

Primary Laryngeal Tuberculosis: Our Experiences at a Tertiary Care Teaching Hospital in Eastern India

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Summary: Introduction. Primary laryngeal tuberculosis is a chronic bacterial infection of the larynx by *Mycobacterium tuberculosis* without affecting the lungs. It is a rare type of extrapulmonary tuberculosis seen in clinical practice.

Objectives. This study aimed to evaluate the clinical presentation, diagnosis, and treatment of primary laryngeal tuberculosis at a tertiary care teaching hospital in eastern India.

Materials and Methods. This is a retrospective study of 11 cases of primary laryngeal tuberculosis managed between December 2013 and January 2018. The detailed clinical presentations, investigations, and treatment of primary laryngeal tuberculosis of the patients were studied.

Results. Primary laryngeal tuberculosis is common in men with mean age of 38.63 years. Hoarseness of the voice is the most common symptom, and the most common site for primary laryngeal tuberculosis is the vocal fold with ulcerative lesion. Endoscopic examinations of the larynx in laryngeal tuberculosis are nonspecific and are to be confused with laryngeal cancer. Histopathological and bacteriological examinations are confirmatory tests for the diagnosis. After confirmation of the diagnosis, all patients had taken antitubercular therapy for 6 months, which gave excellent outcome.

Conclusions. Delayed diagnosis or untreatable laryngeal tuberculosis will lead to high morbidity and mortality of the patient. Although primary laryngeal tuberculosis has nonspecific clinical presentations, it is very important to have a high index of suspiciousness to rule out tubercular lesion in the larynx as this disease is curable.

Key Words: Primary—Laryngeal tuberculosis—Larynx—Extrapulmonary tuberculosis—Antitubercular treatment.

INTRODUCTION

Tuberculosis is a granulomatous infectious disease caused by *Mycobacterium tuberculosis*. This disease mainly affects lungs, referred to as pulmonary tuberculosis, but can also affect extrapulmonary site such as larynx. Tuberculosis is a major public health problem in developing and underdeveloped countries. It often affects the lungs, and the pulmonary tuberculosis accounts for 80% of the cases¹; however, it can involve any other organ of the human body. Primary laryngeal tuberculosis is a rare type of extrapulmonary tuberculosis which constitutes less than 1% of all types of tuberculosis cases.² Because of higher number of immunocompromised patients and increasing multidrug-resistant tuberculosis cases, there are more cases of laryngeal tuberculosis nowadays. Approximately 530,000 children are suffering from tuberculosis in the developing countries around the world.³ The extrapulmonary involvement of the tuberculosis ranges from 30% to 40%.⁴ Larynx is an uncommon site for tuberculosis in the community. Laryngeal tuberculosis may cause mild hoarseness of voice to severe odynophagia and dyspnea due to laryngeal edema and granulations. Clinician or otorhinolaryngologist should be familiar with uncommon site of larynx for tuberculosis as worldwide

recrudescence of tuberculosis due to spread of human immunodeficiency virus (HIV) infection and a misleading cause to be confused with laryngeal cancer. To minimize the misdiagnosis and inappropriate treatment of primary laryngeal tuberculosis, we had performed this study by retrospective analysis of clinical presentations, investigations, and treatment.

MATERIALS AND METHODS

This is a retrospective study based on clinical observation of patients with laryngeal tuberculosis between December 2013 and January 2018. Clinical presentations, investigations, and treatment were documented in each case. The patient details such as age, gender, addictions, and risk factors for facilitating laryngeal tuberculosis are recorded. The investigations such as laryngeal examinations by nasopharyngolaryngoscopy, histopathological test, and bacteriological examinations were done in all cases. The different types of lesions in the larynx such as ulcerative, granulomatous, polypoid, and nonspecific were documented. One chest x-ray was done in all cases. Computed tomography scan of the neck was done in three cases for assessment of laryngeal lesion. After confirmation of the diagnosis, hospital infection control was notified, and the patients were admitted to an isolation ward with immediately antitubercular treatment (ATT) started in all cases.

RESULTS

There were 11 patients detected for primary laryngeal tuberculosis during December 2013 to January 2018. The age of all patients in this study ranged from 22 to 61 years, with mean age of 38.63 years. There were seven male and four female in this study (Table 1). Of 11 patients, 4 had a habit of chronic smoking and 4 had a habit of drinking alcohol (Table 2).

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TABLE 1.
Clinical Profile of the Patients of Primary Tubercular Laryngitis

Serial	Age	Sex	Symptom	Laryngoscopy	Imaging
1	22	Male	Hoarseness of voice and irritating cough	Vocal fold and arytenoids showing lesions	Chest x-ray is normal
2	18	Male	Hoarseness of voice odynophagia and discomfort in throat	Lesions at the vocal fold and epiglottis.	Chest x-ray is normal. CT scan of the neck showing small lesions at epiglottis and vocal folds
3	34	Female	Hoarseness of voice and irritating cough	Lesions at the vocal folds	Chest x-ray is normal
4	41	Male	Hoarseness of voice and breathing difficulty (dyspnea)	A large granulomatous lesion at vocal folds	Chest x-ray is normal. CT scan of neck showing mass at glottis.
5	28	Female	Odynophagia and irritating cough	Lesions at the arytenoids	Chest x-ray is normal
6	45	Male	Hoarseness of voice and discomfort in throat	Lesions at the vocal folds	Chest x-ray is normal
7	58	Female	Odynophagia and irritating cough	Lesions at the arytenoids	Chest x-ray is normal
8	61	Female	Hoarseness of voice and discomfort in throat	Lesions at the vocal folds	Chest x-ray is normal
9	64	Male	Hoarseness of voice	Lesions at the false vocal cords	Chest x-ray is normal
10	33	Male	Hoarseness of voice and irritating cough	Lesions at the vocal folds	Chest x-ray is normal
11	21	Male	Hoarseness of voice	Lesions at the false vocal cords	Chest x-ray is normal

There were family history of tuberculosis in two patients and one patient had personal history of tuberculosis. The most common clinical symptom was hoarseness of voice (n=9), dry irritating cough (n=5), odynophagia (n=3), discomfort in throat (n=3), and dyspnea (n=1) (Table 1). Dyspnea was seen in one patient, which showed advanced stage of laryngeal tuberculosis. The locations for lesions were true vocal cords (n=6), arytenoids (n=3), false vocal cords (n=2), and epiglottis (n=1) (Table 1). The different endoscopic pictures for laryngeal tuberculosis in this study included ulcerative lesions (n=4) (Figure 1), polypoid lesion (n=2) (Figure 2), granulomatous lesion (n=2) (Figure 3), and nonspecific lesions (n=3) (Table 3). All patients showed normal chest x-ray. Of 11 patients, 3 were suffering from diabetes mellitus, 1 was suffering from HIV infection, and 1 was suffering from bronchial asthma (Table 4). The sputum smear test was positive in seven cases. Montoux test was positive in six cases. Polymerase chain reaction (PCR) test was done in five cases, which showed positive results. Three patients had done computed tomography scan of

the neck for assessment of the laryngeal airway and mass in the larynx. All patients had undergone biopsy and histopathological examination (Table 5). The histopathological examination showed granulomatous lesion with caseation (Figure 4). Treatment was antitubercular therapy for all 11 patients, with 2 months of isoniazid, rifampicin, ethambutol, and pyrazinamide followed by 4 months of isoniazid and rifampicin. No serious side effects were seen during treatment period. All patients were completely cured after treatment.

DISCUSSION

Primary laryngeal tuberculosis is a granulomatous disease caused by *M. tuberculosis*, and the tubercular lesion is confined to the larynx only. It is a rare disease accounting for less than 1% of all cases of tuberculosis.⁵ Laryngeal tuberculosis is often associated with pulmonary tuberculosis,⁶ but patients have also laryngeal tuberculosis without history of pulmonary tuberculosis.⁷ Primary laryngeal tuberculosis mostly occurs in

TABLE 2.
Personal History of the Patients Diagnosed for Primary Laryngeal Tuberculosis

History	Chronic smokers	Chronic alcoholics	Family history of tuberculosis	Personal history of tuberculosis
Number of patients	4	3	2	1

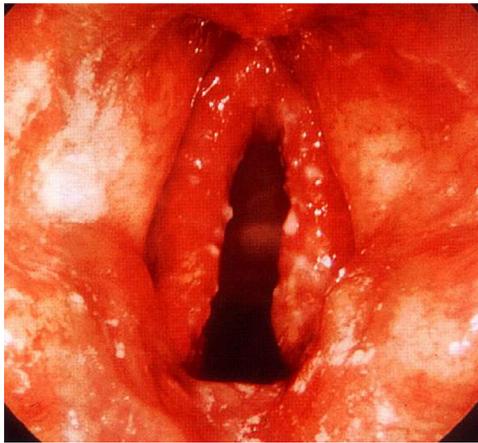


FIGURE 1. Ulcerative lesions on the vocal folds in primary tubercular laryngitis.



FIGURE 2. Polypoid lesion on the vocal fold in primary tubercular laryngitis (arrow mark).

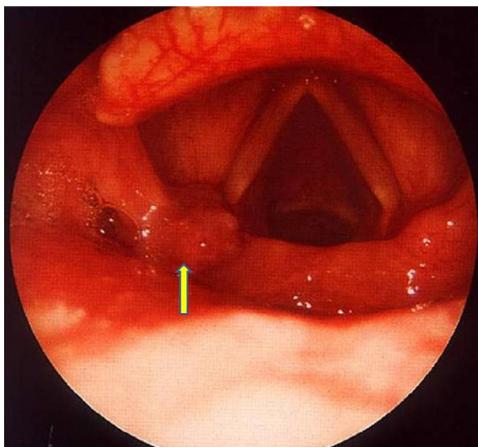


FIGURE 3. Granulomatous lesion on the arytenoids in primary tubercular laryngitis (arrow mark).

adult male aged between 40 and 50 years. It is often seen in person without Bacillus Calmette-Guerin vaccination, with malnutrition, or in patients with acquired immunodeficiency syndrome (AIDS), low immunity, and chronic smoking.⁶ Out of the different predisposing factors, alcohol abuse and smoking are two known risk factors for primary laryngeal tuberculosis.⁸ Of 11 patients, 4 (36.36%) had smoking habit and 3 (27.27%) had habit of alcohol abuse. HIV serology was positive in one patient. The link between HIV infection and tuberculosis is documented in the literature.⁹ Primary laryngeal tuberculosis is a rare clinical entity and is often caused by direct invasion of the inhaled *M. tuberculosis* bacilli.¹⁰ Secondary involvement of larynx often occurs by cough and expectoration from tracheobronchial tree or via bloodstream from other than lungs.¹¹ Lymphatic spread of the tuberculosis to the larynx is rare.

Laryngeal sites affected by tuberculosis are in the decreasing order as follows: true vocal folds (50%–70%), false cords (40%–50%), epiglottis, aryepiglottic folds, arytenoids, posterior commissure, or subglottis (10%–15%).¹¹ The tubercular lesions in the different parts of the larynx may appear as ulcerative, ulcerofungative, polypoid, or nonspecific inflammatory.¹² In this study, four patients presented with ulcerative lesions, two patients presented with granulomatous lesions, two patients presented with polypoid lesions, and three patients presented with nonspecific lesions. Congestion of unilateral vocal cord should be taken as a sign for possibility of tubercular lesion. The laryngeal tuberculosis often presents with hoarseness of voice (80%–100%) and odynophagia (50%–67%), which often mimic other laryngeal diseases. It may lead to severe dyspnea and stridor due to laryngeal edema and granulations. Primary laryngeal tuberculosis can affect any parts of the larynx.¹³ The vocal cords of the larynx are commonly affected in the laryngeal tuberculosis. The laryngeal tuberculosis is characterized by edema, hyperemia, or ulcerative lesions in the larynx. Arytenoids, posterior commissure, and epiglottis are affected in laryngeal tuberculosis if it coexists with pulmonary tuberculosis in case of secondary laryngeal lesions. Primary laryngeal tuberculosis is a highly contagious disease of the human being. Hoarseness of voice is the most common clinical presentation, but odynophagia and dyspnea can also be present in patients with primary laryngeal tuberculosis. The constitutional clinical symptoms such as fatigue, weight loss, fever, night sweats, and hemoptysis are often seen in primary laryngeal tuberculosis. The clinical signs are often minor in primary laryngeal tuberculosis, and the features such as fever, weight loss, and asthenia are essentially seen in advanced form of primary laryngeal tuberculosis with severe odynophagia. The gross laryngoscopic lesions are different from ulcerative lesions to hypertrophic exophytic and polypoid

TABLE 3.
Types of Tubercular Lesions Seen in Larynx

Types of lesions	Ulcerative	Granulomatous	Polypoid	Nonspecific
Number of patients	4	2	2	3

TABLE 4.
Patients of Primary Laryngeal Tuberculosis Having Other Associated Diseases

Associated diseases	Diabetes mellitus	HIV positive	Bronchial asthma
Number of patients	3	1	1

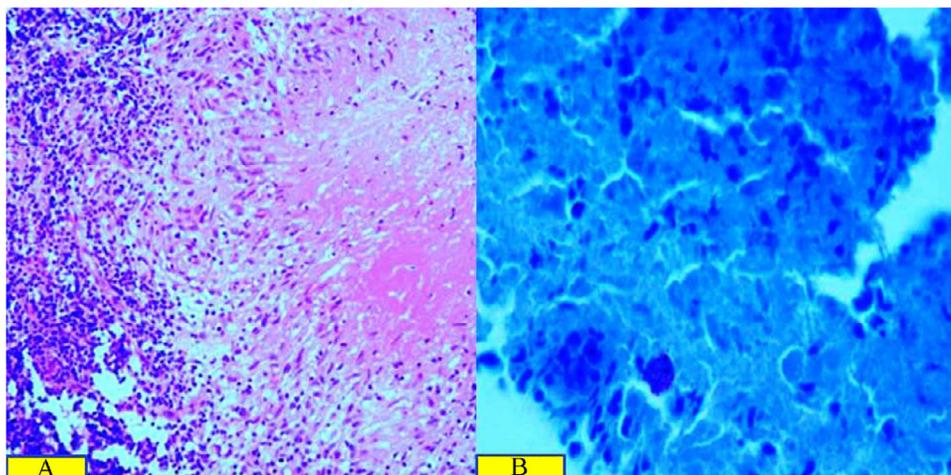
TABLE 5.
Investigations Done in Primary Laryngeal Tuberculosis

Investigations	Montoux test	Sputum AFB	PCR	Histopathological examination
Number of patients	6	7	5	11

lesions.¹⁴ The macroscopic appearance of primary laryngeal tuberculosis is classified into four types: granulomatous, polypoid, ulcerative, and nonspecific. The lesions are either single or multiple. Granulomatous lesions in laryngeal tuberculosis are more common in patients among pulmonary tuberculosis coexisting with laryngeal tuberculosis.¹⁵ The differential diagnoses of primary laryngeal tuberculosis are syphilis, neoplasm, sarcoidosis, Wegner disease, leprosy, actinomycosis, lupus, recurrent polychondritis, rheumatoid arthritis, and amyloidosis.¹⁶ Smoking habit of the person aggravates the laryngeal tuberculosis. Smoking affects the mucosa of the larynx by chronic stimulation and causes decreased defensive capability of the larynx.¹⁷ This consideration suggests that mucosal membrane of the larynx is inflamed by smoking and may be more likely affected by the trans-airway infection from the tuberculosis and so lead to more progressive laryngeal tuberculosis. Primary laryngeal tuberculosis has no gender or age predilection. Primary laryngeal tuberculosis may not reveal abnormality in chest x-ray.¹⁰

Chest x-ray is usually done in laryngeal tuberculosis to rule out pulmonary pathology. In our cases, chest x-ray of the patients was normal, which may mislead the clinician and delay the diagnosis. Fiberoptic nasopharyngolaryngoscopy may show mucosal thickening, ulcerations, or polypoid mass. Malignancy

such as squamous cell carcinoma and tuberculosis may coexist in the same patient, so biopsy is essential in this patient.¹¹ History of pulmonary tuberculosis with scar tissue in the lungs may cause traction neuropathy by affecting the recurrent laryngeal nerve, leading to vocal cord palsy.¹⁸ The difference between laryngeal carcinoma and laryngeal tuberculosis is often difficult to determine. Previously, laryngeal tuberculosis is due to complications of pulmonary tuberculosis, but at present, primary laryngeal tuberculosis is increasing. The tuberculosis of the larynx is often confused with syphilis, fungal laryngitis, and granulomatous lesions such as Wegner granulomatosis and sarcoidosis. In clinical practice, the most important differential diagnosis of laryngeal tuberculosis is laryngeal carcinoma. Both laryngeal tuberculosis and laryngeal carcinoma have similar clinical, endoscopic, and radiological features.¹⁹ The diagnosis of laryngeal tuberculosis is based on pathological and microbiological findings of the biopsy specimen collected from the larynx. Diagnosis of primary laryngeal tuberculosis is confirmed by histopathological examinations with chronic granulomatous inflammatory exudates with or without caseating necrosis. In some cases of histopathology picture showing absence of caseations, the diagnosis is confirmed by recovery of the patients under antitubercular therapy. Routine blood investigations such as total white cell counts, differential count,

**FIGURE 4.** A. Histopathological examination showing granuloma formation with caseous necrosis. B. Z&N (Ziehl-Nielsen) staining from biopsy specimens showing acid-fast bacilli.

and Erythrocyte sedimentation rate are done in all cases. Tuberculin test is also advised in all cases. The tuberculin test, also known as Montoux test, is a standard procedure for the diagnosis of tuberculosis. It includes intradermal inoculation of purified protein which is derived from *M. tuberculosis* for assessing the cellular immune response to the antigens. The inflammatory reaction occurs in *M. tuberculosis*-sensitized patients. Observation of reaction is done after 48–72 hours and is valid for 7 days. The evaluation of tuberculin test is based on the diameter of the inflammatory area calculated transversally against the longitudinal direction of the challenged forearm. The inflammation area of more than 10 mm in immunocompetent persons is considered as positive result. The inflammatory area of more than 5 mm in immunocompromised patient indicates positive for tuberculosis. The Montoux test, although used for diagnosis of tuberculosis, has certain limitations such as low sensitivity in immunocompromised patients, being difficult to perform among children, having a subjective character of interpretation, and requirement for a second visit for confirmation of the diagnosis.²⁰ Sputum microscopy for acid fast bacillus is positive in around 20% of the cases of laryngeal tuberculosis and most of the chest x-ray findings are persistent with pulmonary tuberculosis.²¹ Ziehl-Neelsen staining may directly show acid-fast bacilli. The microbiological culture and drug sensitivities of the infective strain are not usually done in practice, whereas the multiple repeated biopsies are often used for confirming the diagnosis and starting the treatment.²² The PCR test is often used for diagnosis of tuberculosis. The detection of *M. tuberculosis* is increased from 2% to 17% on culture to 89%–100% in PCR.²³ In cases of strong clinician suspicion of tuberculosis with negative cultures, samples can be sent for PCR test.²⁴ QuantiFERON-TB Gold In-Tube (QFT-GIT) is an interferon gamma release assay often used to detect tuberculosis. It is an *in vitro* diagnostic test that needs blood draw. As per updated guidelines for interferon gamma release assays to find out *M. tuberculosis*, the QFT-GIT gives promise in other tests.²⁵ As primary laryngeal tuberculosis is a rare clinical entity and often simulates to malignancy in imaging and during laryngoscopy examination, biopsy is a confirmatory test for the diagnosis.

Laryngeal tuberculosis responds well to ATT. The treatment of laryngeal tuberculosis is similar to pulmonary tuberculosis with surgical intervention to ensure the patient and safe airway if laryngeal airway is threatened by tubercular granuloma. As per the World Health Organization guidelines, the laryngeal tuberculosis or extrapulmonary tuberculosis should be treated with four drug regimens for 2 months followed by two drugs for the next 2 months.²⁶ ATT is the cornerstone of treatment for laryngeal tuberculosis and the role of surgery is only done for early diagnosis and for maintaining airway if compromised.²⁷ The drug combination used includes isoniazid, rifampicin, ethambutol, and pyrazinamide for 2 months followed by isoniazid and rifampicin for 4 months.²⁸ However, in case of drug-resistant *M. tuberculosis*, these guidelines are not appropriate where more drugs are used or treatment is prolonged.²⁹ Many otolaryngologists may not

be familiar with clinical presentations and treatment of laryngeal tuberculosis due to paucity of the laryngeal tuberculosis cases. To avoid untoward outcomes of the patients suffering from laryngeal tuberculosis, health-care workers, and public at large, it is vital for the physicians to be familiar with this contagious disease such as laryngeal tuberculosis.

CONCLUSIONS

Primary laryngeal tuberculosis is a rare clinical incidence compared with pulmonary tuberculosis, but nowadays, its incidence is increasing in endemic area. It should be considered as a differential diagnosis in case of ulcerative or any inflammatory swelling of the vocal fold. Abnormal chest x-ray showing features of tuberculosis along with laryngeal lesion suggests the diagnosis, whereas normal chest x-ray cannot exclude the diagnosis. So the clinician or otolaryngologists should keep in mind the existence of primary laryngeal tuberculosis to avoid delayed diagnosis and treatment. Delayed diagnosis or untreatable laryngeal tuberculosis will lead to high morbidity and mortality of the patient. Although laryngeal tuberculosis has nonspecific clinical presentations, it is very important to have a high index of suspiciousness to rule out tubercular lesion in the larynx as this disease is a curable lesion.

STUDY LIMITATION

This study has a relatively small sample size and may limit the outcome of the above interpretation. However, the outcome of this study will definitely encourage the future research work in the primary laryngeal tuberculosis.

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