

## Clinical Features of Laryngeal Tuberculosis in Iran

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**Abstract-** Tuberculosis is a major health problem in Iran and its laryngeal involvement is not uncommon. Laryngeal tuberculosis is so infectious and delay in diagnosis and treatment could result spread of disease and causes diverting complications. We reviewed clinical and para-clinical characteristics of patients with laryngeal tuberculosis in Iran. In a cross sectional study, patients with laryngeal tuberculosis were studied and followed. All patients admitted from May 2000 to Dec 2011 in Amir-Alam hospital, a referral center for laryngeal diseases in Tehran. We studied 19 cases of laryngeal tuberculosis with typical histopathology (chronic granulomatous inflammation with caseous necrosis and langhans-type giant cells) and 6 cases of laryngeal tuberculosis with atypical histopathology (chronic granulomatous inflammation or chronic inflammation without necrosis). They had laryngeal symptoms and signs from 2 to 12 months before definitive diagnosis. Macroscopic appearances of laryngeal lesions were exophytic in 11 cases and ulcerative in 14 cases. True vocal cords were involved in 22 cases. The primary clinical diagnosis was malignancy in 17 cases, tuberculosis in 5 cases, and nonspecific inflammation in 3 cases. The chest x-ray findings were compatible with tuberculosis in 14 patients. The response to anti-tuberculosis therapy was desirable in all patients. In endemic area, tuberculosis should be considered as an important diagnosis in patients with laryngeal lesions even when histopathology of laryngeal lesions is not typical. Association with pulmonary tuberculosis helps for diagnosis.

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**Keywords:** Hoarseness; Laryngeal lesions; Laryngeal tuberculosis; Tuberculosis

### Introduction

Tuberculosis is one of the most serious health problems in Iran. Laryngeal tuberculosis is an extremely rare presentation of disease even in endemic area (1). It is obvious that larynx is infected by *Mycobacterium tuberculosis* from bronchogenic or hematogenous routes and so patients with laryngeal tuberculosis could be presented with or without pulmonary tuberculosis (2).

Laryngeal tuberculosis is so infectious and it could easily spread to others. It has various presentations that cause diagnostic problems (3). Tuberculosis should be kept in mind when patients present with laryngeal symptoms. Symptoms of laryngeal tuberculosis are usually longstanding and chronic. These are including cough, hoarseness, hemoptysis, dysphagia, odynophagia

and stridor. In laryngoscopy, laryngeal lesions vary from erythema to ulceration and exophytic masses. These laryngoscopic appearances mimic other laryngeal lesions such as neoplasm, severe exudative and fibrinous inflammation and chronic laryngitis. The long delay in diagnosis may cause irreversible damage to vocal cords and permanent narrowing of the airway (4). Laryngeal tuberculosis is usually diagnosed by laryngeal biopsy. The presence of chronic granulomatous inflammation with caseous necrosis is the main histopathological feature that leads to diagnosis (5). If acid-fast bacilli are found in the specimen, diagnosis can be confirmed. The mainstay of treatment is medical therapy by anti-tuberculosis drugs. Surgery may be required in the case of local complications such as laryngeal stenosis or fibrosis. The prognosis of the disease is optimistic with early diagnosis and proper medical

treatment (5,6).

We studied clinicopathological characteristics and laboratory findings of patients with laryngeal tuberculosis in Iran.

## Materials and Methods

In a cross-sectional study clinical and para-clinical characteristics of patients with final diagnosis of laryngeal tuberculosis were reviewed. All patients had been admitted to Amir-Alam Hospital a tertiary referral center for otolaryngology disease, from May 2000 to December 2011. The diagnosis of laryngeal tuberculosis was based on: 1) the existence of chronic granulomatous inflammation with caseous necrosis in the histopathology of laryngeal lesions or 2) the presence of laryngeal lesions with atypical histopathology (chronic granulomatous inflammation or chronic inflammation) which had a complete response to anti-tuberculosis therapy. Demographic data, past medical history, clinical manifestations, laryngoscopic appearances, laboratory and chest x-ray findings and response to anti-tuberculosis therapy were recorded for each patient. All patients were followed up to the end of their medical treatment.

## Results

Twenty five cases (including 19 males) with a diagnosis of laryngeal tuberculosis were gathered. The patients' age ranged between 19 and 74 years with an average of 41 years. Four cases (22.2%) were diabetic and eight patients (32%) were heavy smokers. Three patients were injection drug user. The results of the HIV antibody Eliza test were negative for all cases. Patients' symptoms had begun from 2 to 12 months (an average 7.5 months) before the diagnosis. The complaints of patients in order of frequency were: hoarseness (88%), fever (64%), cough (44%), weight loss (24%), odynophagia (16%), and stridor (8%). According to the laryngoscopy reports, the most common site of lesions was the right side of the larynx (14 cases). The lesions had an exophytic appearance in 11 cases and an ulcerative appearance in 14 cases. In 10 cases (40%) the lesions were single and located in the true vocal cord (7 cases), epiglottis (1 case) and the false vocal cord (2 cases). Fifteen patients had multiple lesions all of which involved the true vocal cords. Overall the primary clinical diagnosis was malignancy in 17 cases, tuberculosis in 5 cases, and nonspecific inflammation in 3 cases. The pathology of laryngeal lesions revealed

chronic granulomatous inflammation with caseous necrosis in 19 cases, chronic granulomatous inflammation without necrosis in 4 cases and chronic inflammation in 2 cases. The chest x-ray findings were compatible with tuberculosis in 14 patients, including 8 patients with typical histopathological appearance of laryngeal lesions and all 6 cases with atypical histopathological studies. These included miliary pattern (4 cases) opacity with cavity (2 cases), and opacity without cavity (8 cases). The results of the sputum smear, sputum culture were available for 18 cases and were reported as positive in 9 and 12 cases, respectively. Unfortunately, two sputum specimens were not available in 7 cases because they didn't cooperate. Tuberculin skin test (PPD) was positive in 20 cases. The response to anti-tuberculosis therapy was desirable in all patients. Fifteen patients became afebrile within 7 to 10 days. In 22 patients, hoarseness completely improved within 2 to 4 months. In 2 patients CO<sub>2</sub> laser therapy was performed to resolve fibrosis and release adhesion bands. The total laryngectomy was performed in one case.

## Discussion

Nowadays, laryngeal tuberculosis is included almost 2% of cases of tuberculosis (7). The characteristics of laryngeal tuberculosis have changed over the years and it has become a challenge for otolaryngologists to distinguish this disease from others. Despite the high prevalence of tuberculosis in Iran, we collected only 25 patients with laryngeal tuberculosis. It seems that early diagnosis and proper treatment of pulmonary tuberculosis has been reduced bronchogenic laryngeal involvement in recent years. In this study males were involved 3 times more than females. This is compatible with results of most other studies that showed male predominance (6,8). Men have more social activity and consequently more tuberculosis exposure in endemic areas. The primary clinical diagnosis was tuberculosis in only 20 percent of the cases in spite of the presence of radiologic findings compatible with pulmonary tuberculosis in almost 60 percent of patients. Indeed, the dominancy and similarity of laryngeal complaints with pulmonary symptoms caused pulmonary involvement to be ignored. In this study, physicians often missed tuberculosis as a differential diagnosis of laryngeal complaints and as a result did not consider airborne precautions during performing laryngoscopy and laryngeal biopsy.

The mean duration of disease until definitive diagnosis was 7.5 months. Our patients referred late

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compared with patients in other reports (6). Physician's knowledge is limited in this issue. One-third of patients were heavy smoker that caused late referral to clinics due to attribution of laryngeal symptoms to smoking.

As other reports, hoarseness was the most common presenting symptom due to true vocal cord involvement (8,9). Significant weight loss was seen in 6 cases because of later referral and longer delay in diagnosis compared to other patients of this study. Two patients had stridor due to epiglottis involvement. Tuberculosis of the epiglottis can obstruct upper airway (10,11). Fever was seen in 64 % of patients with pulmonary tuberculosis. Fever is considered as the cardinal symptom of pulmonary tuberculosis and physicians should pay attention to this symptom in patients with laryngeal lesions (12). In laryngoscopy laryngeal lesions in tuberculosis have variable appearances and mimic other diseases such as contact ulcer, leukoplakia, reflux disorders, polyp and malignancy (13,14). Indeed, laryngeal tuberculosis more closely resembles laryngeal carcinoma on laryngoscopy and imaging than any other diseases of larynx so histological confirmation is mandatory (15,16).

In our study, 19 patients had typical histopathological appearance and 6 patients had atypical histopathology of laryngeal lesions including chronic inflammation or chronic granulomatous inflammation without necrosis. Indeed in these cases, laryngeal lesions did not show typical pathology. All of these six patients had active pulmonary tuberculosis and showed complete improvement of laryngeal and pulmonary lesions after anti-tuberculosis therapy. We suggest the initiation of anti-tuberculosis therapy in any patients with non-malignant laryngeal lesions and concomitant pulmonary tuberculosis especially in endemic area. In one of our patients, primary diagnosis was malignancy. The histopathology of laryngeal sample revealed squamous cell carcinoma and so total laryngectomy was performed. But post-operative laryngeal tissue samples were compatible with tuberculosis. This could be explained by the fact that pseudoepitheliomatous reaction in laryngeal tuberculosis may mimic squamous cell carcinoma (17). The previous reports reveal 48% concomitant HIV infection in patients with head and neck tuberculosis and 25% in patients with laryngeal tuberculosis but in our study we didn't find any coinfection.

In conclusion, in endemic areas, tuberculosis should be considered as an important differential diagnosis in patients with laryngeal lesions even with atypical histopathological features. Association with pulmonary

tuberculosis could help for diagnosis. In addition it is suggested that in endemic area for tuberculosis, samples of laryngeal lesions to be reviewed by two pathologists before performing invasive and radical procedures.

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