

When Tuberculosis Hides in Plain Sight: Diagnosing Rare Extra-Pulmonary Lesions Through Histopathology Case Series

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Abstract

Background: Extrapulmonary tuberculosis (EPTB) constitutes 10–20% of TB cases and may involve unusual sites with nonspecific clinical features, often mimicking neoplastic or chronic inflammatory lesions and leading to diagnostic delay. Recognizing these rare manifestations is crucial in high-burden settings to prevent morbidity and functional loss. We report three cases of EPTB at rare anatomical sites: tongue, middle ear with cholesteatoma, and tarsal bones. These cases underscore that TB should remain an important differential diagnosis in chronic, non-healing lesions of the oral cavity, temporal bone, and small bones of the foot, especially in endemic regions and when routine therapies fail. Early biopsy with careful histopathological evaluation, supplemented by molecular tests where available, is essential for prompt diagnosis and initiation of therapy, reaffirming the central role of tissue diagnosis in atypical EPTB.

Keywords: Extra-pulmonary tuberculosis; lingual tuberculosis; tuberculous otitis media; cholesteatoma; tarsal osteomyelitis; granulomatous inflammation.

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INTRODUCTION

Mycobacterium tuberculosis is the infectious agent that causes tuberculosis (TB). With an estimated 10 million new cases each year, it remains a major worldwide health burden.^[1] While pulmonary involvement is most common, tuberculosis can affect virtually any organ system, with extra-pulmonary manifestations accounting for 10–20% of all TB cases.^[2,3] Since extra-pulmonary tuberculosis often presents with nonspecific symptoms and can affect unusual locations, clinicians and pathologists must remain vigilant for these rare manifestations in chronic, non-resolving lesions.

This study presents a case series of 3 patients with EPTB at rare sites, including the tarsal bone, tongue, and middle ear, who presented with diagnostic and management challenges. Oral manifestations of TB are rare, with an incidence of around <1% of TB cases and often present as non-healing ulcers or mass like lesions that may clinically mimic squamous cell carcinoma, contributing to misdiagnosis.^[4] Tuberculous otitis media with or without cholesteatoma is uncommon but can cause significant bone destruction and hearing loss if unrecognized. Similarly, foot tuberculosis is encountered in only 5–10% of osteoarticular tuberculosis cases, constituting a rare clinical entity.^[5] In all these sites, histopathology showing granulomatous inflammation with or without caseation and demonstrable AFB is critical for diagnosis, especially when microbiological tests are negative or unavailable.

Case 1: Tuberculosis of the tongue

Clinical details

A 45-year-old female presented with a painful non healing

ulcer over the lateral border of the tongue for 2 years, associated with burning sensation and dysphagia, but no significant weight loss or fever. Examination showed a single ulceroproliferative lesion with indurated margins and a granular base, clinically suspected as a malignancy or a chronic traumatic ulcer. There was no cervical lymphadenopathy, and systemic examination was unremarkable.

Routine blood tests and chest radiography were within normal limits. Incisional biopsy from the edge of the lesion showed stratified squamous epithelium with ulceration and underlying granulomatous inflammation composed of epithelioid cell granulomas, central caseous necrosis, Langhans type multinucleated giant cells, and a peripheral rim of lymphocytes and fibrosis [Figure 1]. Ziehl–Neelsen staining demonstrated no AFB. However, a biopsy sample was sent in normal saline for CB NAAT testing, which was positive for the presence of tuberculosis, supporting a diagnosis of tuberculous glossitis. In a similar case report, diagnosis was also supported by a positive tuberculin test and, when available, mycobacterial culture.^[6,7]

Case 2: Tuberculous otitis media with cholesteatoma

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Clinical details

An 8-year-old child presented with chronic ear discharge and progressive hearing loss in the right ear for several months, with intermittent otalgia and occasional low grade fever. Ooscopic examination revealed perforation of the tympanic membrane with granulation tissue and keratin debris suggestive of chronic suppurative otitis media with cholesteatoma.

The patient underwent a modified radical mastoidectomy for presumed cholesteatoma; intraoperatively, extensive granulation tissue and bone destruction were noted. Histopathological examination of the middle ear/mastoid tissue showed keratinizing squamous epithelium consistent with cholesteatoma, along with florid granulomatous inflammation characterised by caseating epithelioid cell granulomas and Langhans giant cells. [Figure 2] Necrotizing granulomas raised suspicion of TB, and AFB staining and culture were advised. AFB may be negative in tissue sections due to the paucibacillary nature. Still, the combination of granulomas, caseation, and clinical response to ATT supports a diagnosis of tuberculous otitis media associated with cholesteatoma as reported in similar cases.^[8,9]

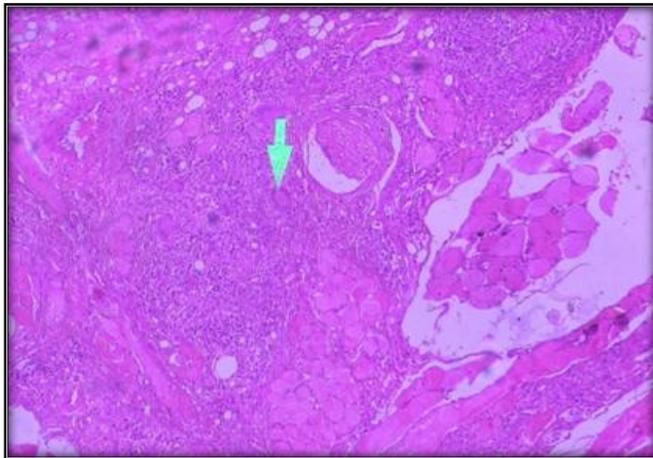


Figure 1: Section from tongue biopsy shows epithelioid cell granuloma with Langhans Giant cell (green arrow) infiltrating the muscle. (H& E 100X)

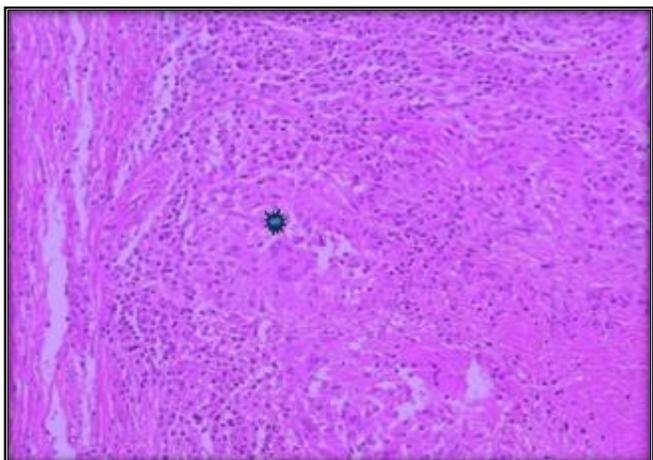


Figure 2: Section shows multiple epithelioid cell granulomas. (H& E 200X)

Case 3: Tubercular osteomyelitis of tarsal bone

Clinical details

A 25-year-old female presented with an insidious onset of pain and swelling over the lateral aspect of the left foot for 9 months, aggravated by weight bearing and walking, with no history of trauma. Examination revealed localised swelling, tenderness over the tarsal region, and restriction of mid foot movements, but no draining sinuses.

Plain radiographs and MRI showed multifocal areas of lytic change with surrounding bone sclerosis and reduced bone mass in cuboid, navicular, all cuneiforms (most prominent in lateral), and in bases of 2nd and 3rd metatarsals, suggestive of mid-foot chronic osteomyelitis with associated collections [Figure 3]

Under regional anaesthesia, a biopsy of the involved tarsal bone was performed. Histopathological examination showed caseating granulomatous osteomyelitis with necrotic bone trabeculae, typical of tubercular osteomyelitis. [Figure 4] Although AFB staining was negative, histology was sufficient to initiate ATT in endemic settings, as reported in other similar studies.^[10,11]

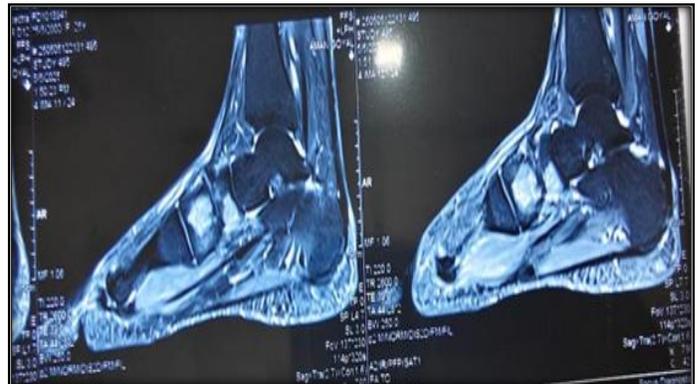


Figure 3: MRI shows multifocal areas of lytic change with surrounding bone sclerosis in cuboid, navicular, all cuneiforms (most prominent in lateral) and in bases of 2nd and 3rd metatarsals.

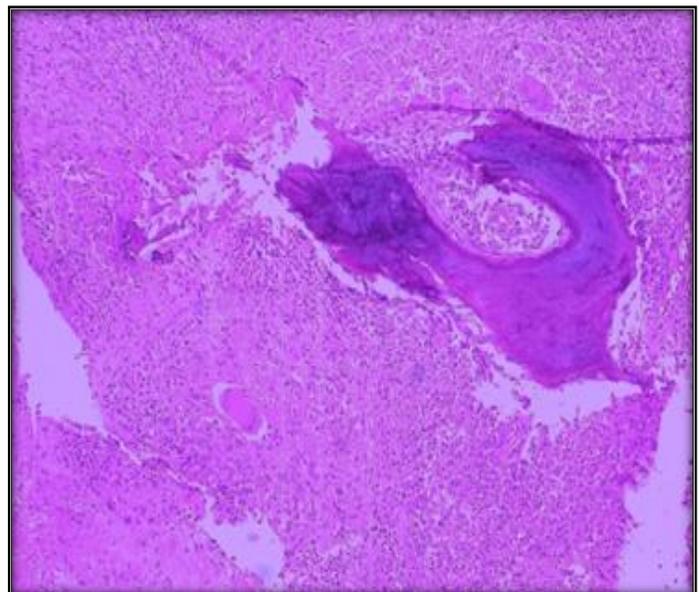


Figure 4: Section examined showed caseating granulomatous osteomyelitis with necrotic bone trabeculae. (H& E 200X)

DISCUSSION

16% of the 7.5 million incident cases reported globally in 2019 were EPTB cases.^[12] Among EPTB, in endemic nations like India, it is usual to come with TB lymphadenopathy, Abdominal Koch's, and osteoarticular TB. Due to their uncommon appearance, absence of particular clinical characteristics, or lack of established diagnostic criteria, TB in sites such as the ENT, bones, oral cavity, and other uncommon locations may go unnoticed.^[13]

Lingual tuberculosis, for instance, is exceedingly uncommon due to the salivary cleaning, continuous movement, and the inherent resistance provided by the tongue's stratified squamous epithelium.^[14] It typically presents as a chronic ulcer or nodular lesion resistant to conventional therapy, often prompting suspicion of malignancy.^[15] Similarly, skeletal TB involving the tarsal bone is rare even among osteoarticular forms, which are more commonly seen in the spine, hip, or knee. When the tarsal bones are affected, symptoms such as localised pain, swelling, and limited mobility are frequently nonspecific and may be mistaken for pyogenic osteomyelitis or neoplastic processes.^[16] Middle ear involvement manifesting as tuberculous cholesteatoma represents another diagnostic dilemma; it may clinically resemble chronic suppurative otitis media or cholesteatoma of other aetiologies, and the diagnosis is often established only after histopathological examination.^[17]

Histopathology, along with ancillary tests, remains the cornerstone for confirming TB at these unusual sites. The presence of caseating granulomas composed of epithelioid histiocytes, Langhans giant cells, and lymphocytic infiltration is highly suggestive of tuberculous aetiology, especially when microbiological results are inconclusive or negative. In many extra-pulmonary lesions, the bacillary load is low, rendering Ziehl–Neelsen staining and culture less sensitive. Therefore, histopathological evaluation not only assists in differentiating TB from other granulomatous or neoplastic conditions but also strengthens the clinical suspicion needed to initiate timely anti-tubercular therapy. Our case series underscores the indispensable role of tissue diagnosis in confirming TB at rare anatomical sites. Clinicians should maintain a high index of suspicion when encountering chronic, non-healing lesions that are unresponsive to standard antimicrobial or anti-inflammatory therapies. Early biopsy and histopathological assessment can prevent disease progression, minimise morbidity, and ensure prompt institution of appropriate therapy. These findings reaffirm that, even in the era of advanced molecular testing, histopathology remains pivotal for accurate diagnosis of extra-pulmonary tuberculosis.^[6,8,10]

CONCLUSION

In endemic areas, tuberculosis should be considered when evaluating potential diagnoses for unexplained lesions. Early biopsy and histopathological examination with appropriate special stains are crucial to establishing a diagnosis and initiating timely ATT, thereby preventing morbidity and functional loss.^[10,18]

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Conflicts of interest

There are no conflicts of interest.

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