Cervical Tuberculosis Lymphadenitis (Scrofula) in Wisconsin: Case Report, Pitfalls and Challenges

Carlos E. Figueroa Castro, MD, MS; April A. Shera, MD

ABSTRACT

Introduction: This case report presents a case of cervical tuberculous lymphadenitis (scrofula) in Wisconsin, illustrating the diagnostic challenges in a low-prevalence setting. It emphasizes the importance of including tuberculosis (TB) in the differential diagnosis of persistent cervical lymphadenopathy, particularly in patients with a history of latent TB infection.

Case Presentation: A 37-year-old woman presented with a persistent, painless left-sided neck mass without local warmth or erythema, characteristic of a cold abscess. Initial imaging demonstrated lymph node abnormalities, while multiple diagnostic tests were inconclusive. After misdiagnosis and unsuccessful treatments, she was eventually diagnosed with TB lymphadenitis. She completed a prolonged course of antituberculous therapy, followed by surgical intervention, with complete resolution of symptoms.

Discussion: This case underscores the need for a high index of suspicion for tuberculosis in patients with chronic cervical lymphadenopathy, even in regions with low TB prevalence. It also highlights the importance of thorough clinical and exposure history and the potential for diagnostic delay in atypical presentations, particularly when medical records are fragmented across health care systems.

INTRODUCTION

In the United States, a recent report by the Centers for Disease Control and Prevention revealed an increase in the incidence of tuberculosis (TB), with 9615 cases (2.9 per 100 000 persons) reported in 2023. This represents a 16% increase compared with 2022, reversing a 27-year decline following the COVID-19 pandemic.[1] Most cases (76%) occurred in people born outside the United States, including 34% among individuals of Asian descent. Multiple factors have contributed to this postpandemic increase, including diversion of staff and resources away from TB control programs. Extrapulmonary TB accounts for 30% of cases, most commonly affecting the lymph nodes.[2] Its proportion has increased over recent decades, from 15.7% in 1993 to 22.4% in 2019.[3] TB lymphadenitis, also known as scrofula, represents the most frequent form of extrapulmonary TB in the United States, accounting for approximately 25% of cases.[2] In areas with low incidence of TB including Wisconsin—where case rates have remained consistently below 1 per 100 000 population (Table)[4]—diagnosis of tuberculous lymphadenitis presents unique challenges. Nonspecific presenting symptoms, combined with the relative rarity of the condition, often lead to delayed diagnosis and inappropriate initial treatment.

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Author affiliations: Department of Medicine, Division of Infectious Diseases, Medical College of Wisconsin, Milwaukee Wisconsin (Figueroa Castro); Department of Otolaryngology and Communication Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin (Shera).

Corresponding author: Carlos E. Figueroa Castro, MD, MS, FACP, Department of Medicine, Division of Infectious Diseases, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226; email cfiguero@mcw.edu; ORCID ID 0000-0002-0789-9261

CASE PRESENTATION

A 37-year-old female of Southeast Asian ethnicity, born in the Philippines and who immigrated to the United States 11 years earlier, sought medical evaluation for a left-sided neck mass. The lump had gradually enlarged over 6 weeks, was approximately grape-sized, persistent, firm to touch, and mildly tender. The node was characteristically cold, without local warmth, erythema, pustule formation, or fever, consistent with a cold abscess. She denied cough, sputum production, emesis, nausea, diarrhea, hematuria, or lymphadenopathy at other sites. Her medical history included asthma, gestational diabetes, hypothyroidism treated with levothyroxine, and polycystic ovarian syndrome.

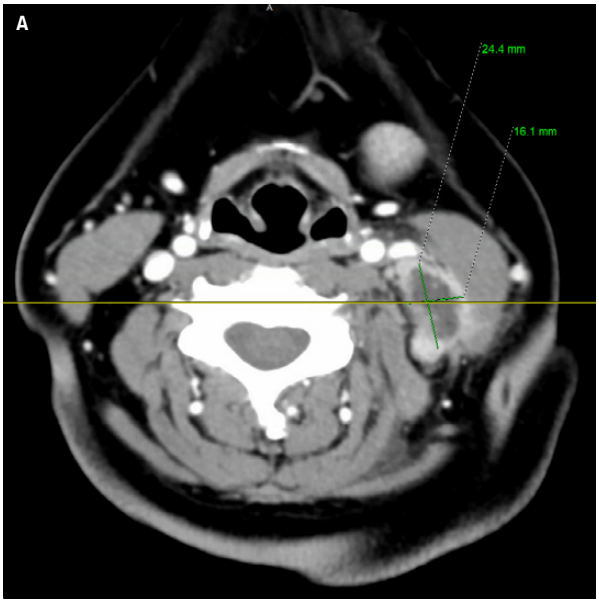
Table. Highest Incidence Rates of Tuberculosis in Wisconsin Counties in 2022[4]

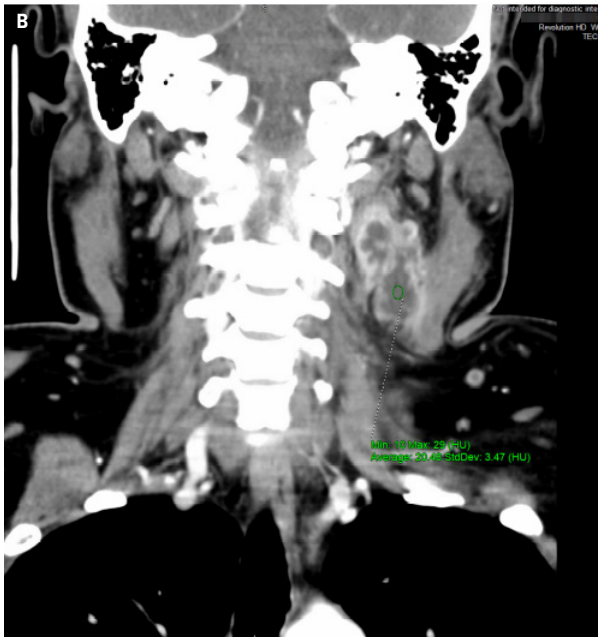
County	Region	2022 Population by Region	Incidence per 100 000
Milwaukee	Southeastern	2 055 647	0.63
Dane	Southern	1 288 908	0.62
Marathon	Northern	497 642	0.60
Kenosha	Southeastern	2 055 647	0.19
Brown	Northeastern	1 287 166	0.15
Winnebago	Northeastern	1 287 166	0.15
Appleton	Northeastern	1 287 166	0.15
Greenfield	Southeastern	2 055 647	0.14
South Milwaukee	Southeastern	2 055 647	0.14
Monroe	Western	819 792	0.12

Physical examination revealed normal vital signs and firm, nonwarm enlarged lymph node (2 cm diameter) in the left anterolateral cervical region without local erythema. Chest examination was unremarkable, and no splenomegaly was noted. Laboratory testing revealed mild leukocytosis with neutrophil predominance (14 200 cells/µL; neutrophils, 93.7%), elevated erythrocyte sedimentation rate (41 mm/h), and C-reactive protein level of 1.66 mg/dL. HIV screening was negative. Neck ultrasound demonstrated hypoechoic, enlarged left-sided lymph nodes at level III (middle internal jugular, 1.1 cm), level IV (lower internal jugular, 0.9 cm), and level V (posterior triangle, 0.7 cm). Additional workup included negative Lyme serology, Epstein-Barr virus serology consistent with prior exposure, negative testing for acute cytomegalovirus infection, and a negative antistreptolysin O titer. Was treated with amoxicillin-clavulanic acid for 10 days but noted increased swelling and development of low-grade fever. Oral prednisone resulted in temporary clinical improvement, but symptoms returned after steroid completion.

Six weeks after initial presentation, the patient was admitted after CT imaging showed a lobulated, peripherally enhancing left level II (upper internal jugular) and level III lesion deep to the sternocleidomastoid muscle, concerning for suppurative adenitis, with prominent left cervical lymph nodes, some demonstrating central cystic change and necrosis (Figure 1A and 1B). No suspicious masses were identified in the nasopharyngeal soft tissues or thyroid. A right apical calcified granuloma was incidentally noted on the same CT scan, which included upper chest structures. She received vancomycin and piperacillin-tazobactam, followed by de-escalation to ampicillin-sulbactam. Percutaneous needle drainage by interventional radiology yielded thick purulent material. Standard bacterial cultures were negative; 16S ribosomal RNA testing was not performed. Fungal cultures were negative. Pathology evaluation revealed granulomatous inflammation with necrosis, without malignancy, and negative stains for acid-fast bacilli (AFB) and fungi. A mycobacterial culture was sent, but results were pending at discharge. She was discharged on clindamycin for 7 days but returned to the hospital with persistent symptoms despite antibiotic therapy.

Figure. Axial (A) and Coronal (B) Computed Tomography Scan of Neck With Intravenous Contrast With Lobulated Peripherally Enhancing Lesion Deep to the Sternocleidomastoid Muscle, and Left Cervical Lymph Nodes With Central Cystic Change and Necrosis





Further history revealed TB screening with a protein purified derivative (PPD) skin test during a job application 7 years before symptom onset. She described a large, tender, and red reaction, though documentation of induration and size was unavailable. A chest x-ray obtained at that time was normal. She was diagnosed with latent TB infection (LTBI), but treatment was not offered

after the reaction was attributed to prior bacille Calmette-Guérin (BCG) vaccination. She denied known contact with individuals with active tuberculosis.

Additional evaluation revealed negative *Bartonella* titers and normal chest x-ray. QuantiFERON TB testing was positive. Given concern for scrofula, a planned incisional biopsy was replaced with a repeat fine-needle aspiration performed 6 days after the initial procedure, again yielding purulent material. Pathologic evaluation showed acute inflammation and necrosis without malignancy. AFB stain was positive (3+). Cultures for common bacteria and fungi remained negative. Testing at the Wisconsin State Laboratory of Hygiene detected *Mycobacterium tuberculosis* complex DNA, with no evidence of *Mycobacterium avium-intracellulare* complex. Three sputum samples were negative for AFB and negative by nucleic acid amplification testing (Cepheid Xpert MTB/RIF assay). The aspirate culture eventually grew *M tuberculosis* after 6 weeks of incubation, but susceptibility results were available because of poor growth.

After diagnosis of cervical tuberculous lymphadenitis (scrofula), the patient began TB therapy in coordination with the local health department. The initial regimen included daily isoniazid, rifampin, ethambutol, and pyrazinamide for 8 weeks, followed by isoniazid and rifampin for 18 weeks, with vitamin B6 supplementation. Complications included pyrazinamide-associated hyperuricemia, managed with allopurinol and discontinuation of pyrazinamide after 6 weeks. Around this time, she developed purulent drainage, with cultures growing *Staphylococcus capitis,* initially treated with doxycycline and later switched to cephalexin because of diarrhea. Repeat imaging revealed enlargement of peripherally enhancing lesions, increased adjacent tracts, and similar enlargement of adjacent lymph nodes. A third ultrasound-guided aspiration was negative for bacteria, fungi, and AFB; mycobacterial cultures remained negative after 8 weeks. The initial phase of therapy with isoniazid, rifampin, and ethambutol was extended for 6 additional weeks after pyrazinamide discontinuation (total, 12 weeks), resulting in resolution of swelling and drainage. She completed a 6-month total course of isoniazid and rifampin.

Mild transaminitis was observed (maximum ALT, 46 U/L; AST, 59 U/L; references ranges ALT, 6-37 U/L; AST 111–33 U/L) and was monitored without therapy modification. Liver ultrasound demonstrated hepatic steatosis. Transaminitis resolved after completion of therapy.

Three weeks after treatment completion, the patient reported recurrent swelling. CT imaging showed a slight decrease in treated adenopathy in the left neck and reduced anteroposterior dimension of the low-attenuation collection medial to the left sternocleidomastoid muscle. Because of progressive swelling, she underwent excision of the left deep cervical lymph node and skin. Local culture grew methicillin-susceptible *Staphylococcus aureus* (MSSA) treated with trimethoprim-sulfamethoxazole for 10 days. Pathology showed granulomatous dermatitis with necrosis; AFB and fungal stains were negative, and AFB cultures remained negative after 8 weeks of incubation. At 12-month follow-up, the patient had complete healing of the surgical site with no swelling, tenderness, erythema, or drainage.

DISCUSSION

This case highlights several important aspects of the current understanding and management of TB lymphadenitis. Although scrofula remains one of the most common forms of extrapulmonary TB, its diagnosis and management continue to present challenges in both endemic and nonendemic settings. Diagnosis requires a high index of suspicion, as several infectious and noninfectious conditions may present similarly.[5] The patient's demographic and clinical features in our case align with current epidemiologic trends. A meta-analysis of head and neck TB (57 studies; 6950 cases) reported a predominance of cervical lymph node involvement (87.9%), followed by laryngeal (8.7%) and other sites (3.4%). Risk factors included age <40 years (83%), female sex (53.8%), HIV infection (31.3%), and foreign-born status (44.2%).[6] A retrospective study from Texas reported cervical lymph node involvement in 96.9% of cases; 52.7% were female, and 26.5% had both extrapulmonary and pulmonary TB (26.5%). Identified risk factors included positive HIV status, homelessness, excessive alcohol use, and drug use.[7]

Whether extrapulmonary TB is increasing overall remains unclear; however, older adults with weakened immune systems represent another important at-risk population, even when cancer initially seems more likely.[8] Our patient exemplified several recognized risk factors, including female sex, age younger than 40 years, and birth in a TB-endemic region. Her presentation as a classic cold abscess – firm, nontender swelling without warmth or erythema – is characteristic of TB lymphadenitis and should prompt suspicion for TB, particularly when appropriate risk factors are present.

This case also illustrates both the utility and limitations of current testing methods. While imaging studies helped delineate the extent of disease, definitive diagnosis required histopathological confirmation. Fine-needle aspiration cytology is a valuable first-line diagnostic tool, whereas excisional biopsy remains the gold standard, particularly when diagnosis is uncertain, alternative diagnosis such as neoplasm is suspected, or response to therapy is poor.[5] Despite the presence of granulomatous inflammation, negative AFB staining does not rule out TB. This may be explained by several factors, including the paucibacillary nature of some tuberculous lesions, sampling error, or prior broad-spectrum antibiotic exposure with partial activity against *Mycobacterium*. The sensitivity of AFB smear in extrapulmonary TB ranges from 0% to 40%, contributing to diagnostic delay. With respect to our patient's positive PPD history, current guidelines do not recommend discounting positive tuberculin skin

tests because of prior BCG vaccination, especially with reactions >15 mm. In such cases, interferon-gamma release assays are preferred because of higher specificity.[9] This represented a missed opportunity for LTBI treatment that might have prevented progression to active disease.

Treatment with standard 4-drug therapy under in coordination with the local health department reflects current TB treatment guidelines. Posttreatment recurrence of symptoms in this case could be related to a paradoxical reaction or postoperative complication, rather than treatment failure. Paradoxical reactions (transient worsening or appearance of new lesions despite appropriate therapy) can occur in 20% to 30% of cases and should not be misinterpreted as treatment failure.[5] Supporting factors include recurrence after therapy completion, granulomatous inflammation with persistently negative AFB stain and cultures for *Mycobacterium*, and lack of further recurrences while off anti-TB therapy. Isolation of MSSA may be related to inadequate initial source control or superimposed infection of the surgical site, may be influenced by the extensive nature of the disease and possibly worsened by the immunomodulatory effects early corticosteroid exposure. Extended therapy (9 months) is considered for extensive or complicated cases, although outcomes are generally favorable.[5] This case underscores the importance of screening for HIV, evaluating pulmonary involvement, reviewing TB history, and ensuring long-term follow-up.[10-12]

From a public health perspective, this case highlights challenges posed by fragmented medical records across different health care systems. Prior TB screening and occupational health records were unavailable to treating clinicians, potentially contributing to diagnostic delays. Improved cross-system health information exchange could facilitate earlier detection and appropriate management.

CONCLUSIONS

This case report emphasizes the need for a high index of suspicion for TB in patients with chronic cervical lymphadenopathy and "cold abscess" features, even in low-prevalence areas such as Wisconsin. It underscores the risk of diagnostic delay, the importance of comprehensive history-taking – including immigration and occupational screening – and the need for close monitoring during and after treatment. Clinicians should recognize the possibility of paradoxical reactions and the potential need for surgical intervention. Accurate interpretation of TB screening tests and appropriate follow-up of positive results remain essential in preventing progression from latent to active TB disease.

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