CASE REPORT

A Rare Case of Pulmonary Tuberculosis Masquerading as Laryngeal Tuberculosis or Malignant Manifestation

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ABSTRACT

Introduction: Laryngeal tuberculosis (LTB) is usually accompanied by pulmonary tuberculosis (TB) involvement. Misdiagnosis often occurs because the symptoms are non-specific and resemble laryngeal malignancy. We reported a rare condition of pulmonary TB masquerading as larynx abnormalities such as malignant manifestations.
Case: A 59-year-old man presented with a main complaint of prolonged hoarseness without clinical respiratory complaints. The patient additionally reported coughing as a symptom while receiving medical treatment in the hospital. A computed tomography (CT) scan of the neck without contrast revealed a glottic tumor invading the vocal cord – T3N2cMx. Laryngoscopy examination revealed T1-T1 tonsils. The pharyngeal mucosa was slightly hyperemic. The arytenoids and epiglottis were less hyperemic. There was no edema, the left vocal fold was paralyzed, could not be adducted, and there was a lump. The glottis rima gap was narrow, size 3–4 mm, and the mass could not be evaluated. Chest X-ray examination was normal, but rapid molecular tests of TB detected very low *Mycobacterium tuberculosis* (MTB) levels. The patient was treated with anti-TB treatment (ATT) according to body weight. An evaluation was performed after 2 weeks, and the patient's clinical and physical condition improved.
Conclusion: Pulmonary TB patients in endemic countries can have clinical manifestations such as LTB or laryngeal malignancy in 1% of cases. The prognosis for LTB with pulmonary T involvement is quite good with ATT administration.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB).[1,2] It can affect pulmonary and extrapulmonary organs, such as the larynx. Sometimes, laryngeal TB (LTB) can also be the first clinical manifestation of asymptomatic active pulmonary TB. Dworetzky first described the pathogenesis of LTB and the clinical syndrome in 1941, and Auerbach followed in 1946.[1]

Currently, LTB is a rare symptom of TB, accounting for 1% of cases overall.[1,2] Even though the incidence rate is low, LTB is the most common granulomatous disease of the larynx.[3] The man-to-woman LTB ratio is approximately 2.5:1, with a mean age of 49.5 years old. Symptoms of LTB are nonspecific and sometimes clinically difficult to distinguish from malignant tumors of the larynx. The most frequent symptoms are hoarseness, dysphonia, weight loss, cough, dysphagia, and odynophagia. LTB infection causes exudation in the subepithelial space followed by round-cell infiltration, leading to fibrosis. In most cases, the scar tissue causes permanent changes in the structure of the vocal cords, resulting in altered glottic vibration and dysphonia. Misdiagnosis frequently occurs because the endoscopic examination is often characterized by exophytic lesions and/or ulcers surrounded by erythema that resembles a malignant laryngeal disease.[1,4]

LTB can manifest either as a primary or secondary infection.[3,5,6] Primary LTB, the less common occurrence, involves direct infection of the laryngeal mucosa by MTB via airborne particles without concurrent pulmonary TB. This route leads to the formation of granulomas in the larynx.[7] In contrast, the more prevalent form is secondary LTB, which arises as a direct extension of pulmonary TB, particularly from highly infectious cavities within the lungs that produce

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sputum laden with MTB. During coughing episodes, these bacteria are expelled from the tracheobronchial system and reach the laryngeal mucosa through bronchogenic spread or hematogenous/lymphogenic routes.[8–10] The response to anti-TB treatment (ATT) has been highlighted by Kulkarni, *et al*. (2006) as a crucial diagnostic criterion, aiding in distinguishing LTB from other laryngeal pathologies such as malignancies.[11]

In this case, we presented a distinctive case of pulmonary TB that clinically mimics LTB or laryngeal malignancy, highlighting the diagnostic challenges faced in distinguishing these conditions. The rarity of primary LTB and the complex presentation of secondary LTB underscore the necessity for a high index of suspicion, especially in patients presenting with laryngeal symptoms and a history suggestive of or conducive to TB.[11] This case emphasizes the importance of considering LTB in the differential diagnosis of persistent laryngeal symptoms, particularly hoarseness, even in the absence of overt pulmonary TB. It illustrates the pivotal role of ATT responsiveness in confirming the diagnosis. Through detailed examination and responsive treatment, this case contributes to the broader understanding of extrapulmonary TB manifestations. It reinforces the critical need for awareness among clinicians to prevent misdiagnosis and ensure timely and appropriate management.

CASE

A 59-year-old man was referred by the Ear, Nose, and Throat (ENT) division with a glottis tumor and suspected LTB accompanied by paralysis of the left vocal folds. The patient complained that his voice had been hoarse for the previous 5 months and worsened in the last month. The patient also had intermittent shortness of breath, difficulty swallowing, a cough with phlegm for the past 2 days, and difficulty sleeping. There was no history of a long-standing cough. Over the preceding month, he had lost around 2 kg in weight. He underwent a thyroidectomy in 2005, and although the patient did not have a history of diabetes or hypertension, he had previously smoked.

During treatment, the patient's vital signs showed increased respiratory rate and peripheral saturation (91% without nasal cannula and 97% with 3 LPM nasal cannula) with a normal body mass index (BMI). Upon physical examination of the lungs, no abnormalities were found during inspection, palpation, or percussion. Meanwhile, bronchovesicular breath sounds were heard on auscultation with minimal crackles in the right lung and stridor sounds. Complete blood cell examination showed WBC 12.7 x10^3/UL, HGB 11.7 g/dl, and others within normal limits.

A computed tomography (CT) scan of the neck without contrast and axial reformats of the coronal and sagittal sections showed a glottic tumor invading the vocal cord, classified as T3N2cMx. The cervical vertebral body was normal (Figure 1). The ENT department then performed a laryngoscopy examination and found T1-T1 tonsils. The pharyngeal mucosa was slightly hyperemic. The arytenoids and epiglottis were less hyperemic. There was no edema, the left vocal fold was paralyzed, could not be adducted, and there was a lump. The glottis rima gap was narrow, the size was 3-4 mm, and the mass could not be evaluated.

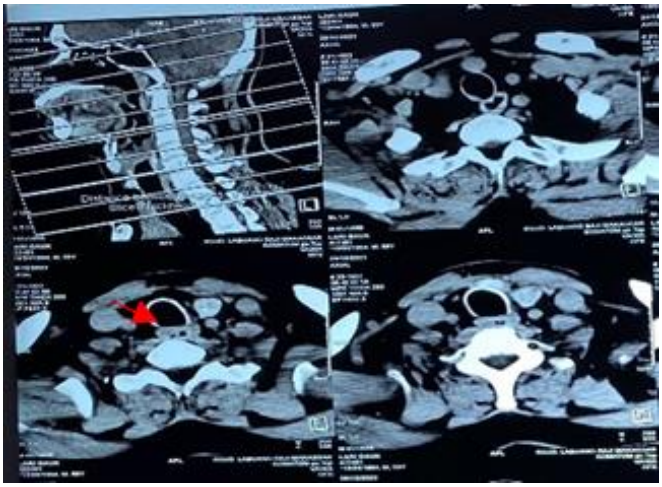

Figure 1. CT scan of the neck without contrast, axial reformat coronal and sagittal sections. The image depicts a glottic tumor (red arrow) involving the vocal cord, classified as stage T3N2cMx.

Chest X-ray examination showed that the cast and lungs were within normal limits (Figure 2). A sputum examination was performed using a rapid molecular test (RMT), and a very low MTB level was detected. Rifampicin resistance was not detected. Based on the results, the patient was diagnosed with bacteriological pulmonary TB, suspected LTB, and suspected glottic malignancy. The patient was given ATT 4FDC 3 tablets. The patient felt clinically better during the first 4 weeks of ATT administration. The

planned duration of treatment for the patient was 6 months, but it could be extended depending on evaluation at the sixth month.

Figure 2. Patient's chest X-ray

DISCUSSION

Pulmonary TB is a chronic inflammation of the lung parenchyma caused by MTB bacteria. Manifestations in the larynx sometimes accompany active pulmonary TB without symptoms such as LTB. At the beginning of the 20th century, LTB was a common complication of pulmonary TB in approximately 25–30% of all infected patients.[1]

This case presented a man with the chief complaint of hoarseness in his voice. LTB is difficult to differentiate from malignant tumors of the larynx clinically.[3,7,8] However, dysphonia is a continuous symptom of LTB and is usually characterized by hoarseness and sometimes loss of voice for the patient. It usually has a chronic course lasting from 1 to 6 months and occurs in 85–100% of cases.[10–13]

Men are more likely to develop LTB than women. The clinical pattern and symptoms of LTB have also changed. Currently, the disease has many similarities with laryngeal carcinoma. In the case report by Smulders, *et al*. (2009), the patient was diagnosed with pulmonary TB quite late because the presenting concerns on admission to the hospital had more similarities to laryngeal malignancy without clinical lung manifestations.[14]

In the head and neck area, cervical lymph nodes account for approximately 90% of cases of extra-pulmonary TB, with the larynx playing a role in 2–6% of cases. Less common sites of involvement include the temporal bone, nasal cavity, eyes, pharynx, thyroid, and skull base. The clinical characteristics of LTB have evolved significantly, posing a diagnostic challenge for otolaryngologists to differentiate this condition from other diseases. Historically, LTB primarily affected individuals in their second or third decade of life who had advanced pulmonary TB, presenting with symptoms such as cough, hemoptysis, fever, weight loss, and night sweats. The disease typically featured ulcerative, granulomatous lesions located on the larynx's posterior section, attributed to sputum accumulation in the bed-bound patient's arytenoid region. In more recent times, LTB predominantly affects individuals in their 50s and 60s, primarily presenting with hoarseness, observed in 80–100% of patients. Other, less common symptoms include odynophagia, dysphagia, dyspnea, stridor, cough, and hemoptysis, with systemic symptoms now being a rarity.[1,14–16]

LTB can affect any part of the larynx, dissociating from the once clear association with pulmonary TB. Infection of the larynx may occur either through direct extension from the lungs or hematogenous spread from non-pulmonary sites. Although less common, the latter is particularly relevant in cases lacking evidence of pulmonary disease. Differentiating LTB from chronic laryngitis, especially laryngeal carcinoma, has become increasingly complex. Odynophagia, a distinguishing symptom given its rarity in laryngeal cancer cases, presents a diagnostic challenge as painful dysphagia is frequently reported in patients with supraglottic laryngeal carcinoma.[14,17]

Physically, the true vocal cords are most commonly impacted by LTB, with the disease also affecting the epiglottis, false vocal cords, ventricles, arytenoids, posterior commissure, and subglottic area. The presentation of LTB can range from edema and hyperemia to ulcerative lesions, nodules, exophytic masses, or obliteration of anatomical structures. This diversity in presentation, alongside the absence of pathognomonic features and its rarity in industrialized nations, frequently leads to misdiagnosis as the more common laryngeal carcinoma. In this case, the patient's extensive smoking history, coupled with symptoms of hoarseness and odynophagia, initially suggested a diagnosis of laryngeal carcinoma. However, LTB can present with identical symptoms, and a notable chest X-ray, distinct from pulmonary metastasis, should prompt consideration of TB by radiologists and otolaryngologists, especially if previous chest X-rays were normal.[14,18,19]

The identification of TB infections relies on laboratory techniques such as histopathological tissue examination with Ziehl–Neelsen histochemical staining for acid-fast bacilli and detection of MTB through polymerase chain reaction (PCR) or bacterial culture, with the latter serving as the reference standard despite its time-intensive nature. A CT scan of the neck, akin to

a chest X-ray, cannot definitively diagnose LTB due to its potential to mimic various diseases. The primary treatment for LTB involves anti-tuberculous agents, with expectations of dysphagia improvement and resolution of cavernous lung lesions within weeks. Delayed treatment can lead to complications such as (sub)glottic stenosis, muscular involvement, and vocal cord paralysis, emphasizing the importance of early detection and intervention.[14]

The patient complained of dysphonia for 5 months, accompanied by odynophagia. This supports the assertion that dysphonia to aphonia is the most frequently reported complaint by patients with LTB.[15] A study by Rubin, *et al*. (2024) on 119 LTB patients in 2000-2022 observed symptoms in 86% of cases, including hoarseness to aphonia (93.4%), odynophagia (80.3%), both dysphonia and odynophagia (68.9%), and productive cough (32.8%).[7] Other symptoms, such as fever, weight loss, and night sweats, are rarely found in LTB.[16]

The patient, in this case, was a 59-year-old man, similar to a study by Zang, *et al*. (2020), which showed that men are more likely than women to develop LTB, especially in their fourth and sixth decades of life.[17] Risk factors for LTB include smoking, a history of malignancy, human immunodeficiency virus (HIV) infection, and the use of immunosuppressive drugs.[17] On the contrary, a case report by Sohil, *et al*. (2019) in India found that LTB patients with atypical symptoms had no history of alcohol consumption and smoking and not a known case of any other co-morbidities.[18]

The patient, in this case, also complained of coughing during treatment. Apart from clinical symptoms in the form of hoarseness of the voice, other non-specific signs are usually also found in the form of dysphagia and odynophagia, aside from productive cough, chest pain, fever, and so on, if there are clinical symptoms indicating lung involvement.[1,19,20]

The patient, in this case, had an indirect laryngoscopy examination undertaken by the ENT department, and the results showed T1-T1 tonsils, hyperemic pharyngeal mucosa, hyperemic arytenoids, and epiglottitis, no edema, left plica vocalis paralysis and the mass could not be evaluated. Theoretically, in patients with LTB, it is usually found in pathological changes involving the entire laryngeal cavity. Three types of lesions were summarized according to their shape: pale edema, where the patient shows pale edematous tissue and the spread of millet white dots; hyperplasia, with a white appearance indicative of polyp-like or granuloma-like vegetation; and ulcer type, characterized by the appearance of mucosal ulcers and seepage erosion.[13,17,18,20]

This case is interesting because the chest X-ray examination was normal. However, the RMT examination detected (+) very low MTB. Rifampicin resistance was not detected, indicating the involvement of MTB in the clinical symptoms displayed by the patient. According to Schluger (2001), the symptoms were productive cough, chest pain, fever, and so on.[13] It must be searched systematically, as it can indicate lung involvement.[13] A chest X-ray and sputum examination should be performed for all patients with a suspected diagnosis of LTB, as approximately 20% of patients indicate positive results in such examinations.[13,20]

The definitive diagnosis of LTB is established by detecting the pathogen MTB from laryngeal samples or sputum. The PCR technique exhibits high sensitivity in the detection of TB. Cultures can be performed while conducting drug sensitivity tests. Direct laryngoscopy examination coupled with biopsy and histopathology represents the most accurate diagnostic method while excluding a differential malignancy diagnosis. Microscopic examination of LTB can reveal caseous necrosis surrounded by clusters of epithelial cells. Through hematoxylin and eosin (H&E) staining, Langerhans cells and acid-fast bacilli (AFB) can be identified with Ziehl–Neelsen staining.[4] The diagnosis of LTB in this case was established after obtaining a positive result for MTB from the RMT examination. The RMT examination is a PCR-based molecular test that detects MTB deoxyribonucleic acid (DNA) and resistance to rifampicin within 2 hours. Sputum is the most frequently used specimen in RMT examinations.[20]

After obtaining RMT results (+) which support the diagnosis of pulmonary TB possibly accompanied by LTB, the pulmonologist recommends that the patient start receiving anti-TB drugs, namely being given ATT 4 FDC 4 tabs/24 hours/orally according to the patient's body weight. The final diagnosis of LTB was made, and then the patient underwent an intensive phase with four drugs for 2 months, followed by three drugs in a continuation phase for 4 months, and monitoring of progress and side effects during ATT drug administration was performed. Treatment monitoring can be conducted by examining the clinical response, laryngoscopy and radiology, and culture examination. Treatment is usually given for a minimum period of 6 months. However, various regimens are available for the type and duration of therapy and may vary according to institutional protocols and clinical, laboratory, and radiological parameters. Cases with drug resistance usually require longer treatment and the need for second-line drugs.[4,14,17–19]

Similar to managing pulmonary TB generally, LTB is treated with ATT for a minimum of 6 months. ATT medication is administered in two stages: the intense phase, which lasts for 2 months and includes rifampicin, isoniazid, ethambutol, and pyrazinamide, and the continuation phase, which lasts for 4 months

and includes rifampicin and isoniazid. Regular treatment can yield positive results in as little as 2 weeks, as seen by improvements in the patient's symptoms.[17–19]

The vestibular folds, vocal folds, epiglottis, and aryepiglottic folds commonly affect the laryngeal structures. Observations during laryngoscopy include edema, hyperemia, mucosal hypertrophy of the posterior third of the larynx, ulcers, white lesion appearances, granulomatous masses, nodules, or polyps.[20–22] However, a laryngoscopy was not performed on this patient. Instead, a non-contrast neck CT scan was conducted as another supportive examination. Laryngoscopy should be the gold standard for identifying specific problems in the patient's larynx for more precise localization of the affected organ or structure. Based on laryngoscopy results conducted by Agarwal, *et al.* (2019) on 15 cases of LTB patients, the involved laryngeal structures were the vocal folds (33.3%), epiglottis (53.3%), vestibular folds (6.6%), anterior commissure (6.6%), and pyriform sinus (6.6%).[23] Multiple lesions were found more often than not.[23]

LTB can be macroscopically classified into four types: granulomatous, polypoid, ulcerative, and nonspecific.[20] The clinical presentation of LTB can also be divided into four stages: infiltration, ulceration, perichondritis, and tumor formation. Diffuse hyperemia, edema, and infiltration of inflammatory cells are characteristics of the infiltration stage, with the laryngeal mucosa appearing pale. Tuberculous granulomas form, enlarging and coalescing, causing the mucosa to stretch and rupture into ulceration. Ulcers that become shallow and enlarge are visible at the stage where tumor formation will result in fibrotuberculosis.[20,21,23] In this case, the patient did not undergo fiber laryngoscopy. However, it is recommended that one be performed if needed in similar cases in the future, which will facilitate the identification of the type of LTB macroscopically.

An early biopsy to exclude malignancy might not always be the initial choice if diagnostic tests (such as chest X-ray, high-resolution CT of the chest, and AFB sputum analysis) yield positive results for TB, and there is a swift clinical improvement following ATT. As Kulkarni, *et al.* (2006) outlined, responsiveness to ATT is a significant diagnostic criterion for identifying LTB.[11] Should the response to ATT be partial or incomplete, a biopsy at that juncture becomes warranted. Adopting this strategy is deemed safe and rational, especially considering the complexities associated with administering general anesthesia for performing a laryngeal biopsy in patients with active pulmonary Koch's disease. The challenges encompass anesthesia-related complications, potential drug interactions, and infectious concerns, thereby underscoring this diagnostic approach's prudence.[13]

Possible complications include airway obstruction leading to respiratory failure.[3] Furthermore, laryngeal stenosis, vocal cord paralysis, and laryngeal muscle disorders may also occur. MTB may spread hematogenously and cause complications in other organs. Differential diagnoses of LTB include laryngeal papilloma, vocal cord polyps, laryngeal tumors, acute epiglottitis, vocal cord cysts, and luetic laryngitis.[20]

CONCLUSION

LTB is a manifestation of extrapulmonary TB, with an incidence rate of 1% among extrapulmonary TB cases, and is often a secondary infection to a primary TB infection occurring in the lungs. This case report presented findings of LTB in a 59-year-old man who presented with hoarseness and a productive cough. The diagnosis was established through anamnesis, non-contrast neck CT scan, chest X-ray, and RMT MTB. The patient was treated in the pulmonary outpatient clinic with ATT, showing clinical improvement after several weeks of treatment. Prompt diagnosis and management can decrease complications and improve the patient's quality of life.

Discussion on this topic remains exceedingly scarce and limited, necessitating further contributions. Recommendations for subsequent researchers include conducting a more in-depth and comprehensive investigation into hoarseness as a clinical manifestation of tuberculous laryngitis and, importantly, updating the latest management protocols and rapid screening methods for patients with LTB.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Wrote the original draft: JM, MF, MA. Conceptualization, corresponding, and revising the manuscript: JM. Review and final approval of the manuscript: BH. All authors contributed and approved the final version of the manuscript.

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