

Disseminated Tuberculosis with Testes Involvement: An Intriguing Case Report

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Abstract

Background: Disseminated tuberculosis (TB) is the presence of two or more noncontiguous sites resulting from hematogenous dissemination of *Mycobacterium tuberculosis*. We report a case of disseminated TB with testicular involvement. **Case:** A 21-year-old male patient presented to the outpatient department with bilateral testicular enlargement and tenderness for last six months. It was suspected to be a case of epididymo-orchitis and empirical antimicrobial therapy was initiated. However, ultrasonography findings were inconsistent with epididymo-orchitis. Two weeks later the patient again presented with increased nodularity in the right testes. Non-seminomatous germ cell tumor was suspected. However, tumor markers came back normal. Magnetic resonance imaging revealed enlarged lymph nodes in the right inguinal and retroperitoneal region raising a suspicion of testicular lymphoma. Positron emission tomography with computed tomography showed multiple lymphadenopathies. Histopathology of the left axillary lymph node finally confirmed the diagnosis to be tuberculosis. No drug resistance were found and the patient responded well to anti-tubercular drugs. **Conclusion:** Diagnosing disseminated TB is difficult as it mimics conditions, such as infarction, cancer, torsion, etc. Attention to small details is necessary. We faced a similar situation in our patient. The patient went through a myriad of tests before finally being diagnosed with TB. Histopathological study was able to get it whereas cytology could not. Similar and totally opposite cases were found in the literature. This highlights the difficulty and importance of these type of cases.

Introduction

Disseminated tuberculosis (TB) is common in low and middle-income countries and especially among children below 15 years of age. However, its prevalence in high-income countries is rising due to various risk factors, such as Human immunodeficiency virus (HIV), immunosuppressive medications, organ transplantation, alcohol consumption, and other comorbidities.¹

Disseminated TB in an immunocompetent adult comprises less than 2% of all TB cases and up to 20% of all extra-pulmonary TB cases.¹ The true global incidence is likely underestimated due to diagnostic challenges.¹ It can involve many organs like lymph nodes, liver, bone marrow, kidney, testis, etc.

Clinical presentation varies widely in disseminated TB, ranging from subacute or chronic constitutional symptoms like fever, weight loss, and night sweats to multi-organ failure in severe cases.¹ Uncommonly it can present as anorexia and pyrexia of unknown origin.¹ Symptoms in children are quite vague, making the diagnosis quite difficult.¹ It often mimics various conditions like torsion and infarction (painful testicular mass) or cancer (widespread involvement).

The key to differentiate between various differential diagnoses is by diagnostic tests like imaging, microbiological tests, tissue

Highlights:

- Diagnosing disseminated tuberculosis (TB) is challenging.
- Disseminated TB mimics various conditions like infarction, cancer, torsion, etc.
- In our case, the patient underwent a myriad of tests before getting a definitive diagnosis.
- This case report highlights the importance of histopathology to diagnose disseminated TB as cytological analysis might miss it.
- Disseminated TB is relatively rare in immunocompetent adults and might be missed initially and a high level of suspicion is needed.

biopsy, etc. Mantoux test (tuberculin skin test, TST) is often negative in disseminated TB thus not reliable.¹ Chest radiograph is often the initial imaging modality, showing characteristic miliary patterns in a majority of cases.¹ Other imaging modalities, including high-resolution computed tomography (CT), abdominal ultrasonography, magnetic resonance imaging (MRI), and positron emission tomographic CT (PET-CT), can assist in

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identifying affected organs and guiding the collection of appropriate specimens for diagnosis.¹

Microscopically there are tuberculous granulomas with or without central caseation. Acid-fast bacilli may be found in epithelioid cells or inside caseation. The nonspecific nature of the symptoms poses a challenge in diagnosing the disease.¹

Here, we describe a rare case of disseminated TB with testicular involvement, mimicking cancer. This case report highlights the critical need for considering tuberculosis as a diagnosis in testicular masses, emphasizing the diagnostic challenges and atypical presentations mirroring other condition(s), and is crucial for timely and accurate management.

The Case

Initial Presentation

A 21-year-old male presented to the outpatient department (OPD) with complaints of bilateral testicular enlargement for last six months. On examination, both testes were tender, hard and enlarged with loss of testicular sensation as reported by the patient. He was of average build and had no other complaints. He was not currently on any medications and denied any addictions or sexual contact in his life. He denied any history of pulmonary disease or problem. A provisional diagnosis of bilateral epididymo-orchitis was made and the patient was started on empirical antimicrobial therapy. To confirm the diagnosis, urine was sent for routine examination, microscopic examination, and culture which came out normal. Ultrasonography of the scrotum and testis was also advised.

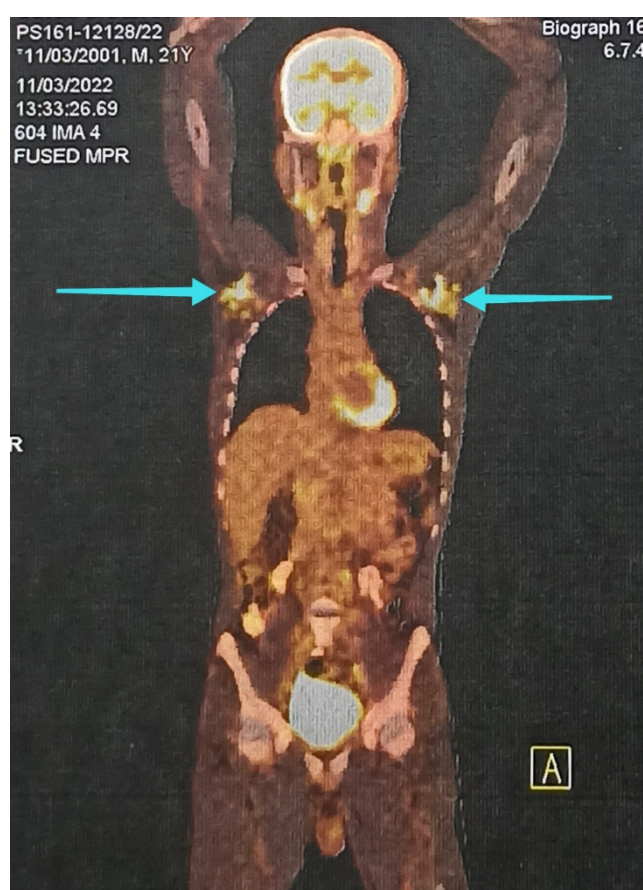
Diagnostic Challenges

A follow-up visit one week after initiating empiric therapy showed improvement, with reduced pain and tenderness. Two weeks later, the patient again presented to the OPD with a new onset nodularity of the right testis with thickening of the spermatic cord which was not present in the previous OPD visit. Based on scrotal edema, clinical findings suggested a suspected non-seminomatous germ cell tumor, clinically categorized as T4 (As per TNM staging system), with invasion of the spermatic cord and pelvic lymphadenopathy.

However, testicular tumor markers were found to be within the normal limits [LDH - 171U/L (120-246U/L), β -hCG - <0.100mIU/ml (<2.6mIU/ml) and α -fetoprotein - <1.3ng/ml (<8.1ng/ml)]. Later on, MRI of the pelvis and scrotum was done which showed ill-defined T2 hypointensities in both testes along with multiple perifocal satellite hypo-intense lesions. Similar involvement is seen in the epididymis and bilateral spermatic cord (more on the right side). A mild right-sided hydrocele was noted. Also, mildly increased fluid in the left testis was observed. Visible parts of the right ureter were dilated. Enlarged lymph nodes in the right inguinal and retroperitoneal region (mainly the left para-aortic region) were noted. A testicular lymphoma was then suspected based on extensive lymphadenopathy and the absence of any history of tuberculosis.

¹⁸FDG whole-body PET-CT was done to determine spread. It showed metabolically active multiple lymphadenopathies (bilateral cervical, axillary, retroperitoneal, iliac and inguinal lymph nodes) and active lymphomatous nodules in bilateral

Figure 1. Positron Emission Tomography with Computed Tomography Showing Metabolically Active Axillary Lymph Nodes (Blue Arrow). It was Done After Malignancy was Suspected to Determine the Extent of Spread.



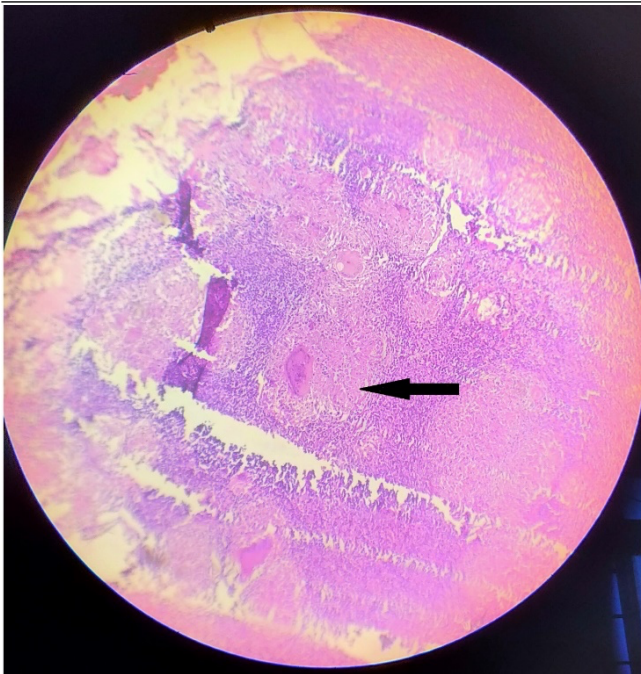
adrenal glands, bilateral epididymis and right testis [Figure 1](#). Then a CT-guided fine needle aspiration cytology (FNAC) of the right inguinal lymph node was done which showed lymphoid cells with foreign body giant cells. No epithelioid tumor or tumor giant cell was seen.

A histopathological examination was advised for confirmation. A left axillary lymph node biopsy was performed and sent for histopathological examination. Preoperative investigations were normal. Mantoux test and triple serology was negative (HIV, Hepatitis B and C). Histopathological examination of axillary lymph nodes showed multiple epithelioid granulomas with Langhans giant cells and foci of caseous necrosis. [Figure 2](#) Histopathological features were in favor of tuberculous lymphadenitis. A diagnosis of disseminated extra-pulmonary TB with testicular involvement was made.

Treatment and Outcome

No drug resistance was detected in line probe assay. The patient was started on anti-tubercular treatment of isoniazid, rifampicin, pyrazinamide and ethambutol for two months followed by 4 months of isoniazid, rifampicin and ethambutol. During treatment,

Figure 2. Histopathological Examination of Axillary Lymph Node Showing Caseating Granuloma (black arrow). This Confirmed the Diagnosis of Tuberculosis.



the patient was followed up at 1 month, 2 months, 4 months, and 6 months. The patient underwent full remission. Testicular enlargement and nodularity went down and no pain or tenderness were further reported. Lymph node swelling was absent on subsequent visits. The patient now follows up regularly every 6 months [Table 1](#).

Discussion

TB can involve many organs like lymph nodes, liver, bone marrow, kidney, testis etc. Acid-fast bacilli may be found in epithelioid cells or inside caseation. Disseminated TB presents with subacute or chronic constitutional symptoms such as fever, weight loss and night sweats. Differential diagnoses include testicular torsion and infarction or cancer. All of these conditions present with testicular enlargement, lump, with or without color changes. Pain is also a common feature but is usually not present in cancer. Also, pain in testicular TB is chronic compared to sudden onset pain torsion and infarction. Specific features of torsion are elevated testis and the absence of cremasteric reflex. Thus, history taking, and clinical examination is important to distinguish between these conditions especially in acute presentations. In testicular masses FNAC is not done due to risk of tumor cell seeding. Only way to do a cytological or histological is an excisional biopsy – This is a significant challenge for the diagnosis of these cases.²

Table 1. Histopathological Examination of Axillary Lymph Node Showing Caseating Granuloma (black arrow). This confirmed the diagnosis of tuberculosis.

Timeframe	Diagnostic tests	Findings	Inferences
Onset	Clinical examination (Initial)	Both testes were tender, hard and enlarged with loss of sensation	Epididymo-orchitis suspected
2 weeks	Clinical examination (Follow up)	Nodularity of right testis and thickening of spermatic cord	Non seminoma germ cell tumor with spermatic cord invasion suspected
1 month	Testicular tumor markers	Normal	Diagnosis of cancer was in doubt
2 months	MRI of pelvis and scrotum	Ill-defined T2 hypointensities in both testes along with multiple perifocal satellite hypo-intense lesions. Similar involvement in the epididymis and bilateral spermatic cord (more on the right side). A mild right-sided hydrocele was noted. Also, mildly increased fluid in the left testis was observed.	Testicular lymphoma was suspected
4 months	¹⁸ FDG whole-body PET-CT	Metabolically active multiple lymphadenopathies (bilateral cervical, axillary, retroperitoneal, iliac and inguinal lymph nodes) and active lymphomatous nodules in bilateral adrenal glands, bilateral epididymis and right testis.	Metastasis of suspected testicular lymphoma
7 months	CT-guided Fine Needle Aspiration Cytology of right inguinal lymph node	Lymphoid cells with foreign body giant cells. No epithelioid tumor or tumor giant cell was seen.	Histopathological analysis suggested
9 months	Histopathology of axillary lymph nodes	Multiple epithelioid granulomas with Langhans giant cells and foci of caseous necrosis	Disseminated TB with testicular involvement

The key to differentiate between various differential diagnoses is by diagnostic tests like imaging, microbiological tests, tissue biopsy, etc. Mantoux test is often negative in disseminated TB

thus not so reliable.¹ Diagnosis of disseminated TB can be confirmed if any one of the following is present - isolation of tubercle bacilli, positive PCR or Histological demonstration of

caseating granuloma in the biopsy specimen.¹ In our case, the symptoms were first interpreted as an inflammatory condition (epididymo-orchitis) which initially improved with later relapse and testicular nodularity. Testicular neoplasms were suspected but it did not fit with the diagnostic tests done later. Ultimately it was diagnosed as a disseminated TB with testicular involvement after histologic evidence of caseating granuloma in the axillary lymph nodes. A case similar to ours was reported in a patient by Namburete EI *et al.*³ The patient was HIV positive in which case dissemination of TB is common.^{1, 3} However, our patient was immunocompetent without any history of pulmonary disease which makes it unique. Najdawi *et al.* reported a totally opposite situation in a case of non-seminoma germ cell tumor presenting with dyspnea and cavitary lung lesions which mimicked TB.⁴ Xiao described a case of testicular TB which was diagnosed after orchiectomy as malignancy was suspected and extensive damage to the testis.⁵ Mohamed Ali *et al.* described two cases of testicular tuberculosis from Somalia in immunocompetent patients.⁶ One had a history of respiratory TB while other one did not. Muttarak M *et al.* described a case where the diagnosis was based on ultrasonography, no response to conventional antibiotics, and response to first line anti-TB drugs.⁷ All of this exemplifies the complexity of diagnosing this condition and the differentials.³ In clinical practice, the presentation and history can vary widely as discussed above. Absence of history of any respiratory illness does not necessarily rule out the existence of TB as in our case

and the one reported by Xiao, Mohamed Ali *et al.*, and Muttarak M *et al.* This can be a challenge when a patient presents acutely with the complaints of pain in testes, enlargement and color changes. Histopathology is likely the most effective method to differentiate these conditions as seen in our case and other reported cases.²⁻⁵ Medical management by anti-TB drugs is the mainstay of treatment but sometimes surgical management becomes necessary.⁸ This case contributes to the existing literature on disseminated TB and will help clinicians to be more aware and cautious while diagnosing conditions with testicular lesions.

Summary – Accelerating Translation

A 21-year-old male presented with bilateral testicular enlargement. Initially it was diagnosed as epididymo-orchitis. Further investigations revealed nodules, thickening and lymphadenopathy. Later on MRI was done and testicular lymphoma was suspected. The PET-CT confirmed multiple active lymphadenopathies and nodules. Axillary lymph node biopsy was done which lead to a diagnosis of disseminated extra-pulmonary tuberculosis with testicular involvement. The patient responded well to anti-tubercular treatment. This case highlights the complexity of diagnosing disseminated TB and underscores the importance of histopathological examination for confirmation in atypical presentations. Similar and opposite cases have been reported in the literature exemplifying the complexity and importance of these types of cases. Recognizing these cases is essential as it reduces the risk of complications if treatment is initiated early.

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Conflict of Interest Statement & Funding

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