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*Case Report*

# Scrofula as a Manifestation of Extrapulmonary Tuberculosis: A Case Report

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## A B S T R A C T

Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis and may present a significant diagnostic challenge due to its nonspecific and insidious clinical manifestations. We report the case of a 36-year-old immunocompetent Portuguese male, residing in a rural area and working in agriculture and livestock farming, who presented with persistent cervical lymphadenopathy without respiratory or constitutional symptoms. The patient had a previous history of necrotizing granulomatous lymphadenitis without definitive diagnosis or treatment. Physical examination revealed a hard right cervical lymph node conglomerate measuring approximately 3 cm. Imaging studies demonstrated multiple right laterocervical lymphadenopathies with nonspecific inflammatory characteristics. Extensive infectious, autoimmune and hematologic investigations were largely unremarkable, except for mildly elevated immunoglobulin levels. Interferon-gamma release assay (IGRA) was positive and lymph node biopsy revealed chronic necrotizing granulomatous inflammation. Although ZiehlNeelsen staining was negative for acid-fast bacilli, mycobacterial culture confirmed Mycobacterium tuberculosis. The patient was diagnosed with cervical tuberculous lymphadenitis (scrofula) and referred for antituberculous therapy. This case highlights the importance of considering tuberculosis in the differential diagnosis of persistent cervical lymphadenopathy, even in immunocompetent individuals and in the absence of systemic symptoms. It also emphasizes the essential role of histopathological and microbiological evaluation in establishing the definitive diagnosis of extrapulmonary tuberculosis.

**Keywords:** Tuberculous lymphadenitis; Extrapulmonary tuberculosis; Constitutional symptoms

## Introduction

Tuberculosis (TB) remains a major global health problem and one of the leading causes of death from infectious diseases worldwide[1]. It is caused by Mycobacterium tuberculosis, also known as Koch's bacillus and is transmitted predominantly through airborne inhalation of infectious droplets that deposit in the lungs[1]. Although pulmonary disease is the most common clinical presentation, hematogenous dissemination may occur, resulting in extrapulmonary involvement of organs such as lymph nodes, the genitourinary tract, bones and the central nervous system[1].

Lymph node TB or tuberculous lymphadenitis, is the most common extrapulmonary manifestation of tuberculosis[2,3]. It affects the lymph nodes, predominantly in the cervical, axillary or inguinal regions[2,3]. Unlike pulmonary tuberculosis, this form is generally not contagious[1]. The diagnosis of tuberculous lymphadenitis may be challenging because of its nonspecific clinical presentation and resemblance to other infectious, inflammatory or malignant conditions[4,5]. Histopathological examination often demonstrates granulomatous inflammation with caseous necrosis, although microbiological confirmation may not always be achieved[4,5]. Several risk factors are associated with an increased prevalence of these forms of tuberculosis, namely extremes of age, female sex and certain ethnic groups[1]. Additionally, immunocompromised patients (including those receiving TNF-α inhibitors, people living with HIV and transplant recipients), as well as medical conditions such as diabetes mellitus, chronic kidney disease and connective tissue diseases, are at increased risk[1,6]. Also significant is the risk associated with substance abuse and poor housing conditions, including homelessness and incarceration[1].

## Case Presentation

A 36-year-old Portuguese man, residing in a rural area, working in agriculture and shepherding. Previously healthy and with no regular medication.

His past medical history included excision of a supraclavicular lymph node with cutaneous fistulization in 2024. Histopathological examination revealed necrotizing granulomatous lymphadenitis. No further investigation or treatment was carried out afterward. He also had recurrent oral aphthosis, previously investigated in an Autoimmune Diseases clinic, but without a definitive diagnosis. He presented to the emergency department referred from the outpatient otorhinolaryngology clinic due to a hard jugular and mobile over deeper planes lymphadenopathy measuring approximately 3 cm, present for the previous 2 months. He denied respiratory symptoms, dysphagia, odynophagia or dysphonia. He also denied B symptoms, namely unintentional weight loss (10% of body weight over 6 months), night sweats or fever. He denied lower back pain, xerostomia or xerophthalmia. There was no history of uveitis, photophobia or skin rashes. He consumed tap water and had contact with animals ranging from small to large livestock, some of which were unvaccinated. On physical examination, he was hemodynamically stable and afebrile. Cardiopulmonary auscultation was normal. The abdomen was soft and depressible, without hepatosplenomegaly palpable. Lymph node examination revealed a palpable cervical lymph node conglomerate, the largest node measuring approximately 3 cm in the right jugular region, without inflammatory skin changes, with a hard consistency and mobile over deeper planes **(Figure 1)**.

Right cervical lymph node conglomerate located in the jugular region, presenting as a visible cervical swelling without overlying erythema or inflammatory skin changes. The lesion was described on palpation as hard and mobile over deeper planes. Imaging studies included a computed tomography (CT) scan of the neck, which revealed prominence of the right palatine tonsil measuring 21 × 9 mm and right-sided lymphadenopathies, the largest measuring 29 × 21 mm, considered suspicious **(Figure 2)**.

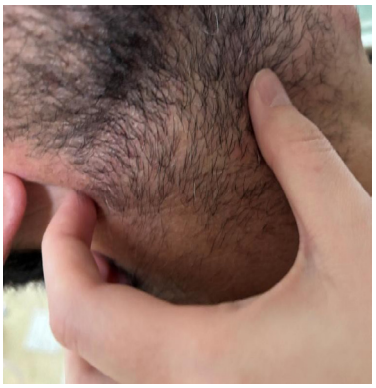


**Figure 1:** Cervical lymph node conglomerate.

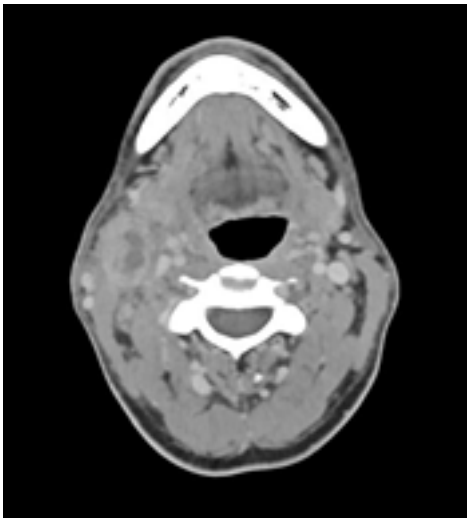


**Figure 2:** Computed Tomography (CT) scan of the neck.

The patient was admitted under the care of Internal Medicine for investigation of the lymph node conglomerate to establish a differential diagnosis between infectious disease, primary tonsillar neoplasm, lymphoproliferative disease and granulomatous disease. An extensive laboratory workup was performed (Table I). Laboratory evaluation revealed a complete blood count with mild microcytosis, normal leukocyte differential count and peripheral blood smear without abnormalities. Autoimmune and infectious screening were negative. Only IgG and IgA levels were slightly elevated.

Thoraco-abdominopelvic CT scan demonstrated right-sided cervical lymphadenopathies and mild hepatosplenomegaly without nodules. The liver measured 18 cm and the spleen 15 cm **(Figure 3)**.

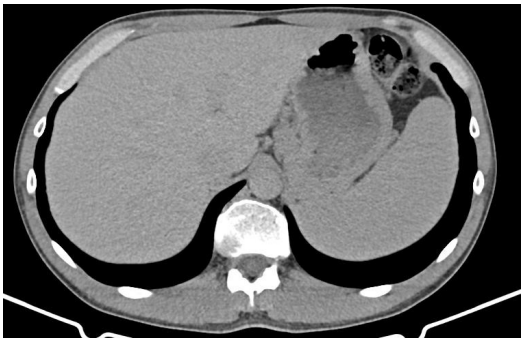


**Figure 3:** Thoraco-abdominopelvic CT scan

A cervical magnetic resonance imaging (MRI) scan was also performed, showing normal appearance of the pharyngolaryngeal

mucosa oral cavity, esophageal segment, tonsils, salivary glands, thyroid, middle ear and cranial compartment, without evidence of inflammatory or neoplastic pathology. Multiple right laterocervical lymphadenopathies were identified, the largest measuring approximately 3.8 cm in the craniocaudal axis, with nonspecific characteristics, considered compatible with chronic granulomatous inflammatory disease. The lesions exerted a mass effect on adjacent muscular structures, including the right sternocleidomastoid muscle, causing bulging of the superficial lobe of the right parotid gland and medial displacement of the right internal jugular vein. Inflammatory changes were also noted in the included paranasal sinuses **(Figure 4)**.

**Table 1:** Laboratory investigation performed during diagnostic workup.

| Parameter | Result | Reference Range |
|---|---|---|
| Hemoglobin (g/dL) | 14.2 | 13.0–18.0 |
| Hematocrit (%) | 41.4 | 43.0–55.0 |
| Mean corpuscular volume (fL) | 84.1 | 87.0–103.0 |
| Leukocytes (×10³/µL) | 3.93 | 4.0–11.0 |
| Neutrophils (×10³/µL) | 1.79 | 1.5–8.0 |
| Lymphocytes (×10³/µL) | 1.21 | 0.8–4.0 |
| Monocytes (×10³/µL) | 0.66 | 0.0–1.2 |
| Eosinophils (×10³/µL) | 0.20 | 0.0–0.3 |
| Basophils (×10³/µL) | 0.05 | 0.0–0.3 |
| Platelets (×10³/µL) | 212 | 150–400 |
| C-reactive protein (mg/dL) | 2.06 | <0.5 |
| Total proteins (g/dL) | 8.7 | 6.6–8.7 |
| Albumin (g/dL) | 4.7 | 3.4–4.8 |
| Sodium (mEq/L) | 139 | 135–147 |
| Potassium (mEq/L) | 3.7 | 3.7–5.1 |
| Corrected calcium (mg/dL) | 9.0 | 8.6–10.0 |
| Urea (mg/dL) | 29 | 0–50 |
| Creatinine (mg/dL) | 0.8 | 0.7–1.2 |
| Total bilirubin (mg/dL) | 0.8 | <1.2 |
| Aspartate aminotransferase (AST) (U/L) | 20.0 | <40 |
| Alanine aminotransferase (ALT) (U/L) | 13 | <41 |
| Gamma-glutamyl transferase (GGT) (U/L) | 16 | 10–49 |
| Alkaline phosphatase (U/L) | 54 | 40–130 |
| International normalized ratio (INR) | 1.06 | <1.2 |
| Immunoglobulin G (IgG) (mg/dL) | 1987 | 650–1500 |
| Immunoglobulin A (IgA) (mg/dL) | 537 | 78–312 |
| Immunoglobulin M (IgM) (mg/dL) | 65 | 55–300 |
| Immunoglobulin E (IgE) (mg/dL) | 155 | <100 |
| Angiotensin-converting enzyme (ACE) | 59 | 20–70 |
| Complement C3c fraction (mg/dL) | 169 | 90–180 |
| Complement C4 fraction | 32 | 12–36 |
| Antinuclear antibodies (IFI) | Negative | <1:160 |
| Anti-neutrophil cytoplasmic antibodies | Negative | <1:20 |
| Anti-glomerular basement membrane antibodies (U/mL) | <0.8 | <7 (negative) |
| Anti-cyclic citrullinated peptide (Anti-CCP) (U/mL) | 1.1 | <7 (negative) |
| Rheumatoid factor (IU/mL) | <10.0 | <14 |
| Anti-myeloperoxidase antibodies (Anti-MPO) (U/mL) | <0.2 | <3.5 (negative) |
| Anti-proteinase 3 antibodies (Anti-PR3) (U/mL) | <0.2 | <2 (negative) |
| Extractable nuclear antigen (ENA) panel | Negative | – |
| Anti-TSH receptor antibodies (U/L) | 1.2 | 0.0–1.8 |
| Anti-thyroglobulin antibodies (IU/mL) | <12 | <40 (negative) |
| Anti-thyroid peroxidase antibodies (IU/mL) | 4.0 | <25 (negative) |
| Venereal Disease Research Laboratory (VDRL) test | Negative | – |
| Total anti-HBc antibodies | Non-reactive | – |
| HBs antibodies | Non-reactive | – |

| | | |
|---|---|---|
| Anti-HBs antibodies | Reactive | – |
| HCV antibodies | Non-reactive | – |
| HAV antibodies | IgM non-reactive / IgG reactive | – |
| HIV 1 and 2 antibodies | Non-reactive | – |
| CMV antibodies | IgM non-reactive / IgG reactive | – |
| EBV antibodies | IgM non-reactive / IgG reactive | – |
| Herpes simplex virus 1 and 2 antibodies | IgM non-reactive / IgG reactive | – |
| Rose Bengal test | Negative | – |
| Brucella abortus antibodies | IgM and IgG non-reactive | – |
| Zoonosis panel (Anaplasma phagocytophilum, Ehrlichia chaffeensis, Borrelia burgdorferi, Coxiella burnetii, Babesia microti, Rickettsia, encephalitis virus) | Negative | – |

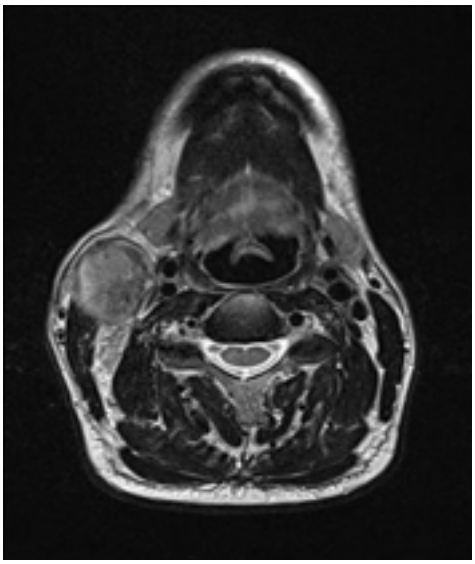
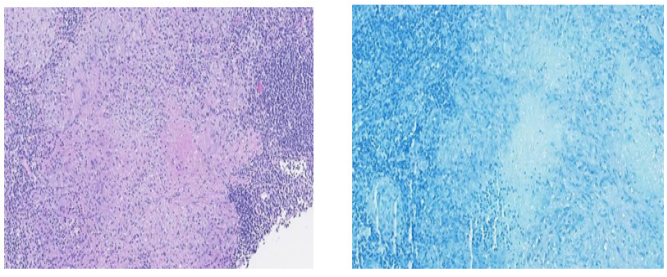


**Figure 4:** Cervical magnetic resonance imaging (MRI).

Following these findings, an interferon-gamma release assay (IGRA) and lymph node biopsy were performed. The IGRA result was positive. Histopathological examination revealed macroscopically filiform fragments and microscopically lymph node tissue involved by chronic necrotizing granulomatous inflammatory processes (Figures 5 and 6). Ziehl-Neelsen staining for acid-fast bacilli was negative; however, mycobacterial culture was positive for Mycobacterium tuberculosis. The patient was diagnosed with cervical tuberculous lymphadenitis (scrofula) and referred to the Pulmonology Diagnostic Center for antituberculous treatment.



(A) (B)

**Figure 5:** (A) Lymph node tissue demonstrating chronic necrotizing granulomatous inflammatory process
(B) Ziehl–Neelsen staining of lymph node tissue negative for acid-fast bacilli

## Discussion

Peripheral lymph nodes, located deep within the subcutaneous tissue, are a very common but also nonspecific finding on physical examination. Generally, a normal lymph node measures less than one centimeter in diameter. The cervical lymph node chain is more frequently affected than other regions. There are numerous causes of lymphadenopathy, including benign local or systemic self-limited infectious disease, solid neoplasms, lymphoproliferative disorders, granulomatous diseases, among others. Obtaining a detailed clinical history is essential, as it may guide the investigation toward the most likely underlying cause. Etiology is strongly influenced by sociodemographic factors; for example, in the African continent, where tuberculosis is endemic, it is a common cause of cervical lymphadenopathy. However, benign etiologies with nonspecific reactive changes remain the most common. When an obvious etiology such as infection is identified, additional tests are usually unnecessary. In other cases, laboratory tests, imaging studies and tissue biopsy are recommended. Imaging modalities, including ultrasound, CT and MRI, can identify the size and distribution of lymph nodes more accurately than physical examination, as well as the involvement of adjacent structures. Despite increasingly precise imaging techniques, fine-needle aspiration biopsy or excisional biopsy remains the gold standard[4,6,7].

Tuberculosis is a worldwide disease and a major global health threat. It is estimated that approximately one quarter of the world's population has been infected with Mycobacterium tuberculosis. Many infected individuals remain asymptomatic and are not contagious; however, approximately 5-10% of infected individuals will develop symptomatic disease. Globally, TB remains the leading cause of death from a single infectious agent and is among the top ten causes of death overall. A total of 1.23 million people died from tuberculosis in 2024 (including 150,000 people living with HIV). TB is preventable and curable and global public health efforts against TB have saved an estimated 83 million lives since the year 2000[1].

Cervical lymph nodes are considered the most common site of tuberculous lymphadenopathy, accounting for 60% to 90% of cases. Classical symptoms of tuberculosis include night sweats, fever, diaphoresis and weight loss[2,3].

Some patients, however, may not present systemic symptoms, as illustrated in this clinical case. The diagnosis of tuberculosis combines clinical assessment with specific diagnostic tests. Immunological tests such as the tuberculin skin test or interferon-gamma release assay (IGRA) are initially used to identify exposure to Mycobacterium tuberculosis, indicating latent or active infection. Sputum tests, including rapid molecular tests and culture, allow direct detection of the bacterium and

confirmation of the diagnosis, with mycobacterial culture still considered the gold standard despite the several weeks required to obtain results. In cases of extrapulmonary disease or difficulty obtaining sputum samples, additional laboratory tests and tissue specimens may be necessary to confirm tuberculosis[8-10].

These tests also allow assessment of antimycobacterial drug susceptibility and resistance. In Portugal, outpatient treatment is generally defined by the Pulmonology Diagnostic Center (CDP). Treatment duration may vary from 3 to 24 months and considers the individual characteristics of the patient as well as antimicrobial susceptibility testing[11]. In the present case, the patient's epidemiological context was highly relevant, together with the prolonged symptomatology and indolent progression of the lymphadenopathy. Although tuberculosis was suspected due to the absence of an obvious etiology, a thorough diagnostic workup was required, culminating in a definitive diagnosis established only through lymph node biopsy[5,12].

## Conclusion

Cervical tuberculous lymphadenitis or scrofula, remains a clinically relevant entity, even in immunocompetent patients and in non-endemic settings and may present insidiously without typical systemic symptoms. This case highlights the importance of considering tuberculosis in the differential diagnosis of persistent cervical lymphadenopathy, particularly when associated with chronic evolution and absence of an evident etiology.

The fundamental role of a systematic diagnostic approach is emphasized, including imaging studies and, above all, lymph node biopsy, which remains the gold standard for diagnostic confirmation. The positive IGRA result and the isolation of Mycobacterium tuberculosis in culture were decisive for the definitive diagnosis, despite the initial negative Ziehl-Neelsen staining. This case further reinforces the importance of correlating clinical, epidemiological and laboratory data, as well as maintaining a high index of suspicion for extrapulmonary forms of tuberculosis. Early diagnosis allows prompt initiation of appropriate therapy, with significant impact on prognosis and disease control.

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