungal culture report, the antifungal was changed if needed. The final diagnosis of FL in the operative group was made based on the KOH mount (Fig. 6), which showed fungal hyphae in all cases.

None of our patients had history of smoking, radiotherapy, chemotherapy, burns, severe reflux, uncontrolled diabetes, HIV, or any immunosuppressant drugs barring a short course of oral steroids or inhalational steroids (nine patients).

Our incidence of FL was (0.7%) and patients were aged between 21 and 66 years (average age was 43 years) with seven (64%) males. All patients presented with hoarseness of voice of a short duration between 1 to 3 months with three patients complained of persistent dry cough. The typical history obtained in most of the patients was either severe cough prior to the onset of hoarseness or a diagnosis of acute laryngitis, for which they had been prescribed oral steroids (8 patients, 73%) or inhalational steroids (1 patient, 9%). None of the patients complained of pain, dysphagia, or breathlessness.



Figs 4A to C: (A) Bilateral FL (B) Following oral fluconazole 200 mg OD at 2 weeks showing some resolution; and (C) at 4 weeks with complete clearance



Figs 5A and B: (A) Bilateral FL that did not resolve with conservative measures and needed excision; (B) surgery performed with CO_2 acublade system (*Figure 5A reprinted with permission from the Atlas of Phonomicrosurgery*)

The ESR was raised in 10 patients (91%) with the average ESR being 42.

All suspected FL patients received oral antifungal therapy consisting of fluconazole 200 mg OD for a period of 2 weeks, after confirming a normal hepatic and renal profile and vocal hygiene measures. Based on the response to this treatment, we categorized the patients into two groups:

Group I: Those who responded completely or partially to the initial therapy—six patients (55%).

Group II: Those who did not respond to the initial therapy and were thus recommended surgical excision—five patients (45%).

The patients in group I (six patients) whose lesions at 2 weeks resolved completely (two patients) were asked to continue with 1 week of antifungals and those in whom the lesions regressed but did not completely resolve were asked to continue with the antifungals for another 2 weeks (four patients).

In the five patients of group II, who underwent excision, KOH mount was positive for fungal elements in all, with culture growing Aspergillus in one (20%) patient (Fig. 6). The histopathological examination showed non-specific chronic inflammation in two, chronic granulomatous changes in one, and necrotizing granulomas in two patients (Fig. 7).

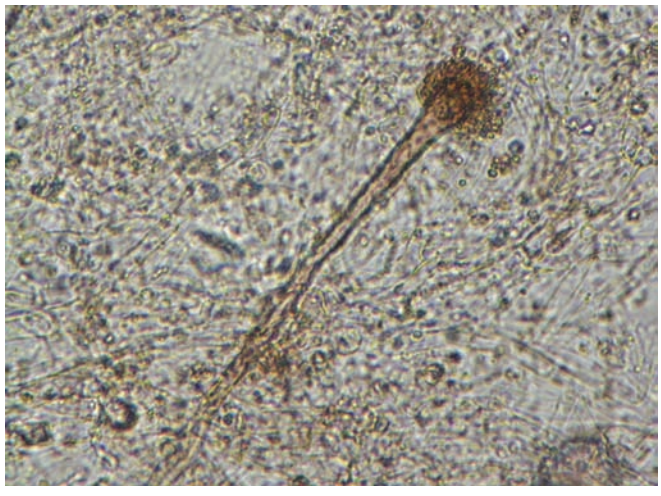
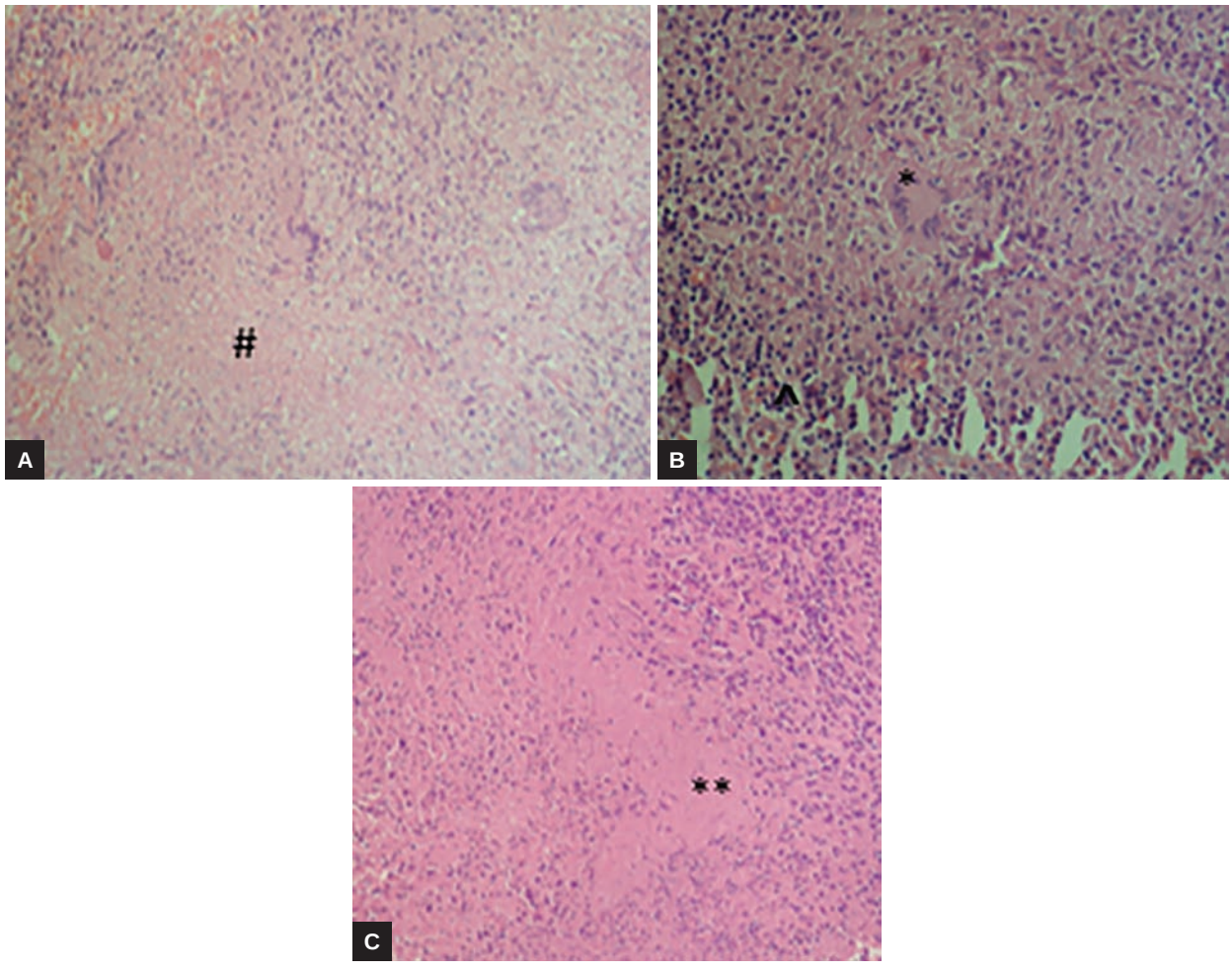


Fig. 6: Aspergillus KOH mount showing an unbranched conidiophore of Aspergillus terminating in a globose vesicle (*) bearing phillades from which the chains of conidia arise (*Reprinted with permission from the Atlas of Phonomicrosurgery*)

Culture for *Mycobacterium tuberculosis* was sent for all operated patients and was found positive in two patients.



Figs 7A to C: Histopathological examination with H&E staining showing: (A) Necrotizing granulomas (#) with; (B) the subepithelial infiltration with multinucleated giant cells (*) formed by pallisading histiocytes (^); and (C) punctuate necrosis (**). (*Reprinted with permission from the Atlas of Phonomicrosurgery*)

Both of these patients had shown extensive lesions on the larynx, and fungal culture in one of these patients had revealed non-invasive aspergillosis for which the fluconazole had been changed to oral voriconazole.

DISCUSSION

The commonest type of FL is laryngeal candidiasis caused by *C. albicans*.[3] Laryngeal candidiasis is typically concomitant with oropharyngeal candidiasis or "thrush". The typical whitish-green to yellow exudate seen in candidial thrush can coat the entire larynx and hypopharynx.[5] Although a majority of our patients of FL responded to fluconazole (91%), suggesting candida infection, none had any obvious concomitant oral thrush.

Historically, FL is described to be found in immunocompromised patients, such as patients with AIDS, leukemia, transplant, chronic renal failure, patients on chemotherapy, chemical injury. However, recent reports have described that laryngeal candidiasis can occur in both immunocompromised patients and healthy patients with predisposing factors, such as the use of corticosteroids, particularly inhaled steroids in asthmatics, broad-spectrum antibiotics, diabetes, burns, alcoholism, endotracheal intubation, and recent laryngitis.[6,7] This may be because of a deficit in the immune system of the host like in immunodeficiency, chemotherapy, etc., or a defect in the mucosal barrier due to mechanical, thermal, or chemical injury.[8]

Two forms of laryngeal candidiasis have been described. One is the benign, isolated laryngeal candidiasis seen in asthmatics with chronic use of steroid inhalers, and the second form is invasive laryngeal candidiasis seen in the immunocompromised patient.[7] Other fungi like Aspergillus, Histoplasma, Coccidioimycosis, Blastomycosis, and Cryptococcus which may be endemic in nature have also been implicated in FL. Aspergillus may cause non-invasive as well as invasive disease.[2]

In our patients of FL (Table 1), we found an elevated ESR value in 10 of the 11 patients. We have not come across a correlation between ESR and FL mentioned in the previous studies and this may be a good diagnostic predictor.

Table 1: Master chart

Age (years)	Gender	Presenting complaint	Duration	Steroid use	ESR	Response to oral anti-fungal	Surgery needed	KOH mount for fungal hyphae	Fungal culture	MGIT TB culture	Histopathology
38	Female	Hoarseness	2 months	Oral	40	Partial	Yes	Positive	No growth	Negative	Chronic inflammation
21	Male	Hoarseness	3 months	Oral	36	Partial	Yes	Positive	No growth	Negative	Chronic nonspecific inflammation
31	Female	Hoarseness, dry cough	1 month	Oral	40	Present	No				
62	Male	Hoarseness	2 months	Nil	38	Present	No				
40	Male	Hoarseness	45 days	Oral	42	Present	No				
39	Male	Hoarseness	45 days	Oral	15	Absent	Yes	Positive	No growth	Negative	Necrotizing granulomas
21	Female	Hoarseness, dry cough	45 days	Nil	56	Partial	Yes	Positive	No growth	Positive	Necrotizing granulomas
48	Male	Hoarseness	3 months	Nil	48	Present	No				
60	Male	Hoarseness, hacking cough	2 months	Inhalation	62	Partial	Yes	Positive	Aspergillus	Positive	Chronic granulomas
52	Female	Hoarseness	3 months	Oral	36	Present	No				
66	Male	Hoarseness	2 months	Inhalation	46	Present	No				

In a study by Wong et al,[3] 54 patients of laryngeal candidiasis were reviewed, 89% of the patients were on steroid inhalers and 7% were on oral steroids. The success rate with the first course of oral antifungals was as high as 96%.[3]

In our series of 11 patients, 9 patients had received steroids, 8 orally and 1 as inhalational steroids. This is unlike previous studies where inhalational steroids seem to be the main culprit predisposing a patient to FL.

Dramatic response to a course of antifungals points toward diagnosis. Previous reports have outlined the importance of biopsy in making the diagnosis of laryngeal candidiasis.[9] However, current opinion does not feel this is necessary in most cases because clinical findings and treatment response can confirm the diagnosis.[10] Furthermore, a premature biopsy might cause vocal fold scarring, which can be extremely difficult to treat.[11]

Accurate diagnosis of FL and early treatment are necessary to prevent extensive damage and systemic dissemination.[3] Amphotericin B used to be the mainstay of treatment[1,12,13] previously, but the azoles especially fluconazole and itraconazole are used widely now.[1,14] Despite a correct diagnosis and appropriate treatment, lack of response is not uncommon. This may be due to thick fungal lesions with central avascularity preventing the antifungals from reaching the site, lack of sensitivity to the prescribed antifungal, or invasive nature of the FL.

With the increasing number of apparently healthy tuberculosis patients in our practice in India, any patient with features suspicious of FL should undergo tests to rule out concomitant tuberculosis especially in extensive lesions.

CONCLUSION

The diagnosis of FL requires a high index of suspicion and should be considered in cases that show white, smooth plaques on the larynx surrounded by erythema. A history of steroid use either inhaled or oral (81% in our series) and elevated ESR (91%) are helpful diagnostic pointers.

A trial of oral antifungals, such as fluconazole is recommended. Some patients may require surgical excision, especially in the case of thick avascular fungal plaques (45% in our series).

In case of extensive lesions or no response to treatment, a possibility of concomitant TB should be considered.

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