

**Tuberculosis lymphadenitis: An unusual swelling of salivary glands, a case series study in Iran**

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**Abstract**

**Background and objective:** Tuberculosis is a chronic granulomatous infection and has become a global concern. This disease is caused by *Mycobacterium tuberculosis*, but other types of *Mycobacterium* can also cause the disease. Tuberculosis usually affects the respiratory system, but other organs, called extrapulmonary tuberculosis, can be involved. Lymph node tuberculosis is one of the manifestations of extrapulmonary tuberculosis, especially in regions where tuberculosis is endemic. The involvement of salivary glands with tuberculosis is an uncommon condition. Here we present three cases (two adults and one child) with tuberculosis salivary gland lymphadenitis.

**Subjects and methods:** Three cases were studied in the current work. The first case was 27-year-old woman without any underlying diseases, was referred to our local hospital due to painful swelling of the submandibular region. The second case was 44-year-old woman without any underlying diseases, was referred to our hospital because of painful swelling in her left parotid gland region. The third case was 7-year-old boy without any underlying diseases, complaining of fever and painful swelling of the right submandibular gland.

**Results and conclusion:** In all the cases, tuberculosis diagnosis was confirmed by biopsy. Although, the diagnosis of tuberculosis was easier in the child due to symptoms like night sweating and fever and positive purified protein derivative test, in adults, there were no abnormalities in the initial laboratory tests, and purified protein derivative tests were negative, which made the diagnosis of tuberculosis more complicated. Although, salivary gland involvement with tuberculosis is not common, it should be considered a differential diagnosis in patients with swelling of salivary glands. In addition, the diagnosis confirmation should be based on biopsy, and normal laboratory tests and negative purified protein derivative tests should not confuse us. An early diagnosis is essential, and early initiation of an anti-tuberculosis regimen can prevent the following complications.

**Keywords:** Case report, Case series, Salivary gland, Tuberculosis lymphadenitis

**1. Introduction**

Tuberculosis (TB) is a chronic granulomatous infection. It is estimated that a quarter of the world's

population is infected with *Mycobacterium tuberculosis* [1]. It is mainly caused by *Mycobacterium tuberculosis*, but other types of *Mycobacterium* can

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also cause the disease [2].

Tuberculosis, which mainly affects the lungs, can affect almost all other organs and tissues in our body [3]. Tuberculosis bacilli enter the lymphatic system and bloodstream to reach the extrapulmonary organs. Lymph node tuberculosis (LNT) is one of the most common causes of lymphadenopathy in areas where tuberculosis is endemic [4]. The diagnosis of LNT may be difficult in countries with a low prevalence of tuberculosis and may delay appropriate treatment [5].

Cervical tuberculosis lymphadenitis should be considered in the differential diagnosis of chronic and painless cervical lymphadenopathy. TB lymphadenitis is often found in the lymph nodes of the neck and causes many benign and malignant conditions of the disease, such as metastatic cancer, malignant lymphoma, nonspecific hyperplasia, metastatic carcinoma, and malignant sarcoidosis. Systemic symptoms such as weight loss, fever, fatigue, and night sweats are sometimes absent, and clinical findings are usually indistinguishable from lymphadenitis due to other diseases [6-8].

In the differential diagnosis of TB lymphadenitis, other granulomatous lymphadenitis conditions, such as non-tuberculous mycobacteria (including *M. scrofulaceum*, *M. avium*, and *M. haemophilum*), tularemia, sarcoidosis, fungal disease, toxoplasmosis, cat-scratch disease, and neoplasm should be considered [9,10]. Patients with long-term lymphadenopathy, with or without systemic symptoms, and especially patients in regions with a high prevalence of TB, should be evaluated for TB lymphadenitis. Symptoms of perforation or compression of surrounding organs may complicate the diagnosis [11]. Identifying TB lymphadenitis, especially in the early stages of lymphadenopathy, is essential and can lead to earlier therapy administration. Here, we present three patients (one child and two adults) with salivary gland TB.

## 2. Case presentation

In 2022, three patients with signs of salivary gland lymphadenitis were referred to Razi hospital

(Rasht, north of Iran). TB lymphadenitis was confirmed by biopsy, and anti-TB drugs were initiated for them. The present study was approved by the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1401.299). More details about the cases, the medical tests, and the treatments are presented as follows.

### 2.1. First case

A 27-year-old woman without any underlying diseases was referred to our local hospital due to painful swelling of the submandibular region. The patient had no other complaints, such as fever or cough. The patient reported that the swelling started five months before his referral to our hospital. Based on the results of the initial assessments, the condition was first diagnosed as bacterial lymphadenitis, and empirical antibiotic therapy was started. The condition got better, and the patient got discharged.

After a couple of weeks, the patient was referred again and reported that the condition flared back, and the antibiotic therapy was ineffective. An X-ray imaging of oral and maxillofacial regions was done to rule out sialolithiasis, sialadenitis, and submandibular gland calcification (Figure 1). Due to the normal X-ray imaging, head and neck Magnetic resonance Imaging (MRI) was requested in the next step. The results of MRI imaging were suggestive of metastatic lymph nodes or infectious lymphadenitis (Figure 2). More laboratory tests, including purified protein derivative (PPD) test and chest X-ray (CXR) (Figure 3) for further evaluation of TB were done. The PPD test result was negative, and no significant finding was observed in CXR; thus, the patient was referred to an infectious disease specialist for a consultation about doing an excisional biopsy. According to the specialist's confirmation, the operation was done, and the lymph node was removed for an excisional biopsy. In pathological evaluation, necrotizing granulomatous lymphadenitis was seen, suggesting tuberculous lymphadenitis. Anti-TB treatment was initiated based on the diagnosis; symptoms faded over time, and laboratory tests demonstrated that the therapy was effective.



Figure 1- X-ray imaging of oral and maxillofacial regions with no significant findings suggestive for sialolithiasis, sialadenitis, and submandibular gland calcification

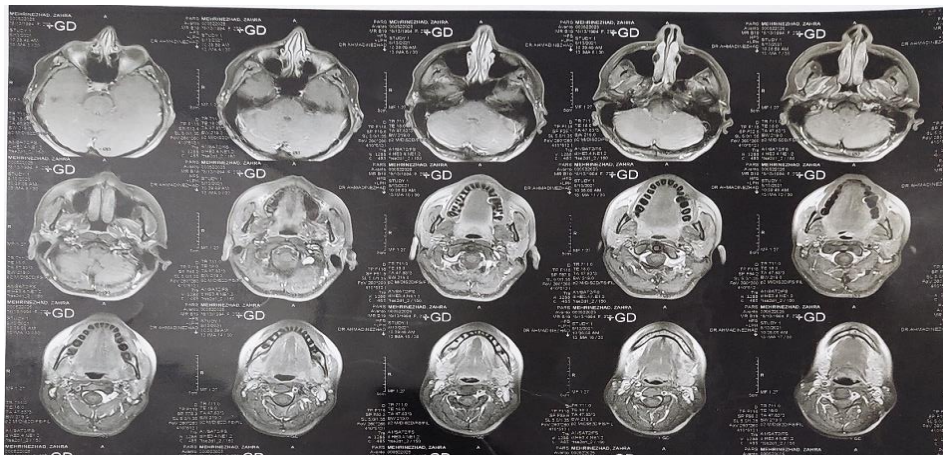


Figure 2- MRI imaging which was suggestive for metastatic lymph nodes or infectious lymphadenitis

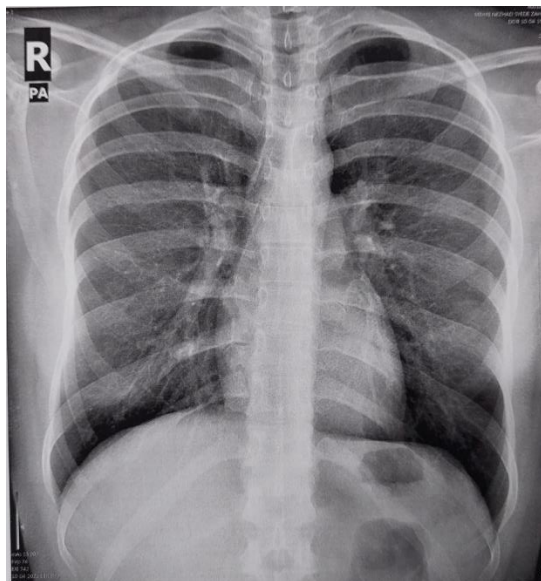


Figure 3- Chest X-ray of the patient with no significant findings

## 2.2. Second case

A 44-year-old woman without any underlying diseases came to our hospital complaining of painful swelling in her left parotid gland region. No other significant symptoms like fever, cough, and weight loss were reported. According to the patient, the swelling started six months before his referral to our hospital and did not improve with empirical antibiotic therapy.

Initial evaluation including laboratory blood exam and physical examination was done. Also, an ultrasound imaging of the parotid gland was done for the patient. In the blood exam, no significant findings were reported. Based on physical examination, the swelling was firm and not mobile (Figure 4). Ultrasound imaging showed a cystic focus with a thick wall of 49×30×37 mm in the inferior parotid region. Also, several hypoechoic lymph nodes were seen with a maximum size of 27×15 mm. The ultrasound imaging findings were suggestive of solid mass, abscess, or infectious lesions (Figure 5).

For more evaluation of the parotid gland, an Axial Computed Tomography scan (CT scan) of the neck

with and without intravenous contrast was carried out. The CT scan results showed diffuse enlargement of the left parotid gland. Also, multiple large conglomerated lymphadenopathies were observed, and some of these lymphadenopathies showed central hypodensity and peripheral enhancement in favor of central necrosis. There was no obvious adjacent organ invasion. Infective processes were considered the most probable diagnosis, including bacterial lymphadenitis, tuberculosis infection, or suppurative parotitis (Figure 6). For assessing infectious diseases also, additional exams (including PPD, Epstein-Barr virus serology, Cytomegalovirus serology, and Toxoplasmosis serology) were carried out, and the results were negative. For more evaluation, a Fine Needle Aspiration (FNA) biopsy was taken, and the result was suggestive of abscess formation and necrotizing granulomatous inflammation, which revealed a final diagnosis of TB.

Regarding clinical presentations and reports, anti-TB drugs were started for the patient, and the swelling healed.



Figure 4- Left parotid gland swelling of the patient

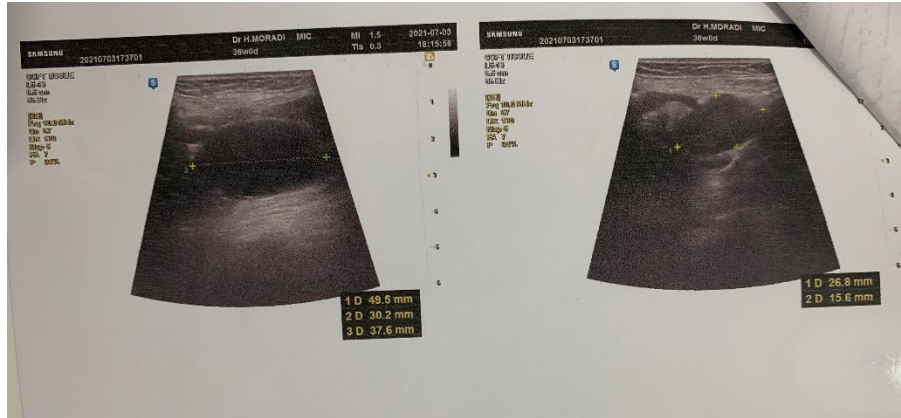


Figure 5- Ultrasound image of the left parotid gland showing cystic focus with a thick wall of 49×30×37 mm in the inferior parotid region. Several hypoechoic lymph nodes were seen with a maximum size of 27×15 mm. Findings were suggestive for solid mass, abscess, or infectious lesions

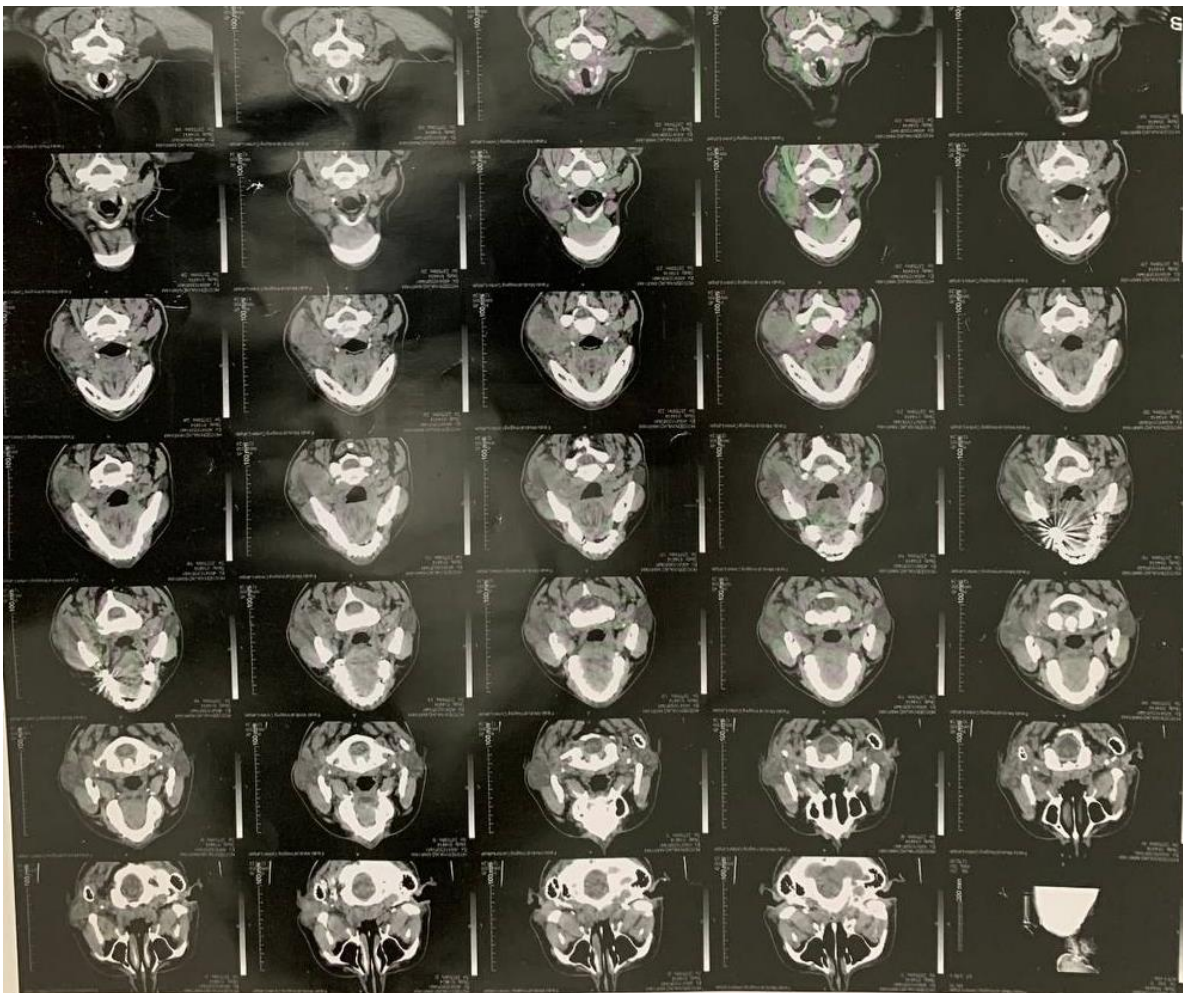


Figure 6- CT scan of parotid glands showing diffuse enlargement of the left parotid gland. Multiple large conglomerated lymphadenopathies were observed which some of these lymphadenopathies showed central hypodensity and peripheral enhancement in favor of central necrosis

### 2.3. Third case

A 7-year-old boy without any underlying diseases was referred to our hospital complaining of fever and painful swelling of the right submandibular gland. The patient also had night sweating and weight loss. The fever had started two months before his referral to our hospital. The patient's mother reported that empirical antibiotic therapy was started for his son before his referral to our hospital, but the condition did not improve. The patient's mother also said the boy's father was in an addiction treatment campus two months ago.

Initial examination and laboratory blood exam were done for the patient. High erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and leukocytosis were seen in the patient's blood examination. Due to the presence of the patient's father in the addiction treatment camp, a PPD test was also done for the patient, and the result was positive. For confirmation of the diagnosis of TB, also right submandibular biopsy was done. The result of the biopsy showed necrotizing granuloma of the tissue suggesting TB.

The anti-TB regimen got started, and the patient's condition got better. After treatment initiation, leukocyte count, ESR, and CRP levels dropped to normal, and the fever disappeared.

### 3. Results and discussion

TB is a disease mainly caused by *Mycobacterium tuberculosis* [12]. This disease is a global concern. The distribution of the disease varies in different countries. Almost 60% of TB death in the world was recorded in six countries, including Indonesia, India, Nigeria, China, South Africa, and Pakistan, in 2015 [13].

TB is a multi-organ disease that mainly affects the respiratory system; however, other organs like the gastrointestinal system, the liver, the central nervous system, the lymph reticular system, the reproductive system, and the musculoskeletal system can also be infected [8,14]. Extrapulmonary forms of TB have increased in recent years, and the referral of three cases to our hospital in two months

is compatible with this phenomenon [11,15,16].

One of the causes of granulomatous lesions of the head and neck is extrapulmonary TB; however, infection of salivary glands by TB is a rare condition [17]. Salivary gland infection by TB is usually unilateral, and parotid gland infection is more common than the other salivary glands [18]. Although, salivary gland infection by TB is uncommon, it should be considered a differential diagnosis of salivary gland lesions [17]. Distinguishing salivary TB from other salivary gland diseases is clinically challenging and requires extra para-clinical assessments. Acid-fast staining, FNA, and polymerase chain reaction can be helpful in the diagnosis of extrapulmonary TB [19].

Here we presented three cases with unusual TB manifestations (two adults and one child). The presence of TB was confirmed by biopsy in all of them.

One of the differences between the child and adults was systemic symptoms. Adults did not complain of fever, weight loss, or cough (constitutional symptoms), while the child had fever and weight loss. In agreement with our findings, some previous studies have shown that adult cases with TB lymphadenitis did not have constitutional symptoms [16,18,20]. Another difference between the adults and the child in this study was the results of their negative PPD tests for adults in contrast to the child. A positive PPD test and fever in the child made TB diagnosis much easier and faster than in adults. The initial blood examination of the adults showed no abnormal findings, while high ESR, CRP, and leukocytosis were observed in the child.

Pulmonary TB can be concurrent with extrapulmonary TB, so all patients with extrapulmonary TB should be assessed in terms of pulmonary TB [21]. For assessing pulmonary TB, we carried out CXR for our patients. The CXR of our cases showed no abnormalities, which is in keeping with the study by Nagalakshmi et al. [22] and Tauro et al. [18]. In contrast, in a study by Nwagbara, lesions of miliary TB were found in the CXR of the patients with TB lymphadenitis [16]. None of our patients were immunocompromised, which is in keeping with other studies [20,23].

#### 4. Conclusion

In conclusion, we presented three uncommon cases of TB lymphadenitis. There were no constitutional symptoms or history of close contact with TB patients in the two cases. Their PPD tests were negative, and blood exams showed no abnormal findings, which complicated the diagnosis of TB lymphadenitis. In the third case, symptoms like fever and positive PPD test helped us to diagnose TB faster. Although, salivary gland involvement with TB is rare, it should be considered a differential diagnosis in patients with swelling of salivary glands, especially in endemic regions of TB. Early diagnosis is essential, and early initiation of an anti-TB regimen can prevent surgery on the salivary glands.

#### 5. Conflict of interest

The authors declare that they have no conflicts of interest.

#### References

- Cohen A, Mathiasen VD, Schon T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *European Respiratory Journal*. 2019; 54(3): 1900655. <https://doi.org/10.1183/13993003.00655-2019>
- Troesch A, Nguyen H, Miyada C, Desvarenne S, Gingeras T, Kaplan P, et al. Mycobacterium species identification and rifampin resistance testing with high-density DNA probe arrays. *Journal of Clinical Microbiology*. 1999; 37(1): 49-55. <https://doi.org/10.1128/jcm.37.1.49-55.1999>.
- Jilani TN, Avula A, Gondal Z, Siddiqui AH. Active tuberculosis. 2018. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK513246/>
- Ganchua SKC, White AG, Klein EC, Flynn JL. Lymph nodes-The neglected battlefield in tuberculosis. *PLoS Pathogens*. 2020; 16(8): e1008632. <https://doi.org/10.1371/journal.ppat.1008632>.
- Mathiasen VD, Hansen AK, Eiset AH, Lillebaek T, Wejse C. Delays in the diagnosis and treatment of tuberculous lymphadenitis in low-incidence countries: a systematic review. *Respiration*. 2019; 97(6): 576-584. <https://doi.org/10.1159/000499052>.
- Khan R, Harris S, Verma A, Syed A. Cervical lymphadenopathy: scrofula revisited. *The Journal of Laryngology & Otolaryngology*. 2009; 123(7): 764-767. <https://doi.org/10.1017/S0022215108003745>.
- Morad NA. Tuberculous cervical lymphadenopathy: should antituberculous therapy be preceded by histological proof? *Tropical Doctor*. 2000; 30(1): 18-20. <https://doi.org/10.1177/004947550003000110>.
- Mathiasen VD, Andersen PH, Johansen IS, Lillebaek T, Wejse C. Clinical features of tuberculous lymphadenitis in a low-incidence country. *International Journal of Infectious Diseases*. 2020; 98: 366-371. <https://doi.org/10.1016/j.ijid.2020.07.011>.
- Asano S. Granulomatous lymphadenitis. *Journal of Clinical and Experimental Hematopathology*. 2012; 52(1): 1-16. <https://doi.org/10.3960/jslrt.52.1>.
- Artenstein AW, Kim JH, Williams WJ, Chung RC. Isolated peripheral tuberculous lymphadenitis in adults: current clinical and diagnostic issues. *Clinical Infectious Diseases*. 1995; 20(4): 876-882. <https://doi.org/10.1093/clinids/20.4.876>.
- Fontanilla JM, Barnes A, Von Reyn CF. Current diagnosis and management of peripheral tuberculous lymphadenitis. *Clinical Infectious Diseases*. 2011; 53(6): 555-562. <https://doi.org/10.1093/cid/cir454>.
- Terracciano E, Amadori F, Zaratti L, Franco E. Tuberculosis: an ever present disease but difficult to prevent. *Igiene e Sanita Pubblica*. 2020; 76(1): 59-66.
- Pan Z, Zhang J, Bu Q, He H, Bai L, Yang J, et al. The gap between global tuberculosis incidence and the first milestone of the WHO end tuberculosis strategy: an analysis based on the global burden of disease 2017 database. *Infection and Drug Resistance*. 2020; 13: 1281. <https://doi.org/10.2147/IDR.S248875>.
- Mbuh TP, Ane-Anyangwe I, Adeline W, Thumamo Pokam BD, Meriki HD, Mbacham W. Bacteriologically confirmed extra pulmonary tuberculosis and treatment outcome of patients consulted and treated under program conditions in the littoral region of Cameroon. *BMC Pulmonary Medicine*. 2019; 19(1): 1-7. <https://doi.org/10.1186/s12890-018-0770-x>.
- Abebe G, Deribew A, Apers L, Abdissa A, Deribie F, Woldemichael K, et al. Tuberculosis lymphadenitis in Southwest Ethiopia: a community based cross-sectional study. *BMC Public Health*. 2012; 12(1): 1-7. <https://doi.org/10.1186/1471-2458-12-504>.

16. Nwagbara VI, Asuquo ME, Ebughe G, Agbor C, Akpan S, Ugbem T, et al. Tuberculous lymphadenitis of the neck: Case series. *International Journal of Medicine*. 2013; 1(1): 4-8.  
<https://doi.org/10.14419/ijm.v1i1.893>.
17. Ataman M, Sozeri B, Ozcelik T, Gedikoglu G. Tuberculosis of the parotid salivary gland. *Auris, Nasus, Larynx*. 1992; 19(4): 271-273.  
[https://doi.org/10.1016/s0385-8146\(12\)80048-4](https://doi.org/10.1016/s0385-8146(12)80048-4).
18. Tauro LF, George C, Kamath A, Swethadri G, Gatty R. Primary tuberculosis of submandibular salivary gland. *Journal of Global Infectious Diseases*. 2011; 3(1): 82.  
<https://doi.org/10.4103/0974-777X.77301>.
19. Mohapatra PR, Janmeja AK. Tuberculous lymphadenitis. *Journal of the Association of Physicians of India*. 2009; 57(6): 585-590.
20. Moualed D, Robinson M, Qureishi A, Gurr P. Cervical tuberculous lymphadenitis: diagnosis and demographics, a five-year case series in the UK. *The Annals of the Royal College of Surgeons of England*. 2018; 100(5): 392-396.  
<https://doi.org/10.1308/rcsann.2018.0021>.
21. Lee JY. Diagnosis and treatment of extrapulmonary tuberculosis. *Tuberculosis and Respiratory Diseases*. 2015; 78(2): 47-55.  
<https://doi.org/10.4046/trd.2015.78.2.47>.
22. Nagalakshmi V, Nagabhushana D, Aara A. Primary tuberculous lymphadenitis: A case report. *Clinical, Cosmetic and Investigational Dentistry*. 2010; 2: 21.  
<https://doi.org/10.2147/ccide.s9733>.
23. Menon K, Bem C, Goulesbrough D, Strachan D. A clinical review of 128 cases of head and neck tuberculosis presenting over a 10-year period in Bradford, UK. *The Journal of Laryngology and Otology*. 2007; 121(4): 362-368.  
<https://doi.org/10.1017/S0022215106002507>.