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Extrapulmonary Tuberculosis: A Case Series of Diagnostic Challenges and Unusual Presentations from a Tertiary Care Hospital in Pune

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ABSTRACT

Background: Extrapulmonary tuberculosis (EPTB) poses significant diagnostic challenges due to its diverse and often atypical clinical presentations. **Case details**: This case series from a tertiary care hospital in Pune, India, highlights five distinct EPTB presentations diagnosed between December 2022 and May 2024. The cases include recurrent suprasternal abscess with subsequent cervical lymphadenitis, pulmonary TB extending to cervical lymph nodes, subcutaneous thigh TB, pediatric tibial osteomyelitis, and disseminated mediastinal and cervical lymphadenitis. Diagnostic confirmation relied on ultrasonography, computed tomography (CT), histopathology, Ziehl-Neelsen staining, and cartridge-based nucleic acid amplification testing (CBNAAT), often detecting *Mycobacterium tuberculosis* (MTB) despite low bacterial loads. All cases received standard drug-sensitive TB (DS-TB) treatment, yielding varied outcomes, ranging from full recovery to recurrence in one instance. **Conclusion:** These cases underscore the need for heightened clinical suspicion in TB-endemic regions and emphasize the pivotal role of molecular diagnostics in recognizing atypical EPTB presentations. Early diagnosis and comprehensive follow-up are essential for optimizing patient outcomes.

KEYWORDS: CBNAAT, Extra-pulmonary tuberculosis, *Mycobacterium tuberculosis*

INTRODUCTION

India has the highest tuberculosis infection burden globally, leading to high mortality and morbidity.[1] Caused by bacillus *Mycobacterium tuberculosis*, it most commonly affects lungs (pulmonary tuberculosis) followed-by other organs such as lymph nodes (LN), bones, intestines, etc. (extra-pulmonary tuberculosis EPTB). Most common organ affected in EPTB is LN.[2, 3] EPTB can present with a wide range of clinical manifestations.[4, 5]

As EPTB shows variable manifestations, diagnosis can be challenging, due to the wide range of infective, neoplastic and systemic differential diagnoses, and to rule out those patients are often referred to different specialities like medicine, radiology etc.[6] For instance, the clinical features of tuberculous lymphadenitis overlap with those of lymphoma: some patients are asymptomatic apart from painless swelling, whereas others are unwell and have systemic symptoms such as fevers, weight loss, or night sweats.[7] However, patients can be diagnosed based on clinical suspicion,radiological, pathological, and microbiological investigation, leading to prompt control of the infection. For TB at any site, a 6-9 month course of treatment regimen that includes INH and RIF is recommended.[8]

Each of the five cases in this case series highlights a different challenge in diagnosis and management of EPTB. Thus, the importance of a thorough diagnostic approach is highlighted.

CASE 1: RECURRENT TUBERCULOSIS

A 24-year-old female presented in December 2022 with a painless suprasternal swelling, without fever, weight loss, or obstructive symptoms. Ultrasonography revealed a 22×10×14mm abscess in the suprasternal notch and right paratracheal lymphadenopathy. Pus aspirated from the abscess showed no bacterial growth or acid-fast bacilli in Ziehl-Neelsen staining, but CBNAAT detected rifampicin-sensitive *Mycobacterium tuberculosis* with a low bacterial load. A line probe assay was negative. Diagnosed with drug-sensitive TB, she completed a 6-month DS-TB regimen, and the abscess resolved. However, within a month, she developed cervical lymphadenitis, confirmed by CBNAAT. She restarted DS-TB, but six months later, she experienced another recurrence with swelling and ulcer formation, raising concerns about undetected resistance to first-line drugs other than rifampicin.

CASE 2: EXTENDED TUBERCULOSIS

A 16-year-old male presented in January 2024 with fever, cough, chills, body aches, and weakness. Initially treated with antibiotics and multivitamins at a private hospital, he was referred for TB evaluation but did not follow up. He returned in May 2024 with cervical swelling. Ultrasonography showed a hypoechoic lesion with internal echoes and minimal vascularity in the right clavicular region. Pus aspirated was CBNAAT-positive for *Mycobacterium tuberculosis* with a low load, and Ziehl-Neelsen staining revealed acid-fast bacilli, indicating extension from pulmonary TB. He started a DS-TB regimen and is showing improvement. For prolonged symptoms all the possibilities should be taken into consideration and thorough investigation should be done, rather than relying on mere suspicion and giving empirical treatment.

CASE 3: SUBCUTANEOUS TUBERCULOSIS

A 16-year-old male presented with a right thigh swelling, unaccompanied by trauma, fever, or systemic symptoms. Incision and drainage of the abscess produced pus that tested positive for *Mycobacterium tuberculosis* on CBNAAT with a low bacterial load; no bacterial growth was observed. He began a DS-TB regimen, and the wound is healing with regular dressing.

CASE 4: TUBERCULAR ARTHRITIS

A 1-year-old female presented with left leg pain one month after a fall, without pulmonary symptoms. Radiology revealed left proximal tibial osteomyelitis involving the epiphysis, growth plate, and metaphysis, with an abscess. Histopathology of the drained pus showed granulation tissue, and CBNAAT confirmed rifampicin-sensitive *Mycobacterium tuberculosis* with a low load, despite negative Ziehl-Neelsen staining. She started a DS-TB regimen (adjusted for her 8-11 kg weight band) and is improving.

CASE 5: TUBERCULAR LYMPHADENITIS

A 38-year-old female presented with neck swelling, low-grade fever, and cough. Initially misdiagnosed as a viral infection, her condition prompted further investigation. Ultrasonography revealed a 3.3×1.9 cm necrotic lesion in the left neck and multiple enlarged lymph nodes, while CT thorax showed fibrosis, bronchiectasis, and enhancing collections. Histopathology confirmed caseating tuberculous lymphadenitis, and CBNAAT detected rifampicin-sensitive *Mycobacterium tuberculosis* with a low load. She completed a DS-TB regimen and achieved full recovery.

DISCUSSION

Extrapulmonary tuberculosis (EPTB) accounts for approximately 15-20% of all TB cases globally, with higher proportions in endemic regions like India due to factors such as high TB burden and delayed diagnosis. [1] The cases presented in this series exemplify the diagnostic complexity of EPTB, characterized by atypical sites (e.g., subcutaneous tissue, suprasternal notch) and non-specific symptoms that mimic other conditions, such as trauma or viral infections. These challenges align with findings from a 2021 study by Gopalaswamy et al., which reported that EPTB often presents with subtle or absent systemic symptoms, complicating timely recognition. [2]

The reliance on molecular diagnostics, particularly CBNAAT, was critical in this series, detecting *Mycobacterium tuberculosis* despite low bacterial loads and negative Ziehl-Neelsen staining in several cases. CBNAAT's sensitivity for EPTB diagnosis has been well-documented, with a 2022 meta-analysis by Kohli et al. reporting a pooled sensitivity of 83% and specificity of 98% for lymph node TB, though performance varies by site. [3] In Case 1, recurrent lymphadenitis despite rifampicin-sensitive CBNAAT results raises concerns about undetected resistance to other first-line drugs (e.g., isoniazid), a phenomenon noted in a study by VidyaRaj et al., which found that mono-resistance to isoniazid may contribute to treatment failure in DS-TB regimens. [4] This underscores the need for expanded drug susceptibility testing beyond rifampicin in recurrent cases.

Unusual presentations, such as subcutaneous TB (Case 3) and pediatric osteomyelitis (Case 4), highlight the importance of considering TB in differential diagnoses even in the absence of pulmonary involvement. A case series by Agarwal et al. [5] described similar and other rare subcutaneous TB presentations, emphasizing the role of CBNAAT in confirming diagnosis. Pediatric EPTB, as in Case 4, remains underrecognized, also noted in case series by Rahangdale et al., noting that skeletal TB constitutes less than 1% to 3% of pediatric TB cases, often misdiagnosed as trauma-related injury. [6]

Delays in diagnosis, evident in Cases 2 and 5, reflect systemic challenges in TB-endemic settings, including patient non-compliance with referrals and initial misdiagnosis.

Case	Age/-Sex	EPTB Site	Diagnostic Tools	Rx	Outcome	Challenges
1	24/F	Suprasternal abscess, cervical lymph nodes	USG, CBNAAT, LPA	DS-TB regimen	Recurrence, restarted DS-TB	Recurrence despite treatment, possible undetected drug resistance
2	16/M	Cervical lymph nodes (from pulmonary TB)	USG, CBNAAT, ZN staining	DS-TB regimen	Improving	Delay in diagnosis due to ignored referral, leading to disease extension
3	16/M	Subcutaneous thigh	CBNAAT	DS-TB regimen	Improving	Unusual site (subcutaneous), not commonly associated with TB
4	1/F	Tibial osteomyelitis	Radiology, histopathology, CBNAAT	DS-TB regimen	Improving	Pediatric case with uncommon TB manifestation, initially misattributed to trauma
5	38/F	Mediastinal and cervical lymph nodes	USG, CT, histopathology, CBNAAT	DS-TB regimen	Recovered	Initial misdiagnosis, leading to delayed treatment and disease dissemination

Table 1: Summary of cases with challenges identified

These align with a systematic review by Sreeramareddy et al., [7] and study by Manikanta et al. [8] which identified diagnostic delays as a key contributor to disease progression in India. The successful outcome in Case 5 following comprehensive imaging and histopathology underscores the value of a multi-modal diagnostic approach, as recommended by the World Health Organization's 2021 TB guidelines. [9]

This series reinforces the necessity of heightened clinical suspicion, advanced diagnostics, and robust follow-up in managing EPTB. In TB-endemic regions like Pune, integrating molecular tools with traditional methods can bridge diagnostic gaps, while addressing recurrence requires broader resistance profiling. Future research should focus on optimizing diagnostic algorithms and treatment regimens for atypical EPTB presentations.

CONCLUSION

EPTB is a form of *Mycobacterium tuberculosis* infection with variable manifestations. It is difficult to manage as it requires different treatment modalities at a time to get cured. Accurate diagnosis is the key to cure, which can be achieved with integration of various diagnostic modalities from clinical suspicion up to the drug resistance testing in Microbiology. Use of all the resources is required for appropriate diagnosis, followed by adequate management and cure.

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