

Head and Neck Manifestation of Tuberculosis

Nezaket Tektaş,¹ İmdat Yüce,² İrfan Kara,² Mehmet Can Kaya,² Sedat Çağlı,²
Emrah Gülmez,³ Özlem Canöz⁴

¹Department of Otorhinolaryngology, Bünyan State Hospital, Kayseri, Türkiye

²Department of Otorhinolaryngology, Erciyes University Faculty of Medicine, Kayseri, Türkiye

³Department of Otorhinolaryngology, City Hospital, Kayseri, Türkiye

⁴Department of Pathology, Erciyes University Faculty of Medicine, Kayseri, Türkiye

ABSTRACT

Objective: The aim of this study was to review cases of extra-pulmonary tuberculosis with head and neck involvement that presented at our clinic.

Materials and Methods: Data from 60 patients were analyzed. All patients were examined with respect to age, gender, symptoms, comorbidities, the head and neck regions sampled, the tuberculin skin test, acid-resistant staining, tuberculosis culture results, and histopathology examination reports.

Results: The patients comprised 41 (68.3%) females and 19 (31.7%) males, with a male-to-female ratio of 1:2.1. The mean age of patients under 18 years was 11.44±4.13 years, and the mean age of patients over 18 years was 51.18±17.06 years. A statistically significant difference was determined between the age groups concerning left-side region 1 and right-side region 4 ($p<0.05$). Involvement of neck regions 1–2 was more common in patients under 18 years, and lymph node involvement of neck regions 2–3–4–5 was more common in patients over 18 years. There was no effect of gender on neck regions ($p>0.05$). Acid-resistant staining positivity was determined in only one patient. Of the patients with culture examinations, *M. tuberculosis* complex was identified in six.

Conclusion: If there are suspicious symptoms and findings in patients with a disease causing immunosuppression or who are using drugs that suppress the immune system, sampling must be performed to rule out tuberculosis. Tuberculosis is seen more often in female patients. When persistent necrotic lymphadenopathy is present in the submandibular region, especially in young patients, tuberculosis should be considered.

Keywords: Extrapulmonary, head and neck, immunosuppression, lymphadenitis, tuberculosis.



Cite this article as:

Tektaş N, Yüce İ, Kara İ, Kaya MC, Çağlı S, Gülmez E, Canöz Ö. Head and Neck Manifestation of Tuberculosis. J Clin Pract Res 2024;46(5):456–462.

Address for correspondence:

İmdat Yüce.
Department of
Otorhinolaryngology, Erciyes
University Faculty of Medicine,
Kayseri, Türkiye
Phone: +90 533 641 07 66
E-mail: imdatyuce@hotmail.com

Submitted: 06.03.2024

Revised: 21.04.2024

Accepted: 31.05.2024

Available Online: 25.10.2024

Erciyes University Faculty of
Medicine Publications -
Available online at www.jcpr.com

INTRODUCTION

Tuberculosis is a disease caused by *Mycobacterium Tuberculosis* (*M. Tuberculosis*) bacillus, which infects the respiratory tract. Although a quarter of the global population encounters these bacilli, the disease does not develop in most people. According to World Health Organization (WHO) data, 10.6 million people worldwide were infected with tuberculosis in 2021, and 1.6 million



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deaths were due to tuberculosis.¹ The bacteria affect adults at the rate of 90%, and tuberculosis is seen more in males than females. Risk factors include Human Immunodeficiency Virus (HIV), poor nutrition, young age, diabetes, air pollution, alcohol consumption, smoking, immunosuppressant drugs, and a low socioeconomic level.² The increasing use of anti-TNF- α group drugs in recent years has been reported to have increased the incidence of extra-pulmonary tuberculosis.³

The lungs are the organs most affected.⁴ Extra-pulmonary tuberculosis (EPTB) cases constitute 20% of all tuberculosis cases.⁵ The diagnosis of EPTB is usually delayed as the bacillus load is low and symptoms are non-specific. The regions where involvement is most often seen are the lymph nodes (19%), followed by the pleura, gastrointestinal system, larynx, bones, central nervous system, and genitourinary system.⁴

The aim of this study was to review cases of extra-pulmonary tuberculosis with head and neck involvement that presented at our clinic.

MATERIALS AND METHODS

Approval for this retrospective study was granted by the Clinical Research Ethics Committee (no: 2023/825). A total of 293 patients who were diagnosed with tuberculosis in our hospital between 2010 and 2023 were retrospectively screened. Of these, 60 patients who were diagnosed with head and neck EPTB were included in the study and analyzed. To examine the distribution of neck regions according to age, the patients were categorized as pediatric (<18 years) or adult (>18 years). The tuberculosis diagnostic criteria were defined as the observation of epithelioid cells in Ziehl-Nielsen staining, Langhans giant cells, acid-resistant bacilli, and caseous granulomatous inflammation in histopathological samples, and the identification of *M. tuberculosis* complex in culture.⁶ All patients were examined with respect to age, gender, symptoms, comorbidities, the head and neck regions sampled, the tuberculin skin test, acid-resistant staining, tuberculosis culture (Löwenstein-Jensen/Bactec culture) results, and histopathology examination reports.

Statistical Analysis

Data obtained in the study were analyzed statistically using R 4.3.2 software (www.r-project.org). To compare the differences, Fisher's Exact and Pearson's χ^2 tests were applied to categorical variables. A value of $p < 0.05$ was accepted as the level of statistical significance.

RESULTS

Of the 293 tuberculosis patients screened, head and neck EPT was present in 60 (20%) patients. This group comprised 41 (68.3%) females and 19 (31.7%) males, with a male-to-

KEY MESSAGES

- Head and neck extrapulmonary tuberculosis (EPT) accounts for 20% of all TB cases, mostly affecting females (68.3%). Patients under 18 often have involvement in neck regions 1–2, while those over 18 show involvement in regions 2–5.
- Diagnosis is delayed due to non-specific symptoms. Excisional biopsy is crucial as bacilli and culture positivity rates are low. Histopathological features like necrotizing granulomatous inflammation and Langhans giant cells are key.
- Persistent necrotic lymphadenopathy in the submandibular region, especially in young patients, should lead to diagnostic sampling for tuberculosis.

female ratio of 1:2.1. The diagnosis was made in 16 patients aged <18 years, with a mean age of 11.44 ± 4.13 years, and in 44 patients aged >18 years, with a mean age of 51.18 ± 17.06 years. A comorbidity causing immunosuppression was present in 28 (46.7%) patients. The distribution of diseases and agents included diabetes, a history of tuberculosis, a history of cancer (ca) (two breast ca, one renal ca, one pancreas ca, one stomach ca, one colon ca, two lymphoma, one endometrium ca), a history of immunosuppressant drug use, rheumatological disease, HIV, Hepatitis C Virus (HCV), and smoking (Table 1).

The symptoms of the patients at the time of presentation included swelling in the neck, B symptoms (weight loss, night sweats, fever), hoarseness, hemoptysis-cough, neck pain, purulent discharge in the mouth, and lymphadenopathy incidentally determined on imaging. The mean duration of symptoms was 5 months (range: 1 week to 3 years) (Table 1).

Laryngeal tuberculosis was present in three patients, nasopharyngeal tuberculosis in one, oropharyngeal tuberculosis in one, and tuberculosis in the submandibular gland in one. In the other 54 patients, tuberculosis manifested as lymphadenitis. Of these patients, scrofuloderma was present in five (Fig. 1).

In patients with laryngeal involvement, findings such as diffuse bulging, widespread polypoid lesions, and Reinke's edema were determined in the laryngeal structures. In the patient with tonsil involvement, only tonsil hypertrophy was present.

In the examination of patients with lymphadenitis, generally hard, semi-mobile, painless lymph nodes were palpated.

Table 1. Comorbidities and symptoms of extrapulmonary tuberculosis patients (n=60)

	n	%
Comorbidity present	28	46.7
Diabetes	8	13.3
Tuberculosis history	5	8.3
Cancer history	9	15.0
Rheumatological disease	4	6.7
HIV/HCV	2	3.3
Smoking	1	1.6
Symptoms		
Swelling of the neck	26	43.3
B symptoms	5	8.3
Weight loss	8	13.3
Hoarseness	2	3.3
Hemoptysis/cough	2	3.3
Incidental LAP	5	8.3
Neck pain	1	1.6
Purulent discharge in the mouth	1	1.6

HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; LAP: Lymphadenopathy.

At the stage of diagnosis, ultrasonography (USG) or neck computed tomography (CT) was requested (Fig. 2).

In the 35 patients with bilateral neck regions 1–5 fully screened with USG or CT, comparisons were made according to age and gender groups. These results showed a statistically significant difference between the age groups in respect to left-side region 1 and right-side region 4 ($p < 0.05$) (Table 2). Involvement of neck regions 1–2 was more common in patients aged < 18 years, and lymph node involvement of neck regions 2–3–4–5 was more common in patients aged > 18 years.

In the comparisons according to gender, no statistically significant difference was determined in the distribution of neck regions ($p > 0.05$) (Table 3).

Excisional biopsy was performed in 47 patients, incisional biopsy in nine, and punch biopsy in four. The excisional biopsies from the neck region were performed most often from the bilateral 2nd region, left 5th region, and left 1st region. In one patient, an excisional biopsy from the left 2nd region and a laryngeal biopsy were performed at the same time, and in another patient, an excisional biopsy from the left 2nd region and a nasopharyngeal biopsy were performed (Table 4).



Figure 1. A pediatric patient diagnosed with tuberculosis presenting with neck discharge.



Figure 2. Cystic tuberculosis lymphadenitis in the left 2nd region on contrast-enhanced computed tomography (CT).

Acid-resistant staining was examined in 42 patients, with positivity determined in only one. Of the patients with culture examinations, *M. tuberculosis* complex was identified in six (Table 5).

Table 2. Involvement of all neck regions determined on imaging (ultrasonography/computed tomography) according to age groups in the 35 patients

Affected region	Age groups of patients				P
	<18 years (n=11, 100%)		≥18 years (n=24, 100%)		
	n	%	n	%	
Left 1					0.021
A	6	54.5	22	91.7	
P	5	45.5	2	8.3	
Left 2					0.709
A	7	63.6	17	70.8	
P	4	36.4	7	29.2	
Left 3					0.657
A	10	90.9	20	83.3	
P	1	9.1	4	16.7	
Left 4					0.657
A	10	90.9	20	83.3	
P	1	9.1	4	16.7	
Left 5					0.657
A	10	90.9	20	83.3	
P	1	9.1	4	16.7	
Right 1					0.297
A	8	72.7	22	91.7	
P	3	27.3	2	8.3	
Right 2					0.435
A	9	81.8	15	62.5	
P	2	18.2	9	37.5	
Right 3					0.146
A	11	100.0	18	75.0	
P	0	0.0	6	25.0	
Right 4					0.037
A	11	100.0	16	66.7	
P	0	0.0	8	33.3	
Right 5					0.146
A	11	100.0	18	75.0	
P	0	0.0	6	25.0	

A: Absent; P: Present.

The histopathology results were generally reported as necrotizing/suppurative/ulcerated, calcified granulomatous inflammation. Calcification was reported in most of the lymph nodes (Fig. 3).

Table 3. Distribution of neck region involvement on imaging modalities (ultrasonography/computed tomography) according to gender in the 35 patients

Variables	Gender				P
	Female (n=25, 100%)		Male (n=10, 100%)		
	n	%	n	%	
Left 1					0.644
P	6	24.0	1	10.0	
A	19	76.0	9	90.0	
Left 2					0.999
P	8	32.0	3	30.0	
A	17	68.0	7	70.0	
Left 3					0.999
P	4	16.0	1	10.0	
A	21	84.0	9	90.0	
Left 4					0.999
P	4	16.0	1	10.0	
A	21	84.0	9	90.0	
Left 5					0.292
P	5	20.0	0	0.0	
A	20	80.0	10	100.0	
Right 1					0.999
P	4	16.0	1	10.0	
A	21	84.0	9	90.0	
Right 2					0.447
P	9	36.0	2	20.0	
A	16	64.0	8	80.0	
Right 3					0.649
P	5	20.0	1	10.0	
A	20	80.0	9	90.0	
Right 4					0.661
P	5	20.0	3	30.0	
A	20	80.0	7	70.0	
Right 5					0.322
P	3	12.0	3	30.0	
A	22	88.0	7	70.0	

A: Absent; P: Present.

At the diagnosis stage, pulmonary tuberculosis was identified in three patients, military tuberculosis in two (with Pott disease present in one), and axillary lymph node involvement in one.

Table 4. Regions of the neck and other regions from which biopsies were taken

Biopsy region	n=60 (100%)	Biopsy region	n=60 (100%)
Left 1	7 (11.7)	Right 1	1 (1.7)
Left 2	11 (18.3)	Right 2	13 (21.7)
Left 3	2 (3.3)	Right 3	1 (1.7)
Left 4	2 (3.3)	Right 4	3 (5.0)
Left 5	11 (18.3)	Right 5	3 (5.0)
Tonsil	1 (1.7)	Larynx	3 (5.0)
Nasopharynx	1 (1.7)	Submandibular gland	1 (1.7)

Table 5. Acid-resistant staining and culture results

	Negative n=60 (100%)	Positive n=60 (100%)
Acid-resistant staining	41 (97.6)	1 (2.4)
Culture	38 (86.4)	6 (13.6)

The patients diagnosed with lymph node tuberculosis according to the histopathology results received treatment for 6 months. In the first 2 months of this period, a treatment regimen of four drugs was given (rifampicin, isoniazid, pyrazinamide, ethambutol), followed by two drugs (rifampicin, isoniazid) for the remaining 4 months. The treatment for patients with scrofuloderma and accompanying pulmonary tuberculosis lasted 9 months, and for the patient diagnosed with Pott disease, the treatment continued for 12 months. No recurrence occurred during the follow-up periods (Fig. 4).

DISCUSSION

Head and neck EPT has been reported to constitute 10% of all tuberculosis cases.^{7,8} In the current study, patients with head and neck EPT constituted 20% of all tuberculosis cases.

In head and neck involvement of tuberculosis, the systemic symptoms and findings are non-specific and may also be seen in tumors or infectious diseases of this region. The diagnostic process may sometimes be prolonged because of local non-specific complaints such as mouth odor, sore throat, nasal discharge, nasal bleeding, and hoarseness, or systemic non-specific complaints such as fever, night sweats, listlessness, fatigue, loss of appetite, and cough.^{9,10} Unlike pulmonary involvement of tuberculosis, symptoms such as fever and night sweats are seen less frequently in EPT (20%).¹¹ This rate was 8.3% in the current series. Diagnosis is generally made from a biopsy performed due to suspicion following ineffective

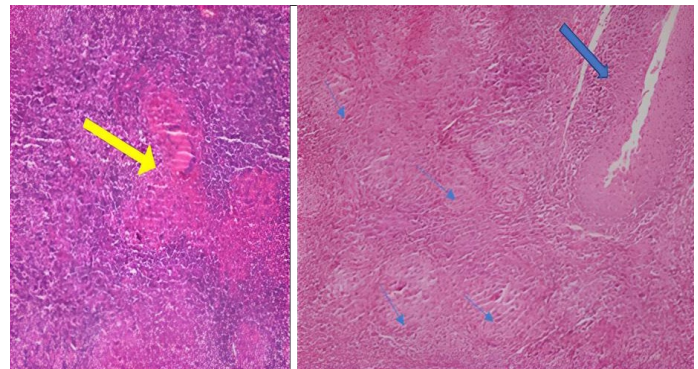


Figure 3. A 22-year-old female patient with larynx and lymph node involvement. Multi-layered smooth epithelium (thick blue arrow), epithelioid histiocytes in the subepithelium and stroma, granuloma structures formed from lymphocytes (thin blue arrow), Langhans type giant cell in the granuloma (yellow arrow).

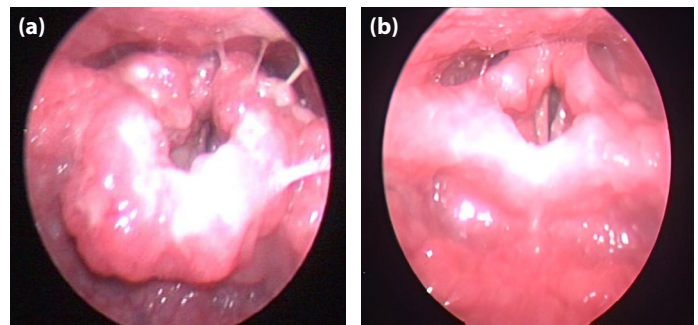


Figure 4. (a) A 22-year-old female with laryngeal tuberculosis at the first examination. (b) A 22-year-old female with the appearance of the larynx following anti-tuberculosis treatment.

antibiotherapy and anti-inflammatory treatments. Infectious diseases such as syphilis, leprosy, actinomycosis, blastomycosis, and leishmaniasis, as well as lymphoma, carcinoma, angiofibroma, sarcoidosis, amyloidosis, and conditions like Castleman disease and Wegener disease, should be considered in the differential diagnosis.¹² There is a 20% risk of malignancy occurring concurrently with head and neck EPT.⁹

According to literature data, the male-to-female ratio of head and neck tuberculosis is 1.43:1.¹¹ However, other studies have reported it to be more common in females.¹³⁻¹⁵ In the current study, there were more female patients. The infected regions are most often the cervical lymph nodes, followed by the larynx, salivary glands, and oral cavity.^{6,7,16} The most frequently involved region in the current study was the cervical lymph nodes, consistent with the literature.

Tuberculous lymphadenitis can develop from reactivation of a latent infection or with local spread from tonsil or adenoid tissue.⁴ The disease usually affects patients in the 30–40 year age range. Bruzgielewicz et al.¹¹ reported involvement of deep jugular lymph nodes in 57.7% of patients and submandibular lymph nodes in 42.3%. In a study of pediatric patients, 79.6% of the involved lymph nodes were determined to be in the suprahyoid region.^{17,18} In the current study, the 1st and 2nd regions of the neck were usually involved in patients aged <18 years, while in those aged >18 years, the lymph nodes in the 2nd, 3rd, 4th, and 5th regions of the neck were infected. These findings were consistent with the literature. In a study by Purohit et al.,¹⁰ unilateral supraclavicular lymph node involvement was reported to be more frequent in females. The current study results showed no significant effect of gender on the neck regions. Fistula formation in the lymph nodes was seen at a rate of 10%.¹⁸

Laryngeal tuberculosis is highly infectious. Clinically, granulomatous, polypoid, and ulcerative changes are seen in the laryngeal mucosa. Lim et al.¹⁹ reported lung involvement in 46.7% of patients with laryngeal tuberculosis. In the three patients in the current study who were diagnosed with laryngeal tuberculosis, there was no lung involvement.

Isolated nasopharyngeal and tonsillar tuberculosis are extremely rare. Clinically, hypertrophy or fibrosis in the nasopharyngeal mucosa is seen in nasopharyngeal involvement, while bilateral hypertrophy, ulcers, or polypoid lesions can be seen in tonsillar involvement.²⁰

Culture examination from mucosal and tissue samples is the gold standard in tuberculosis diagnosis, and smear microscopy, histopathology, nucleic acid amplification tests, and immunological tests are also used.^{16,21} As the bacillus load in the tissue of EPT cases is generally low, the positivity rate of cultures is low.^{7,16} Ziehl-Neelsen staining shows positivity in 27–60% of patients.²² The interferon- γ release assay (IGRA) can be used for rapid diagnosis.²³ In a previous study that compared various tests related to tuberculous lymphadenitis, sensitivity was determined to be highest (95.2%) in histopathological examination performed after excisional biopsy, followed by culture (85.7%) and IGRA (78.8%).²³ It is necessary to histologically identify granulomatous inflammation to be able to predict different etiologies, as the differential diagnosis can be narrowed down by histological patterns (foreign body, necrotizing, non-necrotizing, suppurative, and widespread histiocytic reaction).²⁴ In the histopathological examination of excisional biopsy specimens, the visualization of Langhans giant cells, caseified necrosis, granulomatous inflammation, and calcification is one of the most important means of tuberculosis diagnosis.²⁵

The observation of granuloma with or without caseification histopathologically and imaging methods can be sufficient for treatment decision-making until culture results are received. Children aged <10 years are treated with a combination of three drugs (rifampicin, isoniazid, pyrazinamide).³ For patients aged >10 years, 2 months of intensive four-drug anti-tuberculosis treatment (including ethambutol) is followed by 4 months of maintenance treatment (rifampicin, isoniazid).³ A study published in 2016 showed that the duration of treatment can be shortened with the use of moxifloxacin instead of ethambutol.²⁶

CONCLUSION

Involvement of the head and neck region in EPT can mimic many diseases, so a high level of suspicion is necessary for accurate diagnosis. The frequency has tended to increase with the use of immunosuppressant treatments in recent years. If there are suspicious symptoms and findings in patients with a disease causing immunosuppression or who are using drugs that suppress the immune system, sampling must be performed to rule out tuberculosis. As acid-resistant bacilli (ARB) and culture positivity are low in EPT, excisional biopsy is important for diagnosis. Tuberculosis is known to be seen more often in female patients. When persistent necrotic lymphadenopathy is present in the submandibular region, especially in young patients, tuberculosis should be considered.

Acknowledgements: In this study, head and neck involvement of patients diagnosed with tuberculosis was discussed. We would like to thank the departments that contributed to the diagnosis (Medical Microbiology) and systematic treatment (Chest and Infectious Diseases) of tuberculosis.

Ethics Committee Approval: The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 20.12.2023, number: 2023/825).

Author Contributions: Concept – İY; Design – NP; Supervision – İY; Resource – ÖC; Materials – İK; Data Collection and/or Processing – MCK; Analysis and/or Interpretation – NT; Literature Search – İK; Writing – NT; Critical Reviews – EG, SÇ.

Conflict of Interest: The authors have no conflict of interest to declare.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

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