



## Tuberculous lymphadenitis – still on the scene: a case report

### Tuberkulozni limfadenitis – još uvek na sceni

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#### Abstract

**Introduction.** Tuberculosis (TB) continues to be a global health problem, with various manifestations affecting different organs and organ systems. Tuberculous lymphadenitis (TBL), also known as scrofula or lymph node (LN) TB, is a manifestation of *Mycobacterium tuberculosis* infection primarily affecting the LNs. Our region has a low annual incidence rate of TB, which is why the expected prevalence of TBL is also low. **Case report.** We present two cases of TBL diagnosed three months apart. Both presented patients had the disease localized in the LNs of the neck. These were young people without chronic diseases and previously in good health condition. The diagnosis was confirmed by surgical biopsy of the LNs in the first patient and fine needle aspiration biopsy in the second patient. Both patients were treated with standard protocols for TBL, with favorable outcomes and without significant complications and side effects. **Conclusion.** Presented cases highlight the importance of considering TBL in the differential diagnosis of neck masses, even in regions with a low prevalence of TB. Timely diagnosis and treatment are essential for preventing complications and ensuring a successful outcome.

#### Key words:

biopsy; biopsy, fine-needle; diagnosis, differential; drug therapy; lymphadenitis; neck; tuberculosis; treatment outcome.

#### Apstrakt

**Uvod.** Tuberkuloza (TB) i dalje predstavlja globalni zdravstveni problem, sa različitim manifestacijama koje utiču na različite organe i organske sisteme. Tuberkulozni limfadenitis (TBL), poznat i kao škrofula ili TB limfnih čvorova (LČ), manifestacija je infekcije *Mycobacterium tuberculosis*, koja prvenstveno zahvata LČ. Naš region ima nisku godišnju stopu incidencije TB, zbog čega je niska i očekivana prevalencija TBL. **Prikaz bolesnika.** Prikazana su dva slučaja TBL-a, koja smo dijagnostikovali u razmaku od tri meseca. Oba prikazana bolesnika imala su bolest lokalizovanu u LČ vrata. Radilo se o mladim osobama bez hroničnih bolesti, koje su prethodno bile u dobrom zdravstvenom stanju. Dijagnoza je kod prvog bolesnika potvrđena hirurškom biopsijom LČ, a kod drugog bolesnika aspiracionom biopsijom „finom iglom“. Oba bolesnika lečena su standardnim protokolima za TBL, sa povoljnim ishodom i bez značajnih komplikacija i neželjenih efekata terapije. **Zaključak.** Prikazani slučajevi potvrđuju važnost razmatranja TBL u diferencijalnoj dijagnozi izraslina na vratu, čak i u regionima sa niskom prevalencijom TB. Pravovremena dijagnoza i lečenje su ključni za sprečavanje komplikacija i postizanje uspešnog ishoda lečenja.

#### Ključne reči:

biopsija; biopsija tankom iglom; dijagnoza, diferencijalna; lečenje lekovima; limfadenitis; vrat; tuberkuloza; lečenje, ishod.

#### Introduction

Tuberculosis (TB) remains a global health concern, with various manifestations affecting different organs. According to the latest published statistical data, in 2022, an estimated 10 million people fell ill with TB worldwide. There were approximately 1.5 million TB-related deaths in 2022.

TB is more prevalent in certain regions, with over 95% of TB deaths occurring in low- and middle-income countries. The regions most affected include sub-Saharan Africa and Southeast Asia. These are also the regions with the highest prevalence of human immunodeficiency virus (HIV) infection, which is considered the most important risk factor for TB<sup>1,2</sup>.

Serbia is classified as a country with a low TB incidence rate of around seven to ten people *per* 100,000 inhabitants, which has been slightly increasing in the last five years <sup>3</sup>.

Pulmonary TB is the most common form. However, other organs may also be affected. The most frequently affected sites were lymph nodes (LNs) (48.5%), and the next three ranked were genitourinary TB (20.5%), pleural TB (12.0%), and osteoarticular TB (10.1%) <sup>4</sup>.

Tuberculous lymphadenitis (TBL), also known as scrofula or LN TB, is a manifestation of *Mycobacterium tuberculosis* (*M. tuberculosis*) infection primarily affecting the LNs <sup>5</sup>.

Historically, TBL has been recognized as a significant health issue. It has been documented in ancient Egyptian mummies and was prevalent during the Middle Ages and the Renaissance. In the past, the disease was commonly associated with poor living conditions and malnutrition. However, with advancements in healthcare and the availability of anti-tubercular medications, the incidence of TBL has decreased in many parts of the world <sup>6</sup>.

TBL occurs when *M. tuberculosis* infects the LNs through hematogenous spread or direct extension from a nearby primary focus, usually in the lungs. The bacilli then replicate within LNs, leading to granuloma formation and subsequent caseous necrosis. The immune response often encapsulates the affected nodes, resulting in the characteristic appearance of firm, matted lymphadenopathy <sup>7</sup>.

The clinical presentation of TBL can vary widely, making it a diagnostic challenge. Patients may present with painless, slowly enlarging LNs, commonly involving the cervical region. The LNs are usually firm, non-tender, and may become matted together. Constitutional symptoms such as fever,

night sweats, and weight loss can accompany TBL, mimicking other infectious or neoplastic etiologies such as lymphoma <sup>8</sup>.

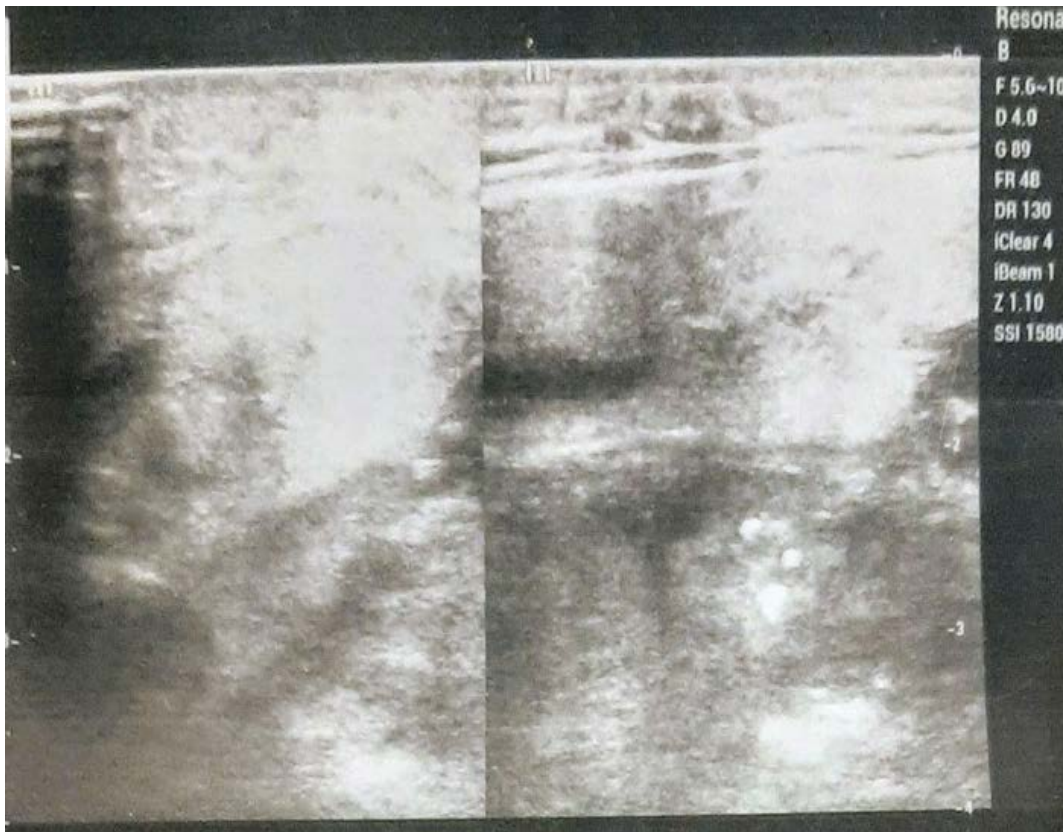
Accurate diagnosis is imperative for appropriate management. TBL diagnosis often involves a combination of clinical, radiological, and laboratory methods. Fine needle aspiration (FNA) biopsy is a commonly employed diagnostic tool, providing a minimally invasive means to obtain tissue for microscopic examination and culture. Polymerase chain reaction assays can enhance sensitivity by detecting *M. tuberculosis* deoxyribonucleic acid. Radiological imaging, such as contrast-enhanced computed tomography (CT) scans, helps visualize the extent of LN involvement and identify associated complications <sup>9-11</sup>.

The cornerstone of TBL management is a multidrug anti-tubercular therapy (ATT) regimen. First-line drugs, including isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z), are typically administered for an extended period. Surgical intervention may be considered for refractory cases, complications (e.g., abscess formation), or diagnostic uncertainty. Ongoing research explores the potential role of novel anti-tubercular agents and immunomodulatory therapies to improve treatment outcomes <sup>12</sup>.

## Case report

### Case I

A 19-year-old male construction worker presented to the outpatient department with complaints of a gradually increasing painless swelling in the left side of his neck for the past four months. He denied any history of trauma, fever, or weight



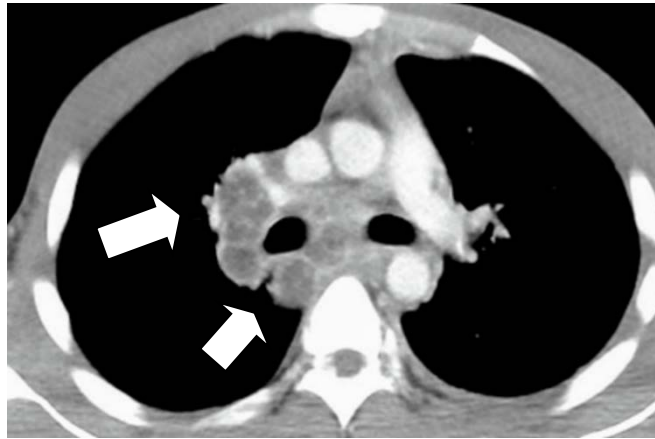
**Fig. 1 – Ultrasound finding of enlarged and necrotic lymph nodes in the left submandibular region.**

loss. On further inquiry, he reported occasional night sweats and a feeling of weakness. He had no significant medical history and was not on any regular medications. Upon physical examination, a firm, non-tender, and mobile LN mass was palpable in the left submandibular region. The overlying skin was normal, and there was no evidence of sinus formation or discharge. General physical examination was unremarkable, with no signs of respiratory distress or abnormal lung sounds. The systemic examination did not reveal any other abnormal findings. The complete blood count was within normal limits. Laboratory tests for viruses (HIV, hepatitis A and B, cytomegalovirus, and Epstein-Barr virus) were negative. Chest X-ray revealed no significant abnormalities in the lungs. Ultrasound examination of the neck showed enlarged and necrotic LNs in the left submandibular region, the largest of which was 4 cm in diameter (Figure 1). Chest CT scan revealed numerous enlarged and necrotic LNs in the mediastinum, the largest of which was  $5.5 \times 6$  cm in the area of the right hilum. No pathological changes were observed in the lungs (Figure 2).

Given the presence of pronounced symptoms and a strong suspicion of lymphoproliferative disease, we decided to perform a surgical biopsy of the LNs. The procedure was done without immediate or delayed complications (Figure 3).

Histopathological (HP) findings showed caseous necrosis and acid-fast bacilli observed under the microscope (Figures 4 and 5).

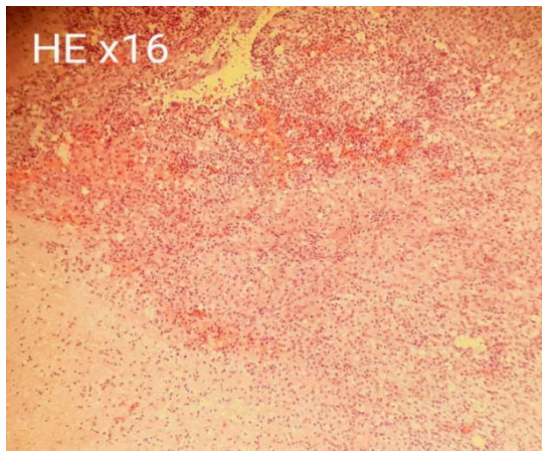
After confirming the diagnosis, we started the treatment. The patient was started on a standard ATT regimen comprising an initial phase of two months of H, R, Z, and E, followed by a continuation phase of four months of H and R, 2HRZE/4HR. He was educated on the importance of medication adherence and the need for regular follow-up. The patient showed significant improvement after two months of treatment, with a reduction in the size of LNs. Repeated chest X-ray remained normal, and the patient reported a resolution of night sweats and weakness. ATT was continued for a total duration of six months.



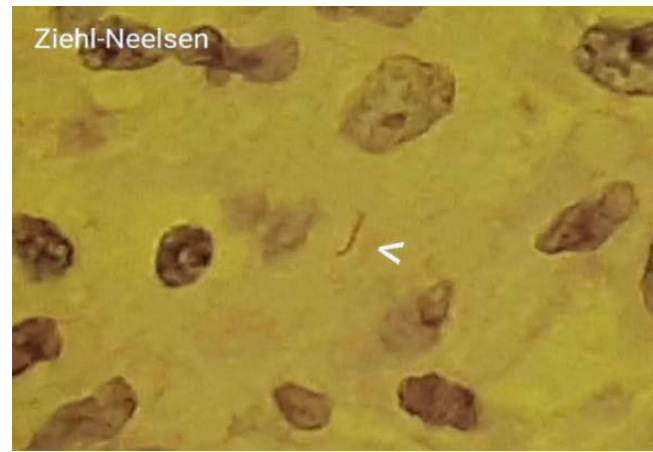
**Fig. 2 – Chest computed tomography scan – numerous enlarged and necrotic lymph nodes in the mediastinum.**



**Fig. 3 – Submandibular mass after surgical biopsy.**



**Fig. 4 – Lymph node histopathological examination: mononuclear cell infiltrate, epithelioid granuloma, and caseous necrosis [hematoxylin-eosin (HE) staining,  $\times 16$ ].**



**Fig. 5 – Microscopic lymph node examination revealed acid-fast bacilli (Ziehl-Neelsen stain,  $\times 100$ ).**

### Case II

A 21-year-old male student of the Military Academy presented with a two-month history of painless neck swelling and low-grade fever. The patient denied any significant weight loss, night sweats, or respiratory symptoms. The patient's training regimen required intense physical activities; he did not notice fatigue and difficulty performing activities.

Physical examination revealed a mass in the left supraclavicular area with a diameter of about 5 cm. The change was dense and fixed to the base with hyperemic skin above. Mild pain was felt during palpation (Figure 6).

Routine laboratory investigations were within normal range, except for a mildly elevated erythrocyte sedimentation rate. Laboratory tests for viruses, including HIV, were negative. Chest X-ray and CT scan revealed no significant abnormalities in the lungs and mediastinum (Figure 7). We decided to perform an FNA biopsy of the neck mass. HP find-

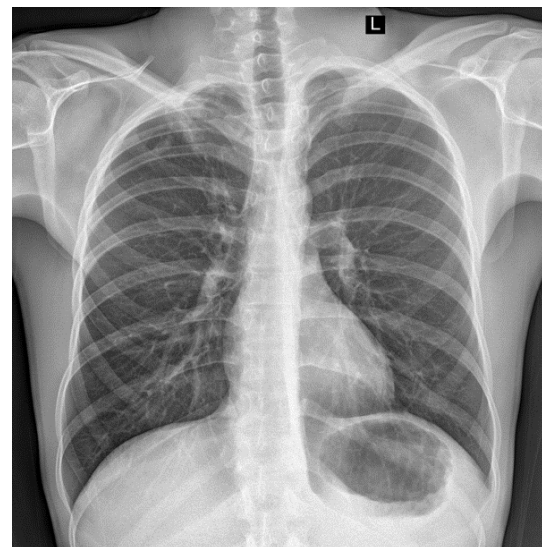
ings revealed granulomas indicative of TB. The Ziehl-Neelsen staining confirmed the presence of acid-fast bacilli, which confirmed the diagnosis of TBL.

Given the patient's military background, strict infection control measures were implemented to prevent transmission to other trainees. The patient was started on a standard ATT regimen, including H, R, E, and Z (2HRZE/4HR). Directly observed therapy was facilitated within the Military Academy setting to ensure treatment adherence.

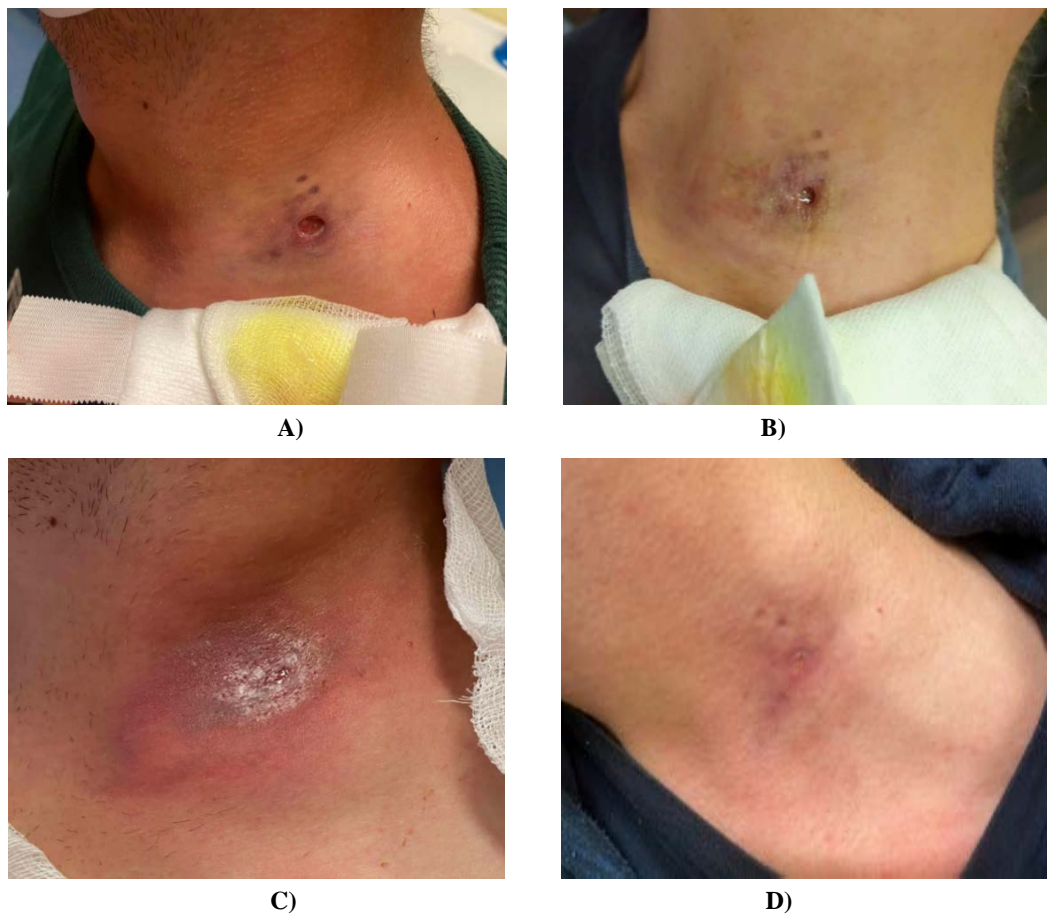
The patient faced unique challenges related to academic commitments and physical training. Special considerations were taken to modify the training schedule, allowing the student to continue academic obligations while accommodating the physical limitations imposed by the disease and its treatment. The importance of bed rest and non-pharmacological therapy in the treatment of TB needs to be emphasized. Close collaboration between the medical team and military authorities was essential to strike a



**Fig. 6 – Initial appearance of the patient: supraclavicular mass with changes in the skin above.**



**Fig. 7 – Chest X-ray: a suspicious infiltrate at the top of the right lung on the computed tomography scan has not been confirmed – no abnormalities in the lungs were found.**



**Fig. 8 – Evolution of cutaneous fistula: development (A and B), closure (C), and residual scar (D).**

balance between academic responsibilities and medical requirements.

After one month of starting ATT, a complication occurred—a cutaneous fistula. We continued ATT with local wound care. In the course of the disease, in four months, the fistula closed, with the presence of a small skin scar (Figure 8).

Regular clinical and radiological assessments were conducted throughout the treatment. The patient responded well to ATT, with a reduction of LN size and resolution of symptoms. The modified training regimen allowed the student to fulfill academic requirements without compromising his health.

### Discussion

Clinical presentation of TBL can vary widely, making diagnosis challenging. Common manifestations include painless, gradually enlarging LNs, usually in the cervical region. These nodes may become fluctuant and form abscesses, leading to the formation of a cutaneous fistula. Constitutional symptoms such as fever, weight loss, and night sweats may also be present<sup>13</sup>.

Early detection of TBL is crucial for several reasons. Timely diagnosis allows for prompt initiation of appropriate treatment, minimizing the risk of disease progression and complications. Considering the localization of LNs, there was a possibility of major blood vessel lesions and fatal bleeding<sup>14</sup>.

Early intervention also reduces the risk of transmission to others, contributing to the control of TB spread within communities. Furthermore, the identification of TB cases at an early stage facilitates contact tracing and preventive therapy for individuals at high risk of infection<sup>15</sup>.

Several conditions can present with similar clinical features, making the differential diagnosis crucial for accurate management. Other causes of lymphadenopathy, such as bacterial or viral infections, lymphoma, and autoimmune diseases, must be considered. FNA biopsy for cytological and bacteriological examination or surgical biopsy of the affected LN is often required for definitive diagnosis, allowing for the identification of acid-fast bacilli and confirming TB. The first presented patient also had mediastinal lymphadenopathy and lymphoma strongly suspected. We decided on a surgical biopsy due to the size of the tissue sample for HP examination. The treatment of TBL typically involves a combination of anti-tubercular drugs, most commonly H, R, E, and Z. However, challenges in the treatment of this condition may arise due to factors such as drug resistance, treatment non-adherence, and the development of adverse drug reactions<sup>16,17</sup>.

TBL has broader implications for public health. Active surveillance and early detection contribute to the overall control of TB transmission within communities. If there is no simultaneous lung localization, this form of TB is not the most infectious. Prompt treatment reduces the reservoir of

infectious individuals, limiting the potential for further spread.

Additionally, effective management of TBL prevents the development of drug-resistant strains, which could pose a more significant threat to public health. This particularly applies to individuals with specific occupations that involve constant presence in large groups. The second presented patient is a professional soldier, which involved numerous measures taken both towards the patient and the members of the military community<sup>18</sup>.

### Conclusion

Tuberculous lymphadenitis is a significant public health challenge that necessitates a comprehensive understanding of its pathogenesis, clinical presentation, diagnos-

tic modalities, and management strategies. Those cases highlight the importance of considering tuberculous lymphadenitis in the differential diagnosis of neck masses, even in regions with low disease incidence. Timely diagnosis and treatment are essential for transmission, preventing complications, and ensuring a successful outcome. This paper aims to contribute to the collective knowledge base, fostering continued advancements in diagnosing and treating tuberculous lymphadenitis. As the global fight against tuberculosis persists, a thorough grasp of tuberculous lymphadenitis is essential for healthcare professionals and researchers.

### Conflicts of interest

The authors declare no conflict of interest.

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Received on March 20, 2024

Revised on June 1, 2024

Revised on July 29, 2024

Accepted on September 27, 2024

Online First November 2024