



Inflammation and infection

# Tuberculosis epididymorchitis masquerading as a testicular malignancy in HIV positive patient: A case report and literature review

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## ABSTRACT

Tuberculosis (TB) remains a significant health concern, with this study focusing on tuberculous epididymo-orchitis. Genitourinary TB (GUTB) diagnosis is difficult using conventional methods like acid-fast staining, culture, and PCR. A case study involves a 22-year-old HIV-diagnosed male with a painless progressive testicular swelling. A radical orchidectomy revealed isolated tuberculosis epididymo-orchitis. The study emphasizes considering this diagnosis for testicular masses, recognizing the diagnostic complexity and potential need for surgical intervention in cases of ambiguity.

## 1. Introduction

Tuberculosis (TB) is a widespread infection caused by Mycobacterium tuberculosis, ranking second in global infectious diseases after HIV.<sup>1</sup> Nearly one-third of the world's population has been infected, resulting in millions of cases and making TB the 9th leading cause of death worldwide.<sup>2</sup> In 2018, the World Health Organization reported 10 million new cases, with a global average incidence of 130 per 100,000 population per year. TB primarily affects the lungs but can also manifest in other sites (extrapulmonary TB), posing diagnostic challenges that radiologists play a crucial role in addressing.<sup>3</sup>

Extrapulmonary TB can affect various sites, with the most common being the skeleton, genital tract, and central nervous system.<sup>4</sup> Genitourinary TB (GUTB) accounts for 8%–15% of all extrapulmonary TB cases, and epididymal involvement occurs in only 27% of GUTB cases.<sup>5</sup> Kidney infection is prevalent in GUTB, while male genital TB (MGTB) is a distinct subset involving the prostate, seminal vesicles, vas deferens, testicles, epididymides, or penis.<sup>4,6,7</sup>

AIDS-related urological complications include epididymitis, orchitis, scrotal and urethral abscesses, neurogenic bladder, erectile dysfunction, infertility, renal failure, and neoplasms. Kaposi's sarcoma, often affecting the penis or urethra, is the most common neoplasm. HIV-positive men have a higher incidence of testicular neoplasms, particularly bilateral tumors. Rarely, testicular abscesses can occur in individuals with diabetes, transplant recipients, or those with prolonged urethral catheter placement.<sup>8,9</sup>

Tuberculous epididymitis is a crucial aspect of genitourinary tuberculosis (GUTB), the second most common form of extrapulmonary tuberculosis. GUTB, apart from tuberculous epididymitis, is infrequent and poses diagnostic challenges in modern medicine, often masquerading under other infections or diseases. Isolated TB orchitis without epididymis is an even rarer occurrence.<sup>4,10</sup> Epididymal tuberculosis, a rare manifestation in young adults, often presents with mild or no apparent symptoms, making early diagnosis challenging. The global increase in male genital tuberculosis, including epididymal tuberculosis, is linked to factors such as multi-drug resistant bacteria, anti-tuberculosis drug resistance, and widespread glucocorticoid use. Pathologically, epididymal tuberculosis leads to extensive tissue destruction and fibrosis, impacting male reproductive system function and causing complications like infertility.<sup>11,12</sup> Tuberculous epididymo-orchitis can mimic testicular tumors, necessitating a high index of suspicion, scrotal ultrasound, and fine needle aspiration for accurate diagnosis.<sup>13</sup>

The case presented involves a patient initially diagnosed with a testicular tumor who underwent radical orchidectomy in a general hospital. However, histopathological examination revealed tuberculous epididymo-orchitis, emphasizing the importance of careful diagnosis to avoid unnecessary surgeries.

## 2. Case presentation

A 22-year-old male presented with a four-week history of

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progressively increasing redness and swelling in the left testicle, without pain (Fig. 1). He underwent hemodialysis due to antiretroviral therapy (ART)-induced acute kidney injury. No prior history of fever, cough, weight loss, night sweats, urinary infection, or surgery. The patient had no prior history of TB exposure. Physical examination showed a moderately ill patient with a non-tender, red, and swollen left testicle mass. Fluctuation was observed in the past week. Lab tests revealed normal blood counts, but antiretroviral therapy (ART) affected kidney function. The patient had an HIV controlled over several months with CD4<sup>+</sup> counts 300 cells/mm. Tumor markers were normal. Testicular ultrasound revealed a 60x40 × 40 mm hypoechoic mass, confirming the clinical diagnosis of left testicular tumor (Fig. 2). Subsequent left radical orchidectomy was performed (Fig. 3).

### 2.1. Histopathology

Histopathological analysis of the examined tissue, a 10x6x2.5 cm specimen, showed extensive necrotic tissue with chronic inflammatory cells through seminiferous tubules predominantly in a state of necrosis, presence of granulomas, tubercles, and Langhans giant cells indicating tuberculous orchitis. No malignant signs were identified (Fig. 4).

### 3. Discussion

Since the advent of HIV infection, tuberculosis has been on the rise worldwide, particularly in developing countries. The disease is most often found in the lungs. All organs may be affected (epididymis and/or testis) during hematogenous, lymphatic, or contiguous dissemination. Isolated genital tuberculosis is rare.<sup>14</sup>

Despite the advancement in anti-TB therapy and the strict implementation of well-known TB measures, TB remains one of the major diseases worldwide. This is compounded by the HIV that had to make it a common infection.<sup>15</sup> TB is currently a global epidemic with more than 2 billion population infected worldwide. An estimated 10 million people fall in people who fell ill with TB in 2018, a number that has been relatively slightly reduced in recent years compared to 2017.<sup>4</sup>

Approximately 7% of extrapulmonary Tuberculosis (TB) are presented as a rare case, namely testicular TB. Patients with HIV infection present an increased risk of genitourinary TB. Genitourinary tuberculosis can result from spread via the bloodstream or originate as a primary lesion in the genital area from prostate or kidney tuberculosis. The more common pathway remains a topic of debate.<sup>16</sup>

The number of tuberculosis patients in China accounted for 10–12% of the total number of tuberculosis patients in the world, ranking second in the world.<sup>17,18</sup> People in Gansu Province of China have a high incidence of tuberculosis and are relatively delayed in seeking medical care.<sup>18</sup> The presentation of tuberculosis is increasingly atypical. Unfortunately, the prevalence of drug-resistant strains of tuberculosis is

increasing.<sup>19</sup> The main treatment of epididymal tuberculosis is early anti-tuberculosis treatment. However, since most of the patients with epididymal tuberculosis in Gansu are in the terminal stage, surgical treatment combined with chemotherapy has been the best treatment modality for this type of patients.<sup>11</sup>

Reproductive system tuberculosis can occur at any age, mainly in men 30–50 years old. Due to the long incubation period, it is not common in children. The most commonly involved organ is the epididymis, followed by the seminal vesicle, prostate, testis, and vas deferens.<sup>20</sup> Isolated epididymal tuberculosis is very rare. A study by Viswaroop et al., indicated that isolated epididymal tuberculosis may be the first or only manifestation of early genitourinary tuberculosis.<sup>1</sup> Similarly, in a study cohort by Man et al., there were 39 cases (82.9%) of isolated epididymal tuberculosis.<sup>11</sup>

TB epididymo-orchitis is a common form of GUTB but when it is isolated, it may mimic testicular tumour. Testicular tumour is rare among blacks and requires surgical removal with adjuvant chemoradiotherapy, unlike testicular TB. Reported cases with clinical diagnosis of testicular tumors that were found to be testicular tuberculosis after surgery sometimes have TB affecting other associated organs like the seminal vesicle, prostate or kidneys.<sup>13</sup>

Scrotal involvement in tuberculosis is typically haematogeneous from a primary source which is usually the lung or kidney. Retrograde extension from the prostate and seminal vesicles to the epididymis and testicles may also occur. Pathologically, the earliest lesions are seen as discrete or conglomerate yellowish necrotic areas in the tail of the epididymis. From here it could extend to the testis. Mycobacterium tuberculosis resulting from haematogeneous spread without epididymal involvement is rare.<sup>16</sup>

Isolated tuberculosis epididymo-orchitis (ITE) refers to tuberculous epididymitis without signs of renal or prostate involvement and is a rare form of genitourinary tuberculosis (GUTB). ITE is the entity that is usually presented without any specific clinical symptoms at a young age, as we have seen in our case; therefore, there remains a probability of misdiagnosis or leads to the diagnosis of the testicular tumor or epididymo-orchitis.<sup>4</sup>

The specific symptoms of ITE include painful scrotal and epididymis swelling, groin pain, dysuria, fever, tenderness, and a painless scrotal mass. Diagnosing ITE can be challenging and delayed due to vague symptoms, typically manifesting after 30 years of age post-exposure to the bacterium.<sup>4,13</sup>

ITE poses diagnostic challenges. Surgical confirmation is sometimes necessary due to the variable sensitivity and specificity of diagnostic tests like urine acid-fast staining, sonography, and MRI. Cold abscess, observed in MRI and sonography, presents a typical finding—a painless cystic lesion contrasting with hot abscess. The concentration of acid-fast bacteria differs in urine and sputum, complicating genitourinary TB diagnosis. In some cases with large scrotal tumors, nonsurgical



Fig. 1. Clinical appearance of swelling and scrotal skin of testicular TB.



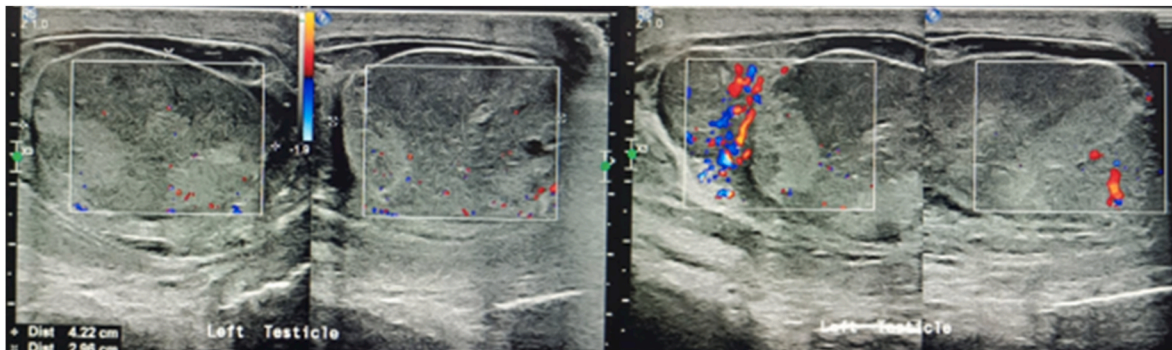


Fig. 2. Testicular and Scrotal Ultrasound with Doppler shows scrotal mass and epididymo-orchitis of left testicle.

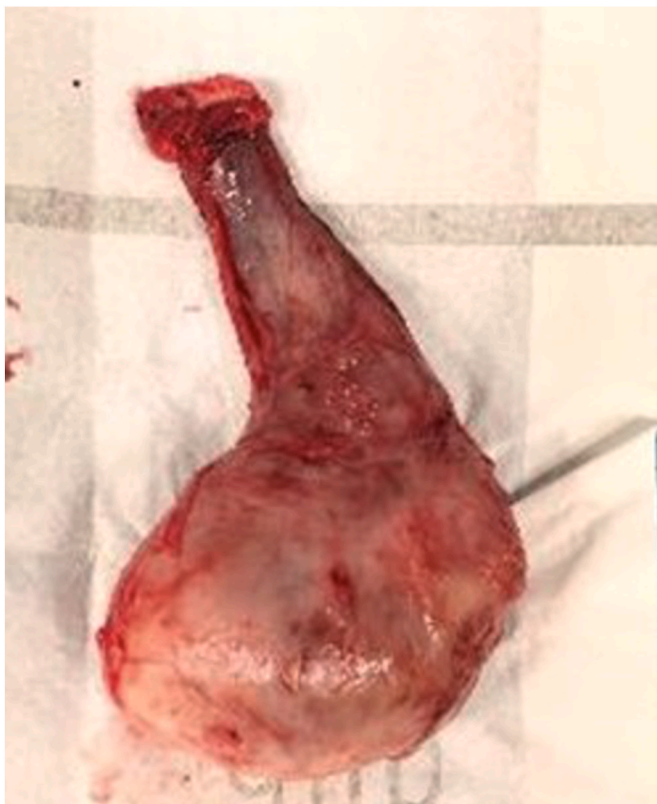


Fig. 3. Testicular mass with size 60x40x40 mm.

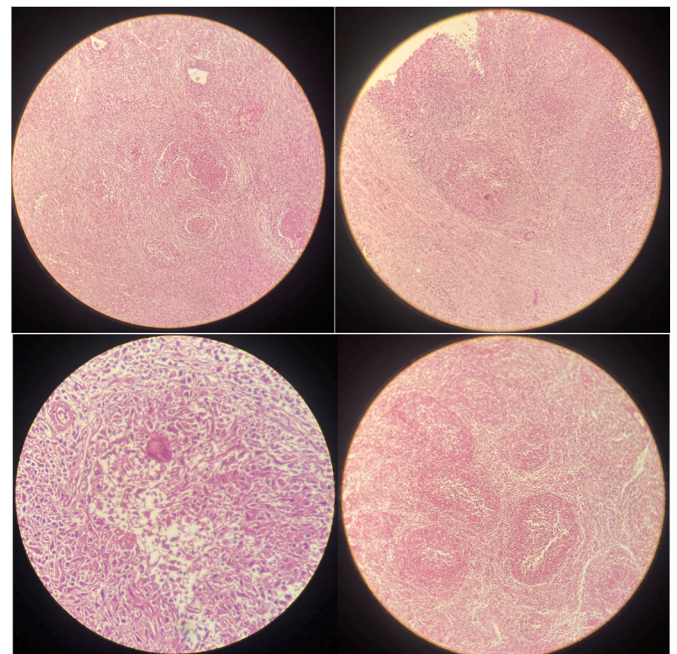


Fig. 4. Histopathological analysis of the examined tissue.

treatment becomes impractical, and due to a vague provisional diagnosis, surgery often becomes the final treatment step.<sup>15</sup>

The major clinical differential diagnosis of scrotal mass with or without pain is inflammatory processes, torsions, and testicular tumour.<sup>16</sup> The gold standard is the isolation and culture of *M. tuberculosis*. In cases of suspected Male genital tuberculosis, we usually look for *M. tuberculosis* in the urine or tissue. Sterile pyuria on microscopic urinalysis is considered to be a typical manifestation of urogenital involvement. Some finds reported that leukocytes in urine were present microscopically or grossly in a majority of cases (50% and 10%, respectively).<sup>11</sup>

Hematuria is a prevalent symptom of urinary tuberculosis, primarily arising from renal and bladder tuberculosis. Acidic urine and hematuria are linked to urinary tuberculosis, but these findings lack specificity. In our patient group, 17.0% exhibited red blood cells in urine, indicative of renal tuberculosis. Leukocyte positivity, aiding diagnosis in 42.6% of patients, had low specificity. Color Doppler ultrasound is the preferred imaging method for analyzing epididymal tuberculosis.<sup>2,11</sup>

Ultrasound is the preferred imaging method for assessing the scrotum. In cases of tuberculous orchitis, ultrasound shows patterns like diffusely enlarged and heterogeneously hypoechoic testis, nodular enlargements, or miliary patterns. Conversely, testicular tumours appear as discrete masses with varying echoic textures. Seminomas and lymphomas are typically homogenous, while non-seminomatous tumours are more heterogeneous.<sup>16</sup>

In the presented case, a comprehensive assessment using testicular and abdominal ultrasound, CT scan, and fine needle aspiration biopsy would have guided management. However, these resources were unavailable at the general hospital, and referral to a tertiary hospital, though ideal, might be cost-prohibitive. Fine needle aspiration cytology (FNAC) has been noted to enhance testicular TB diagnosis when combined with ultrasound and CT scan.<sup>13</sup> FNAC is usually not done in cases with a high suspicion index of neoplastic process based on imaging studies and fear of seeding of tumor cells.<sup>11,13</sup> Hence, the FNAC procedure should be considered in patients with a positive epidemiologic risk for TB, usually in developing countries, and with less suspicion of an underlying neoplasm evidenced by the absence of elevated tumor markers.<sup>11,13</sup>

The principal treatment for genitourinary tuberculosis is antituberculous chemotherapy, an induction treatment period of 2 months of daily isoniazid, rifampicin, pyrazinamide and ethambutol is followed by

a period of 4 or 7 months of daily isoniazid, and rifampicin treatment. Effective antituberculosis chemotherapy would limit the requirement of surgical intervention for the management even in extensive disease and abscesses as sequelae of TB.<sup>16,20</sup> Hence in our case, if the TB orchitis was diagnosed before the orchiectomy, antituberculosis chemotherapy would be sufficient as the principal management instead of the surgical therapy. Surgical therapy is indicated if there is no response to antitubercular therapy in the size of the scrotal mass despite 3 weeks of medications making it highly suspicious for testicular malignancy. No other treatment was used in the case other than antituberculosis chemotherapy as the main therapy.<sup>16,20</sup> Hence, in endemic regions such as ours, patients with chronic epididymitis or scrotal mass must be examined for tuberculosis.<sup>14</sup>

#### 4. Conclusion

Isolated epididymis tuberculosis (ITE) should be considered in the differential diagnosis of testicular masses, despite its rarity and diagnostic challenges. Genitourinary TB diagnosis is difficult using conventional methods like acid-fast staining, culture, and PCR. Surgery may be necessary for confirmation, especially in cases without a definitive diagnosis or with significant clinical indications such as abscesses or cutaneous fistulas. A diagnostic algorithm should incorporate minimally invasive approaches like fine needle aspiration (FNA) for accurate diagnosis. This article aims to discuss extrapulmonary TB, specifically ITE, providing a comprehensive understanding for proper management of this uncommon condition.

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**Aditya Akbar Latief:** Writing – review & editing, Writing – original draft, Validation, Supervision, Formal analysis, Data curation, Conceptualization. **Afdal:** Writing – review & editing, Writing – original draft, Validation, Resources, Investigation, Formal analysis.

#### Declaration of competing interest

None.

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