

Rigid laryngoscope manifestations of 61 cases of modern laryngeal tuberculosis

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Received June 27, 2016; Accepted June 22, 2017

DOI: 10.3892/etm.2017.5167

Abstract. The present study investigated the clinical characteristics and diagnosis of modern laryngeal tuberculosis (TB). A total of 61 patients that were pathologically diagnosed with laryngeal TB between 1998 and 2012 were retrospectively analyzed using laryngoscopy methods. The primary symptoms of laryngeal TB observed in the present study include hoarseness and sore throat, and in the majority of cases, laryngeal TB was not associated with pulmonary TB (ratio 41/61, 67.2%). Systemic symptoms included low-grade fever and night sweats, which were rarely observed (20/61, 32.8%). Laryngoscopy results were summarized into 3 types: Edema type (24 cases), proliferation type (34 cases) and ulcer exudation type (3 cases). The positive rate of purified protein derivative (PPD) examination was 86.9%, which was 63.9% for sputum bacterium analysis. Pathological analysis indicated that there were a large number of phagocytes and giant cell reactions, stroma hyperplasia of epithelioid cells, and the Langhans cells constituted of granuloma and necrotic tissue, with caseous necrosis as a typical manifestation. Modern laryngeal TB is characterized by severe local symptoms like hoarseness and sore throat and mild systemic symptoms like fever and night sweat, and the diagnosis is based on patient history, laryngoscopy analysis, and PPD and sputum bacteria examinations used in combination. However, pathological biopsies and acid-fast bacilli examinations are required for the final diagnosis.

Introduction

Tuberculosis (TB) is harmful to human beings. It has strong infectivity but was almost eradicated 20 years ago due to the use of anti-TB drugs (1). However, in the last decade it has

prevailed in a recurrent state due to resistant strain variation. Furthermore, the incidence of TB has increased worldwide (1) and the number of patients with laryngeal TB has also increased accordingly (1). In the past, laryngeal tuberculosis was almost always associated with advanced pulmonary infections, but in recent decades, patients who have negative findings on radiological examinations of the chest, negative sputum cultures, and negative history have been reported (2). Widespread use of anti-TB agents over a prolonged period of time has led to a change in the characteristics of the signs and symptoms of laryngeal TB. For example, severe sore throat and painful swallowing similar to laryngitis have been observed, without cough and light fever; therefore, misdiagnosis is commonly observed (1-3). Furthermore, as the disease has a potent infectivity, the United States Centers for Disease Control and Prevention have stressed the importance of acknowledging the changes in clinical characteristics, diagnostic points, early diagnosis and timely treatment of the disease (3). For the above reasons, early diagnosis and treatment are very important. Nowadays, laryngoscopy is a primary and effective method for detecting laryngeal TB (4). The present retrospective study analyzed the data of 61 patients at Shanghai General Hospital (Shanghai, China) who had suffered from laryngeal TB for ~14 years, to provide a means of early diagnosis to clinical workers.

Patients and methods

Patients. A total of 61 patients who were admitted to Shanghai General Hospital (male, n=23; female, n=38; age, 22-79 years; mean age, 47.7 years) and underwent laryngoscopy examination between January 1998 and December 2012 were included in the present study. Ethical approval was received from the Ethics Committee of Shanghai General Hospital (Shanghai, China) and informed written consent was obtained from all patients in the present study. The time interval between the onset of symptoms and laryngoscopy examination ranged between 1 and 17 months (mean, 7.4 months). The 61 cases included 26 cases of acute or chronic laryngitis (first diagnosis), 18 cases of vocal polyps or throat tumors (first diagnosis), 8 cases of epiglottitis (first diagnosis), 8 cases of laryngeal lesions and 1 case of laryngeal keratinization disorder. Excluding the 8 cases of laryngeal lesions, the misdiagnosis

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Key words: laryngeal tuberculosis, rigid laryngoscopy

rate was 86.8%. The local and systemic signs and symptoms were recorded for all patients, and the condition of the throat was observed using a rigid laryngoscope (8706 CJ; Kal Storz GmbH & Co. KG., Tuttlingen, Germany) or a fiber laryngoscope (ENF TYPE T3; Olympus Corp., Tokyo, Japan) when the patient's tongue was too large. All cases under the fiber laryngoscope, rigid laryngoscope (or support laryngoscope if the former two methods failed) underwent biopsy, chest X-ray, and tuberculin purified protein derivative (PPD) skin test. The PPD test was considered to have a positive result if skin showed red spots with a diameter >5 mm after 0.0002 PPD was injected into the skin (2). A total of 36 patients underwent sputum smear tests for acid-fast bacilli examination; 0.1 ml sputum was smeared to 20x25 mm and stained according to the Ziehl-Neelsen method (3). A total of 30 patients underwent pathological examination to identify TB bacterium DNA (via polymerase chain reaction).

Diagnosis criteria. In addition to the laryngoscope results, local lesions were required to satisfy one of the following criteria: i) Pathological section was positive for the acid-fast stain; ii) pathological section exhibited caseous necrosis foci; iii) positive PPD skin test; iv) presence of *Mycobacterium tuberculosis* in the sputum smear and culture; or v) diagnostic treatment was effective. Diagnostic treatment consisted of short-term trial anti-TB medications (rifampin, 600 mg daily for 2-3 weeks, isoniazid, 450 mg daily for 2-3 weeks). Any changes in the patient's condition, such as less edema or fewer ulcers in the laryngeal lesions, were considered to potentially indicate laryngeal TB. Following confirmation, all patients were transferred to the Shanghai Tuberculosis Hospital (Shanghai, China) for regular chemotherapy treatment.

Results

Symptoms and history. Patients presented with local symptoms, which included hoarse voice problems and aphonia in 57/61 cases (93.4%); sore throat and painful swallowing in 49/61 cases (80.3%), both hoarse voice problems/aphonia and sore throat/painful swallowing in 42/61 cases (68.9%); cough and sputum production in 20/61 cases (32.8%); and dysphagia in 9/61 cases (14.8%). Systemic symptoms included mild and severe fever, weakness, weight loss, a maximum temperature of 39.5°C in 2/61 cases (mean, 37.9°C) and a minimum of 37.4°C in 16 cases (26.2%). A total of 4 patients had a history of TB, 2 of whom had been cured 20 years prior, 1 was cured 25 years prior and 1 case was cured 50 years prior. Of the 61 patients, 41 cases had no history of TB nor any clinical manifestations to indicate primary laryngeal TB.

Of the 61 cases, 6 had enlarged lymph nodes in the neck, of which 4 cases were on the left-hand side and 2 cases on the right-hand side with hard texture and distinct margins. Furthermore, there were 2 cases of large activity of lymph nodes, and 1 case of restricted movement of lymph nodes. A maximum diameter of the lymph nodes was 2.5 cm and a minimum was 0.3 cm, and tenderness was noted in all 6 cases.

Laryngoscopy examination. A total of 25 cases exhibited 2 or more pathological changes, including 8 cases involving 3 parts and 2 cases involving the whole laryngeal cavity. In 36 cases,

only one area was affected: Vestibular folds were associated with 4 cases, 20 cases were in the vocal cords, 8 cases were in the aryepiglottic folds and 4 cases were in the epiglottis. The 3 types of lesions were summarized according to their form: Pale edema (24 cases), where patients exhibited pale edema tissue and spreading of millet white dots, as shown in Fig. 1; hyperplasia (34 cases), indicated by a white appearance and polyp-like indications or granuloma vegetation, as shown in Fig. 2; and ulcer type (3 cases), defined by the appearance of mucosa ulcer and erosion seepage, as shown in Fig. 3.

X-ray examination. Of the 61 patients, 40 patients were negative for laryngeal TB according to X-ray results, 11 cases were diagnosed with active TB (infiltrating type in 9 cases and blood seeding type in 2 cases), with a positive rate of 18.0%. A total of 4 cases were diagnosed with bronchiectasis, 4 cases with pleural effusion and 2 cases with double lung interstitial lesions.

Laboratory and pathology analysis. Of the 61 patients, PPD skin test results were positive in 53 cases (1:2,000), with a positive rate of 86.9%. A total of 30 patients were examined for pathological TB bacterium DNA and 18 cases were positive, with a positive rate of 60.0%. Of the 36 patients who underwent sputum smear examination for acid-fast bacilli, 23 cases were positive, with a positive rate of 63.9%. All patients underwent routine biopsy and pathological examination, and 43 cases were confirmed once, 12 cases were diagnosed twice and 6 patients were confirmed by biopsy and pathology >2 times. One patient underwent biopsies 4 times prior to diagnosis. The majority of pathological changes observed included squamous cell dysplasia, interstitial phagocytes and giant cell reaction, the presence of epithelioid cells, Langhans cell hyperplasia and granuloma, and the presence of necrotic tissue; 26 cases were confirmed by the presence of typical caseous necrosis foci under the microscope.

Discussion

Laryngeal extrapulmonary TB is the most prevalent laryngeal granulomatous disease (1). Widespread use of anti-TB agents over a prolonged time period has led to a change in the common signs and symptoms of laryngeal TB (2). Early laryngeal lesions occur at the posterior larynx, and have been indicated to appear at the anterior larynx, including the vocal cord, vestibular fold and epiglottis (4-6). In the present study, 28/36 cases had single-area involvement at the anterior larynx (77.8%), and only 8 cases involved the posterior larynx, particularly at the aryepiglottic folds (22.2%). This is similar to previous results (5,6). Previous findings have indicated that, laryngeal TB was typically caused by bacterial infection from TB sputum and the patient being bedridden for a long duration, which led to the infective sputum bacteria remaining at the posterior larynx; however, it has more recently been determined that laryngeal TB spreads predominantly by blood and lymphatic fluid, indicating a notable change in TB manifestation (5).

Previously, laryngeal TB had typically been considered secondary to severe TB; therefore, weight loss and mild laryngeal symptoms occurred (3). Patients with severe TB typically

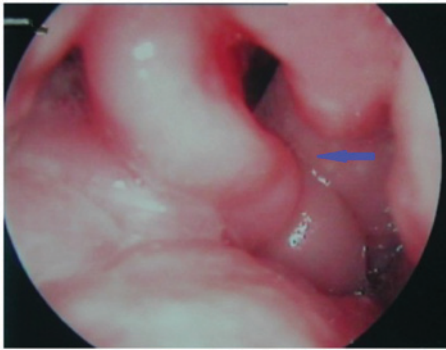


Figure 1. Edema type as shown using a rigid laryngoscope of the epiglottis and arytenoid region. Arrow indicates pale tissue edema, spreading of millet white dots.

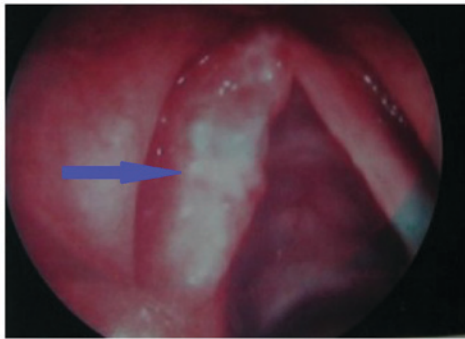


Figure 2. Hyperplasia type using a rigid laryngoscope of the left vocal cord. Arrow indicates polyp-like granuloma hyperplasia.

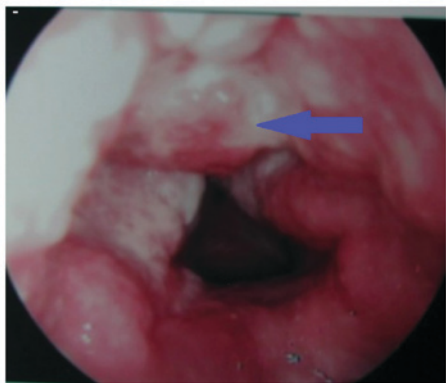


Figure 3. Ulcer exudation type of the whole larynx. Arrow indicates mucosa ulcer and erosion seepage.

exhibit severe symptoms, including low-grade fever, cough and expectoration, weakness, weight loss, rare hoarseness, and sore throat (5-8). Currently, hoarseness and sore throat are the most common symptoms of laryngeal TB, and systemic symptoms and signs are rarely observed or even absent (3). Of the 61 patients in the present study, 41 cases had no history of TB or presented TB clinical manifestations, and were considered to have primary laryngeal TB. Furthermore, 2 cases had a history of TB but exhibited no signs of recurrence of TB and only 11 laryngeal TB cases in 61 patients (18%) were considered secondary to active pulmonary TB according to the X-ray and chest scan. Similarly, this rate has been observed

in various studies (5,6). It is clear now that laryngeal TB may occur independently of pulmonary TB and its local symptoms, including hoarseness, sore throat, dysphagia, serious, and systemic symptoms, which include fever, night sweats, weakness and weight loss, may be absent. Previous findings have suggested that the inoculation, widespread use of long-term anti-TB agents, and the variation of *Mycobacterium tuberculosis* L-type bacteria have contributed to the change in clinical characteristics between laryngeal and pulmonary TB stated above, which has resulted in the increase in misdiagnosis and missed diagnosis (6).

Accurate diagnosis of laryngeal TB is dependent on the patient history, physical examination, chest X-ray, sputum and PPD examinations, and biopsy results (2,3). Laryngeal TB is highly contagious and therefore its early diagnosis is critical (2). Most modern laryngeal TB cases are not secondary to pulmonary TB. Furthermore, the clinical characteristics of TB are not obvious, whereas the local laryngeal symptoms are more noticeable (4). Throat symptoms of laryngeal TB are easily confused with those of other illnesses, including laryngitis (4,5). Therefore, missed diagnosis and misdiagnosis are prone to occur (1,2). In the present study, 53 of 61 patients were diagnosed with other laryngeal disorders, such as laryngitis, vocal polyps or throat tumors, epiglottitis or laryngeal keratinization. In general, attention should be paid to several diagnostic methods. Initially, the indication of any history of pulmonary TB (if patients exhibit laryngeal symptoms with pulmonary TB) should be considered as potential laryngeal TB cases. In addition, laryngeal lesions should be carefully examined by all types of laryngoscopes, and if any one of three types of lesions are observed, a biopsy should be performed immediately. Furthermore, sputum examinations must be evaluated, including a direct smear, which is simple and quick, with a low positive rate (3,5), and sputum culture, which is typically used and is a longer process but with a high positive rate (2). Notably, laboratory examinations should be applied, including the PPD test, where a positive result strongly suggests TB bacterium infection; however, this test does not indicate the site of infection (1). Patients who received the PPD test had a positive rate of 87.9%. In addition, novel technology has been constructed to detect TB bacterium, including TB bacterium DNA probe techniques; however, the false-positive and false-negative rates of these techniques are high and clinical application is limited to a certain extent (5,6). The final diagnosis of laryngeal TB is confirmed by histopathological examination and detection of *Mycobacterium tuberculosis*. Slices showing epithelioid cells, macrophages, hyperplasia of Langhans cells and caseous necrosis are key characteristics (3,7). If an acid-fast stain is positive, laryngeal TB may be confirmed; however, the positive rate of acid-fast stain is considered too low to be reliable alone (3,8). In some cases, the characteristics of pathological images are not clear or the acid-fast stain may be negative, the PPD, PCR tests and fast erythrocyte sedimentation rate may provide a strong positive result (6). Therefore, the use of these multiple techniques may provide a clear diagnosis of laryngeal TB. Diagnostic treatment is also a type of diagnostic method. For some patients for whom diagnosis cannot be made through repeated biopsies, short-term trial anti-TB medications (rifampin and isoniazid) may be used and any changes such as less edema or fewer ulcers to the laryngeal lesions may indicate laryngeal TB.

During the 9 years between January 1998 and December 2006, the present authors analyzed 33 cases of laryngeal tuberculosis and the findings were published in the Journal of Chinese Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery (4). Subsequently, cases were collected until December 2012, and a further 28 cases were detected. Findings in the authors' laryngoscopy room following this 6-year period were similar with what was initially detected in the first 9 years. In addition, the first 9 years of laryngeal inspection methods were the same as those used in the following 6 years. Although various methods are available for detecting laryngeal TB, there are no testing methods that exhibit effective specificity. Following a total of 15 years of continuous research, the present findings indicate that detection of laryngeal TB relies still on rigid laryngoscope and fiber laryngoscopy methods combined with patient history, PPD, sputum bacteria examinations, pathological biopsies and acid-fast bacilli examinations for the final diagnosis. Furthermore, it should be noted that the detection rate is also associated with the diligent observation and experience of medical staff.

This study used long-term laryngoscope experience to observe the modern laryngeal tuberculosis under laryngoscope in three forms (edema, hyperplasia and ulcer exudation types). It laid a solid technical foundation for the early diagnosis and

treatment of laryngeal tuberculosis. But due to limitations on the conditions, only pathological reports without images could be obtained. This affected the data integrity, and remains to be improved in future research.

References

1. Benwill JL and Sarria JC: Laryngeal tuberculosis in the United States of America: A forgotten disease. *Scand J Infect Dis* 46: 241-249, 2014.
2. Rizzo PB, Da Mosto MC, Clari M, Scotton PG, Vaglia A and Marchiori C: Laryngeal tuberculosis: An often-forgotten diagnosis. *Int J Infect* 7: 129-131, 2003.
3. Rieder HL: The infectiousness of laryngeal tuberculosis: Appropriate public health action based on false premises. *Int J Tuberc Lung Dis* 13: 4-5, 2009.
4. Zhao NJ, Sun YJ and Sun ZF: Clinical analysis of the diagnosis of laryngeal tuberculosis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 23: 261-263, 2009 (In Chinese).
5. Shin JE, Nam SY, Yoo SJ and Kim SY: Changing trends in clinical manifestations of laryngeal tuberculosis. *Laryngoscope* 110: 1950-1953, 2000.
6. Ling L, Zhou SH and Wang SQ: Changing trends in the clinical features of laryngeal tuberculosis: A report of 19 cases. *Int J Infect Dis* 14: e230-e235, 2010.
7. Yench MW, Linfesty R and Blackman A: Laryngeal tuberculosis. *Am J Otolaryngol* 21: 122-126, 2000.
8. Wang HE: *Mycobacterium tuberculosis* L form. *Zhonghua Jie He He Hu Xi Za Zhi* 25: 579-580, 2002 (In Chinese).