



Primary Laryngeal Aspergillosis in the Immunocompetent Patient

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ABSTRACT

Introduction

Fungal infections of the larynx are truly rare in immunocompetent people with only a handful of cases reported in the past five decades. Here we present a case series of 3 people (from 2019 to 2021), with no comorbid conditions, who presented with primary laryngeal aspergillosis.

Case Series

Three patients with primary aspergillosis of the larynx were seen in the ENT outpatient department from 2019 to 2021, aged between 40-50 years of which two were females and one patient was a male. We describe the clinical presentation of each patient.

Discussion

Aspergillosis of the larynx usually occurs secondary to bronchopulmonary infections in the immunocompromised. The usual etiological factors include prolonged use of inhaled steroids, cytotoxic drugs, radiotherapy, smoking, mucosal injury, and antibiotic abuse. Persistent hoarseness of voice is the most common presenting symptom. Video laryngoscopy reveals erythema, oedema, hyperkeratosis, adherent white plaques, shallow ulcerations, and grey or white pseudo membrane formation over the vocal cords. Definitive diagnosis is done by the demonstration of hyphae either by KOH staining, culture in Sabouraud Dextrose Agar at 28 degrees Celsius, or tissue biopsy.

Conclusion

Primary aspergillosis of the larynx has occurred more frequently in recent times. Aspergillosis of the larynx can often mimic malignant or premalignant lesions. Persistent hoarseness of voice not responding to treatment should also raise a suspicion of fungal laryngitis, in the clinician and relatively simple treatment be done before significant morbidity occurs.

Keywords

Larynx; Laryngeal Diseases; Aspergillosis

Larynx is an uncommon location for fungal infections of the body and are typically a sequela of bronchopulmonary infections by the fungus.^{1,2} Laryngeal mycoses are known to occur in immuno-

compromised states and are usually associated with the prolonged use of inhalational steroids and cytotoxic drugs.³ However, isolated laryngeal mycosis is a rare clinical entity, especially in immunocompetent individuals. Here we present a case series of 3 immunocompetent patients who developed isolated primary laryngeal mycosis.

Case Series

Three patients with primary aspergillosis of the larynx were seen in the ENT outpatient department from 2019 to 2021, aged between 40-50 years of which two were females and one patient was a male. A methodical clinical examination was done. Investigations done and treatment

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given were recorded in each case. The patient details such as age, sex, addiction, and risk factors for primary laryngeal aspergillosis were documented. We describe the clinical presentation of each patient below and discuss the rise of primary laryngeal aspergillosis as a more common disease entity in present times.

Case Reports

Case 1

A 51-year-old lady presented with hoarseness of voice for 2 months. She had a history of tobacco chewing for

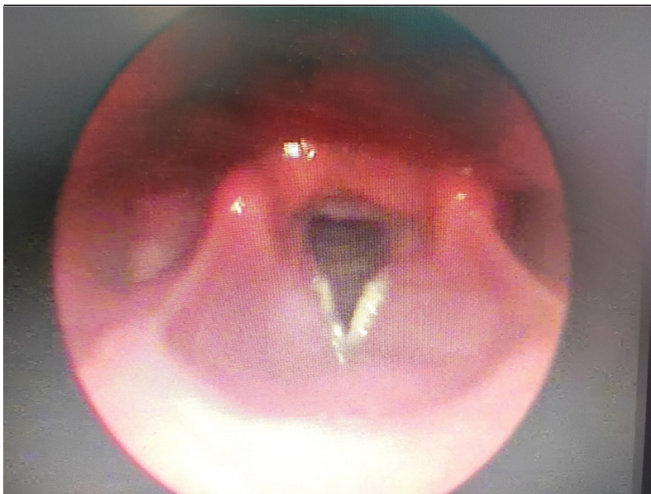


Fig. 1: Whitish plaque like lesion on both vocal cords in case 1



Fig. 2A: Culture on SDA at 25°C showing rapidly growing yellowish green, velvety colonies

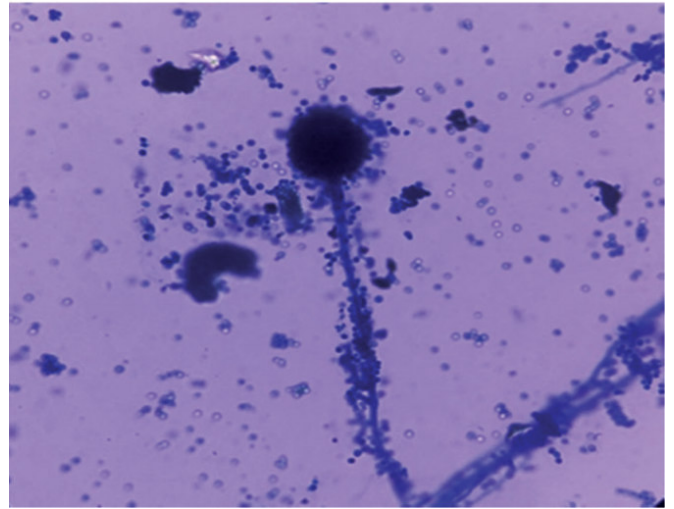


Fig. 2B: Microscopic examination of the colony by Lactophenol cotton blue (LPCB) 40X magnification shows smooth walled conidiophores with subglobose vesicle covered by double row of phialides bearing spherical conidia in case 1.

the past 30 years and complained of reflux symptoms. There was no history of voice abuse, alcoholism, comorbidity, or prolonged use of any drugs. Video laryngoscopy revealed whitish plaque like lesions on the superior surface of mobile thickened vocal cords. (Fig. 1) Microlaryngeal excision of the lesion was done

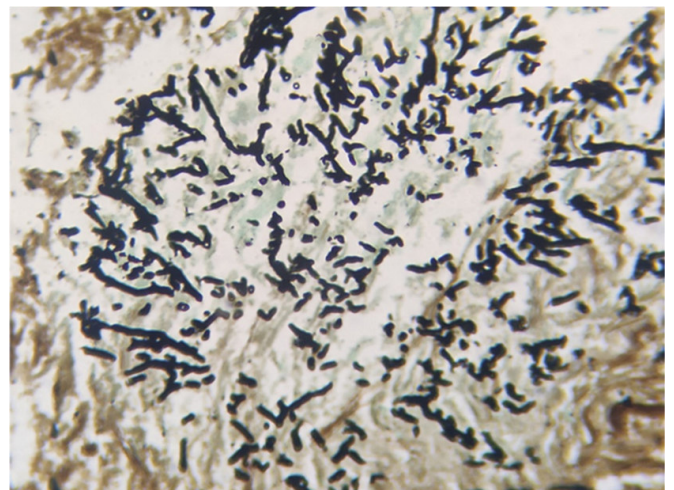


Fig. 3: Grocott-Gomori's Methenamine Silver stain showing slender hyphae branching at acute angles at 400x magnification in case 1

under general anaesthesia. Histopathological examination of the excised tissue revealed ulcerative lesions with colonies of filamentous fungus, and it grew *Aspergillus flavus* on culture. (Figs. 2A, 2B & 3) The post operative course was uneventful, and she was started on Tablet Itraconazole 100mg once daily for 3 weeks, after due discussion with the department of internal medicine. Patient recovered well and was asymptomatic at 3 months follow up.

Case 2

A 41-year-old male with no generalized immuno-deficiency presented with the complaints of change in voice for the past 1 year. He had no history of voice abuse, comorbidity, reflux symptoms or addictions. On examination, chalky white lesions were observed on the superior surface and medial edge of both vocal cords. The cords were mobile, and airway was adequate. The patient was taken up for microlaryngeal excision and biopsy under general anaesthesia. Histopathological examination of the excised tissue revealed filamentous fungi and growth of *Aspergillus fumigatus* was observed on culture. (Fig. 4) Patient had no problems postoperatively and was started

on Tablet Itraconazole 100mg once daily for 3 weeks. There was no recurrence at 3 months follow up.

Case 3

A 44-year-old lady came with hoarseness of voice for the past 1 year. Patient had a history of taking ayurvedic medications for the voice change, during which she had an episode of cough with blood-stained sputum. She was evaluated for tuberculosis and was found to be negative. She had received her first dose of COVID vaccine in August 2021. No other related history of significance was noted. Video laryngoscopy showed a single broad based multi lobulated polyp covered with white plaques arising from the upper surface of the membranous right vocal cord not involving the anterior commissure. (Fig. 5) Microlaryngeal excision was done under general anaesthesia and the tissue sent for biopsy. Histopathology revealed a polypoidal lesion lined by squamous epithelium with foci of ulceration with underlying edema, fibrin, granulation tissue, histiocytes and inflammatory cells consistent with vocal cord polyp. Phaeoid slender septate hyphae were seen on KOH smear suggestive of *Aspergillus* spp. (Fig. 6) The patient was started on oral

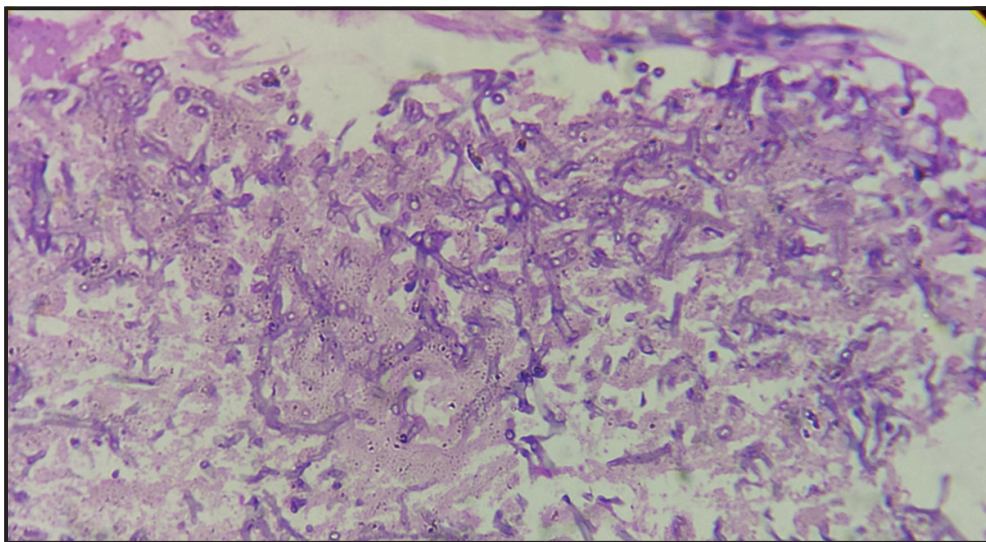


Fig. 4. Periodic acid–Schiff stain showing colonies of filamentous fungi with delicate septate hyphae branching at acute angles at 400x magnification in case 2.

Itraconazole 100mg once daily for 3 weeks. The symptoms had not recurred at 3 months follow up.

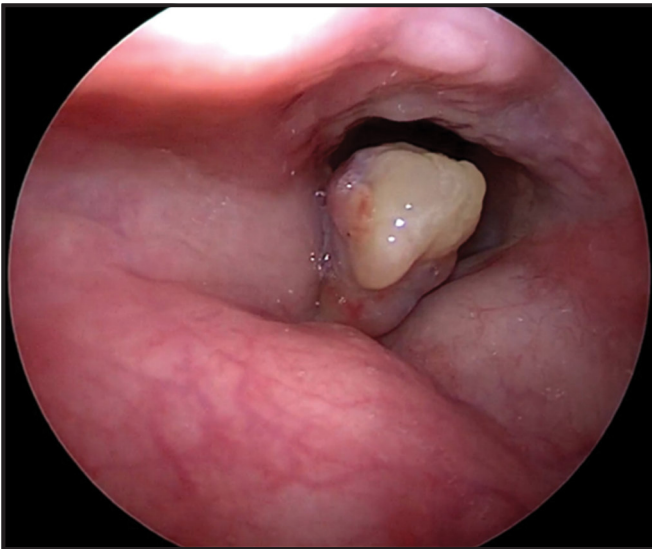


Fig. 5. Single broad based multi lobulated polyp covered with white plaques on the surface, arising from the upper surface of the membranous right vocal cord seen in case 3



Fig. 6. KOH mount showing slender, dematiaceous, septate hyphae with acute branching at 40x magnification in case 3

Summary :

In this series, there were two females and one male aged between 40-50 years. One patient had a history of chewing tobacco while another had been taking ayurvedic medicines. One patient had no known risk factors. None

of the patients had any comorbidities and were apparently immunocompetent. It should be noted that all three patients were from Bankura district of West Bengal, India and were into farming. The predominant complaint was hoarseness of voice. All were taken up for microlaryngeal excision and responded well to postoperative oral Itraconazole and no recurrence or residual lesion was seen on follow up.

Discussion

Aspergillus sp. are ubiquitous, saprophytic fungi that grow on soil and decaying matter. They also result in opportunistic infections in the immunocompromised.³ But primary isolated aspergillosis of the larynx is truly rare, with less than 50 cases documented over the past 50 years.⁴ However, there has been an increase in reporting especially over the recent past, highlighting the fact that it is an emerging disease entity.³ (Table I)

There could be a multi factorial aetiology for laryngeal mycosis in immunocompetent people. Local factors, such as radiotherapy, steroid inhaler use and laser treatment, are more likely to be associated with the onset of localized aspergillosis than decreased immunity. Mucosal injury because of voice abuse, laryngopharyngeal reflux, smoking or use of tobacco may lead to the loss of the local barrier allowing for laryngeal infection and subsequent invasion by the fungus. Antibiotic abuse alters the local bacterial flora leading to the overgrowth of *Aspergillus*.⁵ A review of literature shows that there was no significant identifiable cause in a vast majority of patients. In this study, of the 3 patients, one had a history of tobacco chewing while another had been taking ayurvedic medicines. All 3 patients were from the same district and were engaged in farming which suggests that the type of soil, quality of air and occupation could be important predisposing factors for laryngeal aspergillosis in immunocompetent people.

Persistent hoarseness of voice is the most common complaint in other reports, as in the present series. The other symptoms could be cough, discomfort of the throat and difficulty in breathing. Laryngeal aspergillosis often mimics premalignant, malignant, or granulomatous lesions.

Early diagnosis of laryngeal aspergillosis prevents dissemination of infection.⁶ Video laryngoscopy reveals erythema, oedema, hyperkeratosis, adherent white plaques, shallow ulcerations, and grey or white pseudo membrane formation over the vocal cords.^[1] Definitive diagnosis is done by the demonstration of hyphae either by KOH staining, culture in Sabouraud Dextrose Agar at 28 degrees Celsius, or tissue biopsy.¹ Histopathology shows septate hyphae with dichotomous branching at a 45-degree angle. Species identification can be done by

studying culture patterns or gene extraction and subsequent amplification by polymerase chain reaction.³

Surgical excision followed by oral Itraconazole 100 mg od for 3 weeks is the preferred treatment, in our experience. Though the use of anti-fungal drugs is still being debated, most published reports recommend oral itraconazole for three-to-four weeks as the standard treatment in primary laryngeal aspergillosis, irrespective of invasion.^[3] Further study is required to ascertain whether conservative management with anti-fungals alone, is sufficient in laryngeal aspergillosis.

Table I: Details of the published reports of primary laryngeal Aspergillosis including the present study

CASE	REFERENCE	AGE/ GENDER	CLINICAL PRESENTATION	TREATMENT	FOLLOW UP PERIOD AND OUTCOME
1.	Rao PB. 1969	48/M	Hoarseness of voice	No treatment	2 Months asymptomatic
2.	Ferlito A. et al. 1974	76/M	Hoarseness of voice	No treatment	2 Months asymptomatic
3.	Kheir SM et al. 1983	50/M	Hoarseness of voice	Topical nystatin powder	24 Months asymptomatic
4.	Benson-Mitchell R et al. 1994	62/M	Hoarseness of voice	No treatment	2 Months asymptomatic
5.	Nong D, et al. 1997	30-40 4 M+4F	Hoarseness of voice leading to aphonia, sore throat	NA	NA
6.	Beust L, et al. 1998	53/M	Hoarseness of voice, respiratory distress	Laryngectomy	3 Months asymptomatic
7.	Fairfax AJ, et al. 1999	75/M	Hoarseness of voice, 1999	Amphotericin lozenges, 10 mg -4 Weeks	1 Month Improved aphonia
8.	Dean CM, et al. 2001	17/F	Hoarseness of voice, vocal fatigue	NA	NA

Table I: Contd.

Table I (Contd.) : Details of the published reports of primary laryngeal Aspergillosis including the present study

CASE	REFERENCE	AGE/ GENDER	CLINICAL PRESENTATION	TREATMENT	FOLLOW UP PERIOD AND OUTCOME
9.	Ogawa Y, et al. 2002	73/M	Hoarseness of voice (History of Radiotherapy and DB)	Oral Itraconazole 8 weeks and Amphotericin-B gargle	2 Months- No recurrence
10.	Wittkopf J, et al. 2006	62/F	Fluctuating hoarseness	Surgery	NA- No recurrence
11.	Ran Y, et al. 2008	36/F	Hoarseness of voice, vocal fatigue	Oral Itraconazole (200 mg bd-4 weeks)	1 Month asymptomatic
12.	Liu YC, et al. 2010	30/F	Hoarseness of voice	Oral Itraconazole (200 mg bd-4 weeks)	1 Month asymptomatic
		32/F			
13.	Ran Y, et al. 2011	30/F	Hoarseness of voice, vocal fatigue, expectoration, and occasional vomiting	Oral Itraconazole (200 mg bd-first 2 weeks, 200 mg qd next 2 weeks)	1 Month asymptomatic
14.	Sundarray C et al. 2011	NA	NA	NA	NA
15.	Ran Y, et al. 2013	23/F	Hoarseness of voice, severe paroxysmal cough, tachypnea	Oral Itraconazole (200 mg bd-4 W)	1 Month asymptomatic
16.	Doloi PK, et al. 2014	35/F	Hoarseness of voice, cough	Oral Itraconazole (100 mg qd-3 weeks)	3 Weeks asymptomatic
17.	Al-Ogaili Z, et al. 2014	77/F	Dysphagia and hoarseness	NA	NA

Table I: Contd.

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CASE	REFERENCE	AGE/ GENDER	CLINICAL PRESENTATION	TREATMENT	FOLLOW UP PERIOD AND OUTCOME
18.	Gangopadhyay M, et al. 2014	42/M	Hoarseness, fever, cough with expectoration	Oral Itraconazole	18 Months asymptomatic
19.	Ravikumar et al. 2014	34/F	Hoarseness, cough, Dysphagia, vocal fatigue	Oral Itraconazole (100 mg bd - 3 Weeks)	3 Weeks asymptomatic
		52/F			
		38/M			
20.	David et al. 2014	59/F	Hoarseness of voice	Oral Itraconazole	NA: No recurrence
21.	M Dutta, et al. 2015	45/F	Hoarseness of voice	Oral Itraconazole (300 mg qd- 3 Weeks)	6 Months asymptomatic
22.	JCR Villanueva, et al. 2015	28/F	Hoarseness of voice	Oral Voriconazole (400 mg qd- 4 Weeks)	1 Month asymptomatic
23.	Arpita Saha, et al. 2015	28/F	severe dysphonia	Voriconazole (200 mg bd- 8 days)	2 Weeks asymptomatic
25.	Richard H. et al. 2016	73/F	persistent hoarseness	Oral Itraconazole 20 Weeks	5 Months asymptomatic
27.	Soumen Chatterjee et.al. 2017	43/F	Hoarseness of voice	Oral Itraconazole 100 mg bd- 8 weeks	1 Month asymptomatic
28.	Subramanya, S.H. et al 2018	22/M	hoarseness and frequent expectoration	Oral Itraconazole 4 weeks	1 Month asymptomatic
					No recurrence

Table I: Contd.

Table I (Contd.): Details of the published reports of primary laryngeal Aspergillosis including the present study

CASE	REFERENCE	AGE/ GENDER	CLINICAL PRESENTATION	TREATMENT	FOLLOW UP PERIOD AND OUTCOME
29.	Swain SK et al 2020	15-63 y 2F+4M	Hoarseness of voice	Surgery + Oral Itraconazole 100mg bd- 3 weeks	1 Month- 1 Year No recurrence
30.	Present study	40-50Y 2F+1M	Hoarseness of voice	Surgery+ Oral Itraconazole 100mg OD- 3 weeks	3 Months No recurrence

Conclusion

The incidence of primary laryngeal aspergillosis in the immunocompetent is on the rise recently. The presence of white patches on the vocal cords, or vocal polyp covered by white plaques and persistent hoarseness of voice, not responding to conservative treatment should alert the clinician regarding the possibility of laryngeal aspergillosis, thereby facilitating the diagnosis of this entity before significant morbidity occurs.

References

- Swain SK, Debta P, Shajahan N. Primary fungal laryngitis: Our experiences at a tertiary care teaching hospital of Eastern India. *Int J Health Allied Sci* 2020; 9:153-8.
- Subramanya SH, Jillwin J, Rudramurthy SM, et al. Primary invasive laryngeal mycosis in an immunocompetent patient: a case report and clinico-epidemiological update. *BMC Infectious Diseases*. 2018 Jul;18(1):323. DOI: 10.1186/s12879-018-3219-1. PMID: 29996788; PMCID: PMC6042277.
- Dutta M, Jotdar A, Kundu S, Ghosh B, Mukhopadhyay S. Primary laryngeal aspergillosis in the immunocompetent state: a clinical update. *Braz J Otorhinolaryngol*. 2017; 83:228-34.
- Gandhi SS, Shenoy SB. Primary aspergillosis of bilateral vocal cords in an immunocompetent individual. *J Laryngol Voice* 2018; 8:43-5.
- Liu YC, Zhou SH, Ling L. Aetiological factors contributing to the development of primary laryngeal aspergillosis in immunocompetent patients. *J Med Microbiol*. 2010 Oct;59(Pt 10):1250-1253. doi: 10.1099/jmm.0.021634-0. Epub 2010 Jun 24. PMID: 20576752.
- Biswas KD, Choudhary A, Ghosh SK, Biswas S. Primary Laryngeal Aspergillosis in an Immunocompetent Host. *BJOHNS [Internet]*. 2020Jul.27 [cited 2022Feb.8];26(2):131-3. Available from: <https://bjohns.in/journal3/index.php/bjohns/article/view/190>.