Tuberculosis in Larynx

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Abstract

Introduction: Laryngeal tuberculosis (TB) has shown increase in incidence in recent years and the increase in immunosuppressive conditions has altered the clinical profile of the disease. The aim of this study was to evaluate the changing trends of laryngeal TB and to highlight its site of involvement, type of lesion, and degree of involvement. **Patients and Methods:** This prospective study included 54 patients with a diagnosis of laryngeal TB. All patients were evaluated in terms of their age, chief complaints, lesions, and site of involvement on flexible fiber-optic bronchoscopy, and they also underwent a variety of laboratory investigations as indicated. **Results:** The study showed that true vocal cords + false cords + epiglottis were involved in 48.1% ($n = 26$), arytenoids + interarytenoid + posterior part of true cords in 24.1% ($n = 13$), true cords + false cords + arytenoids + interarytenoid in 18.5% ($n = 10$), true vocal cords alone in 5.5% ($n = 3$), interarytenoid in 1.8% ($n = 1$), and interarytenoid + arytenoid involvement was seen in 1.8% ($n = 1$) of patients. These lesions were categorized into four different appearances as follows: granulomatous lesions in 50% ($n = 27$), ulcerative lesions in 27.7% ($n = 15$), hyperemia and hypertrophic in 16.7% ($n = 9$), and papillomatous mass in 5.6% ($n = 3$) based on fiber-optic bronchoscopy. **Conclusion:** In this study, the disease was most rampant in the age group of 31–60 years, with a predilection seen in low socioeconomic groups, rural groups and in individuals addicted to smoling and alcoholism. Hoarseness and odynophagia are the major symptoms. Multiple subsites are involved, and the lesions show a predilection for the anterior part of the vocal cord.

Keywords: Bronchoscopy, hoarseness, laryngeal tuberculosis, odynophagia, vocal cords

INTRODUCTION

One in three people in the world is infected with tuberculosis (TB) bacteria.^[1] However, the changing behavior of the disease in the face of emergence of acquired immunodeficiency syndrome and other immunosuppressive diseases has drawn attention to the altering spectrum of TB.^[2-4] The clinical picture is rapidly changing because of antituberculous drugs and early interventions. Most physicians do not consider TB in the differential diagnosis of various laryngeal symptoms, and this oversight leads to misdiagnosis and inappropriate treatment.^[2] Laryngeal tubercular granuloma may often be passed off as carcinoma.^[5] Our aim was to unveil and evaluate the changing trends of laryngeal TB with respect to a review of literature.

MATERIALS AND METHODS

The present prospective study comprised 54 patients referred by the department of otorhinolaryngology and head-and-neck surgery after indirect laryngoscopy in which there were some laryngeal findings; in order to have a closer and clearer view, these patients were subjected to bronchoscopic evaluation and

biopsy, which were performed at the department of TB and respiratory diseases, in a tertiary care institute over a period of 10 years between May 2008 and March 2018. The criteria for diagnosis were presence of acid-fast bacilli (AFB) either in the sputum smears or in the histological specimens, or the histopathological findings conclusive of laryngeal TB in the biopsy specimen. In patients in whom the histopathological findings were not conclusive of TB, the diagnosis was made on clinical evaluation and their responsiveness to antitubercular therapy. All the patients were evaluated in terms of their age, chief complaints, lesions, and site of involvement on flexible fiber-optic bronchoscopy, and they also underwent a variety of laboratory investigations ranging from routine blood tests; urine tests; chest radiography; and some special tests such as Veneral Disease Research Laboratories, viral markers, sputum for AFB

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staining, Mantoux test, sputum cultures, and polymerase chain reaction (PCR) as indicated. Contrast-enhanced computerized tomography (CECT) of the larynx and chest was done wherever required (in AFB-negative cases and in cases where there was a suspicion of laryngeal malignancy). The features of laryngeal TB were evaluated, discussed, and compared with that of other reports. Antitubercular treatment was administered in all the cases. An initial regimen of isoniazid, rifampicin, and pyrazinamide for initial 2 months with added ethambutol or streptomycin was prescribed in case of suspected drug resistance. Isoniazid and rifampicin were continued for a further 4 months. Completion of therapy was determined by a repeat bronchoscopic examination and findings of chest radiographs. None of the patients enrolled in our study were or suffering from multidrug resistant-TB.

RESULTS

The study explored many important aspects of laryngeal TB. The disease was common in rural patients. The age range was 13–74 years, with an average of 49.7 ± 4.78 years. The disease was most rampant in the age group of 31–60 years. Thirty (55.55%) were males and 24 (44.45%) were females. The youngest patient affected was 13 years of age, while the oldest was 74 years of age.

Clinical symptoms of the disease encountered in order of frequency included hoarseness of voice (90.7%, $n = 49$), odynophagia (74%, $n = 40$), cough with expectoration (70.37%, $n = 38$), loss of appetite and weight (37%, $n = 20$), low-grade fever (33%, $n = 18$), hemoptysis (33%, $n = 18$), and dysphagia (22.2%, $n = 12$). Only one patient had distressing stridor.

The flexible fiber-optic bronchoscopic findings [Table 1] revealed a striking feature that the involved sites were multiple in majority of the cases. The true vocal cords + false cords + epiglottis were involved in 48.1% ($n = 26$) of patients, arytenoids + interarytenoid + posterior part of true cords in 24.1% ($n = 13$), true cords + false cords + arytenoids + interarytenoid in 18.5% ($n = 10$), true vocal cords alone in 5.5% ($n = 3$), interarytenoid in 1.8% ($n = 1$), and interarytenoid + arytenoid involvement was seen in 1.8% ($n = 1$) only.

The flexible fiber-optic bronchoscopy revealed a variety of laryngeal lesions [Table 2]. These lesions were categorized into four different appearances as follows: granulomatous lesions in 50% ($n = 27$), ulcerative lesions in 27.7% ($n = 15$), hyperemia and hypertrophic in 16.7% ($n = 9$), and papillomatous mass in 5.6% ($n = 3$). In these three cases with papillomatous mass, a suspicion of laryngeal malignancy was made on admission. As the correlation between pulmonary involvement and laryngeal lesions was concerned, chest radiography formed the cornerstone. Fifty-one (94.44%) out of the 54 cases had positive findings on radiological examinations of the chest. Overall 61.1% ($n = 33$) had a lesion in the apex, 16.67% ($n = 9$) had lesions both in the apical and middle lobes, 7.4% ($n = 4$)

Table 1: Site and pattern of involvement

Site of involvement	Number of cases (%) age
TVC + FVC + epiglottis	26 (48.1)
Arytenoids + IA + postpart of TVC	13 (24.1)
TVC + FVC + arytenoids + IA	10 (18.5)
TVC	3 (5.5)
Arytenoids + IA	1 (1.8)
IA	1 (1.8)

TVC: True vocal cord, FVC: False vocal cord, IA: Interarytenoids

Table 2: Types of laryngeal lesions

Gross appearance	Number of patients (%)
Granulomatous lesions	27 (50)
Ulcerative lesions	15 (27.7)
Hyperemia and hypertrophic	9 (16.7)
Papillomatous mass	3 (5.6)

showed extensive lesions in both the lung fields, and 3.7% ($n = 2$), each, showed involvement of the lower lobe and hilum, and 1.8% ($n = 1$) had transudative pleural infusion. In 5.5% ($n = 3$) of cases, the radiological study of chest did not reveal any pathology. The nature of pulmonary lesion on radiology of the chest was infiltration with cavity formation in 48.1% ($n = 26$), infiltrates in the lung fields in 20.4% ($n = 11$), single or multiple cavitory lesions in 18.5% ($n = 10$), and fibrotic lesions in 7.4% ($n = 4$). The sputum for AFB was positive in 48.1% ($n = 26$), indicating the involvement of larynx secondary to active pulmonary TB. CECT of the larynx and chest was done in AFB-negative cases ($n = 28$) and in cases with a suspicion of laryngeal malignancy (cases with papillomatous mass [$n = 3$]) [Figure 1]. The CECT findings of the larynx in sputum negative cases were not specific but bilateral or unilateral diffuse nodular laryngeal lesions were seen without distortion of the laryngeal.

Histopathological examination revealed specific tubercular granuloma with AFB in 23% ($n = 12$) and specific tubercular granuloma without AFB in 7.7% ($n = 4$). The incidence of nonspecific granuloma was 68.5% ($n = 37$), whereas a mixed picture of both granuloma and malignancy was found in 1.8% ($n = 1$). Ten cases out of 37 which revealed nonspecific granuloma on histology showed positive AFB in sputum smears, whereas the rest 27 cases were clinically evaluated for TB based on fever, chest radiograph, CECT of the larynx and chest, and erythrocyte sedimentation rate findings. Based on the above clinical evaluation, antitubercular treatment was started, and these cases were repeatedly evaluated for progression or regression of the disease.

Finally, an epidemiological survey was conducted on the proven cases. The survey was based on certain salient features such as socioeconomic status, area of inhabitants, occupation, and personal addiction. It revealed that 68.5% ($n = 37$) were habitants of rural areas and 53.7% ($n = 29$) were laborers by occupation. As far as addiction was concerned, both smoking

and alcohol consumption were seen in 51.8% ($n = 28$), smoking alone in 22.2% ($n = 12$), and alcohol consumption in 18.5% ($n = 10$) of cases. The study also gave due consideration to the time that has lapsed between the appearance of pulmonary and laryngeal symptoms [Table 3]. The criterion of the time lapse between the pulmonary and laryngeal symptoms was totally based on the history of appearance of cough with expectoration followed by laryngeal symptoms such as hoarseness or odynophagia. In 46.3% ($n = 25$) of patients, the time lapse between the appearance of pulmonary and laryngeal symptoms was 6–12 months, while it was 2–6 months in 22.6% ($n = 12$), more than 12 months in 16.6% ($n = 9$), and < 2 months in 9.2% ($n = 5$), whereas there were no pulmonary symptoms in 5.5% ($n = 3$) of cases.

Multiple drug antitubercular treatment was administered to all confirmed cases and also in those in whom histopathological examination was inconclusive of TB and diagnosis was made by clinical evaluation with responsiveness to antitubercular therapy. An initial regimen of isoniazid, rifampicin, and pyrazinamide for 2 months followed by isoniazid and rifampicin for 4 months was prescribed. Overall 24.1% ($n = 13$) of cases were cured after 6 months, whereas 66.7% ($n = 36$) were cured after 1 year of therapy, 5.5% ($n = 3$) were lost to follow-up, and 1.8% ($n = 1$) each died of chronic renal failure and HIV.

DISCUSSION

TB is reported as the leading cause of death from a single infective agent.^[3,6,7] The reason of resurgence and increase in the incidence of this disease for the past two decades is associated with increases in HIV infection, immunosuppressive diseases or treatments, the aged, immigrants coming from high-endemic areas, and the emergence of antituberculous-resistant organisms and atypical mycobacterium.^[6,7] Laryngeal TB has been reported to emerge with clinical patterns that differ from those seen in earlier times.^[2,3,6] This means that a pulmonologist needs to be more alert to the new emergence of laryngeal TB with atypical clinical manifestations and consider it in their differential diagnosis of laryngeal or disseminated diseases.^[6]

In this study, the age range was 13–74 years, with an average of 49.7 ± 4.78 years. The disease was most rampant in the age group of 31–60 years. The male: female ratio was 1.25:1. Lim cited Auerbach (in 1946) and stated that the period of greatest incidence of laryngeal TB was in young adults between 20 and 30 years of age, and there was no difference in the sex

distribution.^[3,7-9] This shift to older ages corresponds with the results of other studies.^[3,7,9] We also found a male predominance in the sex distribution, and findings from other studies too reported similar sex ratio distribution.^[7,8] These results suggest that there have been a shift in predilection for age and sex in laryngeal TB.

The symptomatology of laryngeal TB has also changed. Constitutional symptoms such as fever, weight loss, night sweat, fatigue, and hemoptysis had been the major symptoms in the past due to progressive pulmonary TB.^[10,11] However, in this study, most cases had hoarseness and odynophagia as the major symptoms. Symptomatology similar to this study has been reported in many studies.^[8,12]

The flexible fiber-optic bronchoscopic findings in our study [Figures 2–10] revealed a striking feature that the involved sites were multiple in majority of the cases. The disease showed a predilection for true vocal cords + false cords + epiglottis followed by arytenoids + interarytenoid + posterior part of true cords. The incidence of lesions involving solitarily a single area like the true vocal cords or the interarytenoid region was less. The classical posterior laryngeal involvement due to pooling of the infected sputum in a recumbent patient^[12] is no longer a cardinal sign for laryngeal TB. Our result and that of Lim *et al.*,^[8] Levenson *et al.*,^[5] and Nishiike *et al.*^[13] revealed that the number of patients with lesions involving multiple subsites was larger than that of patients with lesions involving a single subsite. In this study, the nature of the lesions was predominantly granulomatous followed by ulcerative, nonspecific hyperemia with hypertrophy, and papillomatous in decreasing order of frequency. Literature suggested that multiple areas of ulceration and hypertrophic lesion were more common, whereas Lim *et al.*^[8] and Wang *et al.*^[12] concluded that granulomatous laryngeal TB continues to be prevalent and the prevalence of polypoid or nonspecific laryngeal TB may be increasing, a finding very similar to our study. Polypoid lesions in the larynx often masquerade as malignancy, and a typical patient with laryngeal TB is also at a high risk for laryngeal carcinoma.^[13] Moreover, laryngeal carcinoma is more common than laryngeal TB.^[5] The risk of misdiagnosis of laryngeal TB as laryngeal cancer is evident.^[2] Hence, chest physicians should keep laryngeal TB in the differential diagnosis of all the cases presenting with hoarseness of voice.

As correlation between pulmonary involvement and laryngeal lesions was concerned, chest radiography formed the cornerstone. The disease showed a predilection for apical area followed by lesions both in the apical and middle lobes. In three cases, the chest radiograph showed no abnormality at all. The nature of pulmonary lesion on radiology of the chest revealed that infiltration with cavity formation was the most common, followed by infiltrates in the lung fields. Although a negative chest film does not exclude the diagnosis of laryngeal TB, as seen in our study, a positive chest film with a suspicion of pulmonary TB is a strong clue of laryngeal TB infection and a warning for medical care providers to protect themselves

Table 3: Time lapse during pulmonary and laryngeal symptoms

Time interval between laryngeal and pulmonary symptoms	Number of cases (%)
<1 months	5 (9.2)
1–6 months	12 (22.2)
6–12 months	25 (46.3)
12–24 months	9 (16.6)

Figure 1: Computed tomography scan showing lesion over the right true vocal cord

Figure 3: Granulomatous lesions involving the false cords

Figure 5: Granulomatous lesion involving aryepiglottic folds

from infection during clinical procedures. Therefore, chest X-rays are strongly recommended to all patients with suspected laryngeal TB or malignancy.^[12] Sputum for AFB, though positive in 48.1% of cases in our study, did not seem to be a

Figure 2: Ulcerative lesions over epiglottis

Figure 4: Granulomatous lesions involving the ventricles

Figure 6: Granuloma of epiglottis

reliable test for screening of TB infection as also reported by Wang *et al.*^[12]

Biopsy is still mandatory for diagnosis because laryngeal TB and carcinoma may coexist.^[14] Positive histology of specific tubercular granuloma with AFB was noted in 23% of cases in our study and specific tubercular granuloma without AFB in 7.7% of cases, while 68.5% of cases demonstrated nonspecific granulomas, so in these patients, the criteria of diagnosis

Figure 7: Nonspecific lesion over the left true vocal cords

Figure 8: Granulomatous lesion involving true cords + false vocal cords + ventricles + arytenoids + interarytenoid region

Figure 9: Granulomatous lesion involving true cords + false vocal cords + ventricles + arytenoids + interarytenoid region

Figure 10: Granulomatous lesion over arytenoid + interarytenoid lesion

of laryngeal TB were purely based on clinical evaluation of the patient and response to antitubercular treatment, and these patients were regularly followed up for progression/regression of disease. Although a high rate of positivity can be found on sputum culture and PCR testing, sputum culture generally requires several weeks, and PCR testing may give false-positive results as reported in literature.^[13] Because each examination has its own advantages and disadvantages and is not very specific for TB, physicians should combine the clinical evaluation and repeat examinations for definitive diagnosis of laryngeal TB. After confirmation of the diagnosis, treatment with antitubercular drugs should be started as soon as possible. Resolution of lesions and improvement of symptoms usually occur within several weeks of medical therapy.^[12] However, as the larynx heals, fibrosis of laryngeal tissues can occur, resulting in cricoarytenoid joint fixation, posterior glottis stenosis, subglottic stenosis, or persistent dysphonia.^[14] Surgical treatment, although rarely required, may be necessary if airway obstruction or laryngeal fibrosis results from the disease.

CONCLUSION

In this study, the disease was most rampant in the age group of 31–60 years, with an average age of 49.7 ± 4.78 years. The male: female ratio was 1.25:1, with a predilection seen in low socioeconomic groups, rural groups and in individuals addicted to smoking and alcoholism. Time lapse of 6–12 months is required for the pulmonary TB to manifest itself as laryngeal lesions. Hoarseness and odynophagia are the major symptoms. Multiple subsites are involved, and the lesions show predilection for anterior part of the vocal cords + false cords + epiglottis in combination. Lesions are predominantly granulomatous followed by ulcerative. Polypoidal lesions in the larynx often masquerade as malignancy. The disease shows a predilection for apical area followed by lesions both in the apical and middle lobes. Infiltration with cavity formation was the most common finding in chest radiographs. Sputum for AFB, though positive in our study, did not seem to be a reliable test. Biopsy is still mandatory for diagnosis because laryngeal TB and carcinoma may coexist. A complete course of anti-tubercular treatment

is the treatment of choice. Complete cure is achieved by the end of 12 months of therapy.

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Conflicts of interest

There are no conflicts of interest.

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