ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 09 | September - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A TALE OF FEVER – RETROPERITONEAL TUBERCULOUS LYMPHADENOPATHY MIMICKING LYMPHOPROLIFERATIVE DISORDER

General Medicine

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ABSTRACT

Pyrexia of Unknown Origin (PUO) still remains one of the diagnostic challenges, often presenting as the sole clinical clue in systemic illnesses. In tuberculosis-endemic countries like India, extrapulmonary tuberculosis (EPTB) must always be considered in PUO workups, even in immunocompetent individuals. EPTB constitutes approximately 15–20% of all TB cases and can involve virtually any organ system. Diagnosing TB especially extra pulmonary TB is often challengeing due to its complexity and atypical clinical presentation Retroperitoneal tuberculous lymphadenopathy is a rare manifestation that lacks specific symptoms and often presents with nonspecific findings, mimicking malignancy or inflammatory disorders leading to delayed diagnosis and management. We report the case of a 51-year-old immunocompetent female presenting with a 15-day history of high-grade, continuous fever with absence of localizing signs or symptoms. Initial routine investigations, including blood cultures, imaging studies, yielded inconclusive results. However, positron emission tomography (PET) of the abdomen revealed metabolically active retroperitoneal lymphadenopathy. Based on imaging features, an initial clinical suspicion of lymphoma was raised. Bone marrow biopsy was performed but returned inconclusive findings. Definitive diagnosis was established through histopathological examination of the lymph nodes, which demonstrated caseating granulomas consistent with tuberculosis, and were positive for acid-fast bacilli. This case underscores the diagnostic challenges associated with extra pulmonary tuberculosis (EPTB), particularly in the absence of definitive clinical and laboratory findings. It highlights the importance of maintaining a high index of suspicion for tuberculosis in patients presenting with prolonged unexplained fever, especially in endemic regions. In this scenario, early utilization of advanced imaging and targeted tissue sampling proved instrumental in establishing the diagnosis, thereby enabling prompt initiation of anti-tubercular therapy and contributing to a favourable clinical outcome.

KEYWORDS

Tuberculous Lymphadenopathy, Fever, Lymphoproliferative Disorder

INTRODUCTION

Tuberculosis (TB) continues to be a major public health concern globally, with India accounting for a significant burden of cases. According to the WHO Global Tuberculosis Report 2023, India contributes approximately 26% of the global TB caseload [1]. While pulmonary tuberculosis remains the most prevalent form, extra pulmonary tuberculosis (EPTB) represents 15–20% of all TB cases. EPTB may affect lymph nodes, pleura, abdomen, bones, meninges, and the genitourinary tract. The clinical manifestations of EPTB are often subtle and non-specific [2], making diagnosis particularly challenging.

Retroperitoneal lymphadenopathy as a presentation of EPTB is rare [3,4], especially in immunocompetent patients. Such presentations are often classified under fever of unknown origin (FUO)—defined as persistent fever above 38.3°C for more than three weeks, with no clear diagnosis after one week of standard evaluation. The differential diagnoses for FUO are extensive and include infections, malignancies, autoimmune conditions, and drug fevers. In TB-endemic countries like India, TB must be a prime suspect [5,6], even when initial investigations such as chest radiographs and sputum analysis are normal.

The diagnosis of EPTB is further complicated by the poor sensitivity of conventional tests like the Mantoux test and AFB staining [7], particularly in non-pulmonary samples. Imaging modalities like ultrasound or contrast-enhanced CT [8], followed by histopathological and molecular testing (e.g., CBNAAT or GeneXpert) [9], are often necessary for accurate diagnosis.

This report presents a case of a middle aged woman with prolonged high-grade fever and no evident source of infection on initial evaluation. Despite normal chest imaging and inconclusive laboratory findings, detailed imaging studies revealed retroperitoneal lymphadenopathy. Histological analysis confirmed tuberculosis, enabling prompt initiation of anti-tubercular therapy with subsequent clinical improvement.

The case underscores the importance of a methodical approach to PUO and highlights the need to consider extrapulmonary TB early in the diagnostic algorithm, especially in endemic regions. A combination of clinical vigilance, appropriate imaging, and tissue diagnosis is essential for timely treatment and prevention of complications.

Case Presentation

A 51-year-old female, a homemaker residing in a urban area in southern India, referred from a private hospital to BGS GIMS, Bangalore in July 2025 presented with complaints of high-grade, continuous fever for 15 days. The fever was associated with chills and fatigue but lacked diurnal variation or rigors. She denied cough, breathlessness, night sweats, weight loss, urinary or gastrointestinal symptoms. No recent travel, drug use, she is a known case of old pulmonary TB had completed therapy

On examination, she was febrile (39.2°C), tachycardic (106/min), normotensive, and had no lymphadenopathy or organomegaly. Systemic examination revealed basal crepitation's. Initial labs revealed hemoglobin level of 11.3mg/dl suspected normocytic normochromic anemia, elevated ESR (52 mm/hr), and CRP (96 mg/L) with a white blood cell count of 3940 cells/mm3 and a platelet count of 2,20,000cells/mm3. Liver and renal function were within normal range. Chest X-ray showed left basal consolidation. Serology for dengue, malaria, scrub typhus, leptospirosis, enteric fever, and HIV was negative.

Sputum and Broncho alveolar lavage (BAL) samples were smear and polymerase chain reaction (pcr) – negative for Mycobacterium tuberculosis. Abdominal ultrasound was inconclusive too. Contrast-enhanced CT (CECT) of the abdomen showed lymphadenopathy in the retro peritoneum and mild hepatomegaly with fatty infiltration, PET CT was done which showed Hyper metabolic retroperitoneal group of lymph nodes showing early conglomeration in the para aortocaval region partially encasing aorta and right renal hilar vessels with largest lymph node measuring 2.1x3x7.5 cm and Hyper metabolic splenomegaly which was suggestive of lymphoproliferative disorder.

A CT -guided FNAC of the lymph node revealed necrotizing

granulomatous lymphadenitis with acid fast bacilli suggestive of tuberculous lymphadenitis but AFB rapid culture of tissue specimen using automated BACTEC MGIT 960 yielded no acid fast bacilli, Modified Middle Brook 7H9 broth yielded no mycobacterium species growth on culture.

Bone marrow biopsy was done showed normocellular marrow with trilineage hemopoiesis and granulomatous inflammation, AFB staining and GeneXpert was negative. The patient was started on anti tubercular therapy. Fever resolved by day 10 of therapy. She showed clinical and radiologic improvement at follow-up.

DISCUSSION

Tuberculosis (TB) is a disease with protean clinical manifestations, and its extrapulmonary forms often mimic malignancy, autoimmune diseases, or other chronic infections. Retroperitoneal tuberculous lymphadenopathy is one of the rarest forms [3,10] of extrapulmonary TB (EPTB), and its insidious presentation makes it a diagnostic conundrum. In our case, a immunocompetent woman presented with prolonged fever without respiratory symptoms, no lymphadenopathy on clinical examination, and unremarkable initial workup. This delayed the consideration of TB in the differential diagnosis. The diagnosis was eventually clinched through PET CT and histo-pathological confirmation, underscoring the importance of imaging and targeted diagnostics in persistent fever cases in TB-endemic settings.

India, being a high TB-burden country, contributes nearly 26% [1] of the global TB incidence according to the WHO Global TB Report 2023. While pulmonary TB constitutes the majority, extrapulmonary TB is seen in 15–20% of cases and often remains undiagnosed due to non-specific clinical signs. Lymph node TB is the most common form of EPTB [2], especially cervical. Retroperitoneal involvement, although uncommon, must not be underestimated due to its capacity to mimic lymphoproliferative disorders such as lymphoma or metastatic adenocarcinoma.

Pyrexia of unknown origin (FUO) as defined by Petersdorf and Beeson [5] includes fever higher than 38.3°C on multiple occasions for at least three weeks, with no diagnosis after one week of hospital investigation. In the Indian context, tuberculosis remains a leading cause of PUO [6]. The differential diagnosis includes malignancy (particularly lymphoma), autoimmune diseases (e.g., SLE, Still's disease), and infections (like EBV, CMV, brucellosis, or enteric fever).

In our case, the lack of site-specific symptoms, the absence of night sweats, cough, or weight loss, and nonspecific findings in chest radiograph initially led the evaluating team to consider alternative causes like enteric fever, malaria or autoimmune disease. Only after initial blood tests, serologies, and imaging studies returned inconclusive, was a more detailed abdominal imaging undertaken. PETCT provided a key breakthrough, revealing lymphadenopathy in the para-aortic and aortocaval chains which was highly suggestive of TB in endemic areas, although they are not pathognomonic and may also occur in lymphoma and fungal infections.

Radiologic imaging, especially contrast-enhanced computed tomography [8] (CECT), is a cornerstone in detecting abdominal TB. Features such as centrally necrotic lymph nodes, rim enhancement, calcifications [11], and conglomerate nodal masses are characteristic of tubercular etiology. Retroperitoneal TB may also be associated with peritoneal thickening, ascites, or mesenteric involvement.

Despite radiological suspicion, microbiological confirmation is necessary to establish the diagnosis and guide treatment. In this case, FNAC of the lymph node demonstrated classic caseating granulomas. While Ziehl–Neelsen staining for acid-fast bacilli (AFB) is often insensitive [7] in extrapulmonary samples, molecular assays like GeneXpert (CBNAAT) have revolutionized [9] TB diagnostics. It offers not only rapid identification of Mycobacterium tuberculosis DNA but also detects rifampicin resistance with high specificity.

Lymphomas, particularly non-Hodgkin lymphoma [12], remain a major differential diagnosis of retroperitoneal lymphadenopathy. Clinical presentation with fever, fatigue, and deep-seated lymph node masses, especially in the retroperitoneal or mesenteric regions, often misleads clinicians toward malignancy. However, histopathological differentiation is clear-cut. In lymphoma, architecture is effaced by neoplastic lymphoid cells, whereas in TB, there is granulomatous inflammation with caseation and Langhans giant cells. In our case, histology ruled out malignancy and confirmed granulomatous inflammation.

This mimicry highlights the importance of not proceeding directly to empirical chemotherapy in patients with suspected lymphoma unless histologic confirmation is obtained. In resource-limited settings, where TB prevalence is high and oncologic diagnostics may be delayed or unavailable, clinical judgment becomes critical.

EPTB is often associated with immunocompromised states [13], such as HIV/AIDS, diabetes, or immunosuppressive therapy. Interestingly, our patient was immunocompetent, with negative HIV serology and no comorbidities. This reinforces the understanding that EPTB, especially lymph node TB, can affect healthy hosts and should not be excluded based solely on immune status.

It is believed that hematogenous dissemination of Mycobacterium tuberculosis [14] bacilli from an occult pulmonary focus or during primary infection may seed the lymph nodes. In many cases, the primary pulmonary lesion may heal or be subclinical, while extrapulmonary sites harbor active disease.

Standard first-line anti-tubercular therapy (ATT) [15] as per India's National TB Elimination Programme (NTEP) includes 2 months of intensive therapy (HRZE) followed by 4 months of continuation phase (HR). The total duration of therapy for lymph node TB is typically 6 months unless complications arise.

Our patient responded favorably to standard therapy, with resolution of fever within 10 days of treatment initiation and improvement in systemic symptoms. Follow-up imaging showed regression of lymphadenopathy, confirming treatment response.

CONCLUSION

Retroperitoneal tuberculous lymphadenopathy remains a diagnostic challenge, particularly in immunocompetent individuals with nonspecific symptoms such as prolonged fever. This case underscores the importance of maintaining a high index of suspicion for extra pulmonary tuberculosis in endemic regions, even in the absence of respiratory findings or immunosuppression. Advanced imaging and molecular diagnostics like GeneXpert play a critical role in timely identification and initiation of therapy. Accurate diagnosis prevents mismanagement with empirical chemotherapy for lymphoma and reinforces the value of FNAC and histopathology. Prompt anti-tubercular treatment led to symptom resolution, highlighting the impact of targeted intervention in atypical TB presentations.

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