CASE REPORT

Epididymo-Orchitis: A Rare Manifestation of Tuberculosis Infection

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ABSTRACT

Introduction: Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (MTB) and now represents a significant global health concern, with an estimated 10 million people infected with TB in 2022, equivalent to 133 incident cases per 100,000 population. Indonesia faces a substantial burden. The World Health Organization (WHO) estimates 969,000 TB cases, with 717,941 confirmed cases reported. Extrapulmonary TB, contributing to 15% of TB cases, affects various areas such as bones, pleura, lymph nodes, genitourinary system, peritoneum, and meninges. Tuberculous epididymo-orchitis, a rare type of extrapulmonary TB, is characterized by MTB infection in the epididymis or testis.

Case: A 31-year-old male was presented to the Emergency Department of Budi Rahayu General Hospital, Pekalongan, with a fever, bitter taste, body aches, and cough. Initially hospitalized for five days and discharged upon improvement of symptoms, the patient returned with fatigue, cough, and black stools. After being admitted under internist and pulmonary specialist care due to a suspected left lung TB apical lesion, biomolecular testing (GeneXpert) was performed. Consultation with a urologist revealed scrotal pain, prompting further tests including urine acid-fast bacilli (AFB) examination, testicular ultrasound, and aspiration culture. The patient was diagnosed with TB epididymo-orchitis and treated with a Category 1 TB regimen.

Conclusion: TB epididymo-orchitis is a rare case requiring thorough diagnostic evaluation encompassing anamnesis, physical examination, and diagnostic procedures. Early detection and appropriate management are vital in combating this challenging disease.

INTRODUCTION

Mycobacterium tuberculosis (MTB) is the leading cause of morbidity and mortality worldwide. It is estimated that approximately 25% of the world's population has been infected with tuberculosis (TB), with the greatest impact on developing countries. In 2023, the World Health Organization (WHO) reported that more than 10 million people were infected with TB, and there were 7.5 million newly diagnosed TB cases in 2022, the highest number since 1995. In 2019, there were 10.3 million cases, increasing to 5.8 million cases in 2020 and 6.4 million cases in 2021.[1] This incidence may dramatically rise in the coming years due to factors such as the prevalence of human immunodeficiency viruses (HIV), population migration, and malnutrition.

Southeast Asia records the highest number of TB cases, accounting for 46%. Meanwhile, according to the Global TB Report 2022, Indonesia ranks second in the world for the highest prevalence of TB after India. WHO estimates 969,000 TB cases in Indonesia, with the current number being 717,941, based on ages from 15 to 54 years old.[1–3]

MTB enters the lungs through inhalation, as it can survive in the air for several hours depending on environmental conditions. MTB then enters the respiratory tract, reaching the alveoli and bronchi. If only a small amount of MTB is inhaled, the bacteria will be phagocytosed by macrophages. However, if the amount of TB bacteria exceeds the macrophages' capacity to phagocytose and digest, the TB bacteria will

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persist and replicate intracellularly within the macrophages. When the macrophages die, replicating MTB exits the cells. Subsequently, MTB lodges in lung tissue, forming a primary focus, from which inflammation in the lymphatic vessels and the formation of primary complexes occur. When primary complexes develop, dissemination can occur via hematogenous or lymphatic spread.[4]

The diagnosis of pulmonary TB can be established based on clinical symptoms, which are categorized into two groups, 1) Respiratory symptoms that include productive cough lasting more than two weeks; and 2) Additional symptoms, such as coughing up blood, shortness of breath, fatigue, unintentional weight loss, loss of appetite, malaise, night sweats without physical activity, subfebrile fever lasting more than one month, and chest pain.[4] Extrapulmonary TB refers to clinical manifestations of TB involving organs other than the lungs.

In extrapulmonary TB, the affected areas typically include bones, pleura, lymph nodes, genitourinary system, peritoneal joints, and meninges.[5,6] Genital TB in men is a part of urogenital TB (UGTB). UGTB accounts for nearly 8-15% of all types of TB outside the lungs.[6,7] UGTB usually involves the prostate up to the penis. Involvement of the epididymis is less common, accounting for approximately 28% of UGTB. In various literature sources, it has been mentioned that men aged between 20-40 years old are more prone to testicular TB, which is very rare in children due to the long latent period.[8–10]

Manifestations of these rare cases can vary significantly. The majority of cases present with pelvic pain, dysuria, and subsequent fever. Scrotal swelling without pain or tenderness occurs in about ⅓ of cases, and it may also be accompanied by symptoms of lower urinary tract irritation, such as increased frequency of urination (initially during the day and then at night as the disease progresses), suprapubic pain, and presence of pus in the urine.[9,11,12] Ancillary tests such as scrotal ultrasound and fine-needle aspiration can be very helpful in diagnosis. Cases of tuberculous epididymo-orchitis are rare. However, if they occur, a comprehensive assessment of the patient is necessary to avoid potential complications.

We presented the case of a 31-year-old male who was presented to the hospital with initial complaints of fever, cough, and swelling of the testis, which was later diagnosed as tuberculous epididymo-orchitis.

CASE

A 31-year-old male patient was presented to the Emergency Department of Budi Rahayu General Hospital with a complaint of fever for the past three days. The fever was described as intermittent, accompanied by a bitter taste in the mouth, generalized body aches, weakness, and cough. The patient denied coughing up blood, shortness of breath, unintentional weight loss, night sweats, chest pain, loss of appetite, or decreased fluid intake. The patient has been a heavy smoker since he was 15 years old, consuming one to two packs of cigarettes per day. The patient has a history of asthma and hypertension, for which the patient regularly takes medication. Additionally, the patient has a history of treatment for pulmonary TB in 1990.

The patient was hospitalized for five days under the care of internal medicine and pulmonary specialists. On the first day, a molecular rapid test (TCM) showed MTB positive for rifampicin sensitivity. The chest X-ray revealed basal left-sided pulmonary TB with no enlargement of the heart (Figure 1). The pulmonary specialist prescribed anti-TB therapy (ATT) with anti-TB drugs (ATD) three tablets per 24 hours as a single dose.

On the third day of treatment, the patient complained of a swollen and painful scrotum, with no complaints of dysuria, penile discharge, suprapubic pain, or pelvic pain. Subsequently, testicular ultrasonography (USG) was performed, revealing that the Doppler examination showed an increase of vascularity observed in the epididymis and right and left testes and a hypoechoic mass with internal echoes seen in the right epididymis with a diameter of 1.82 cm (Figure 2). After the patient underwent USG, they were referred to the Department of General Surgery and scheduled for surgery due to suspicion of tumor presence based on the patient's USG results. Then, after being observed for several days, the patient was allowed to go home, as their condition improved.

Six days after being discharged from outpatient care, the patient returned to the Emergency Department complaining of weakness, cough, and black-colored bowel movements. The patient was readmitted and treated by a pulmonary specialist, along with internal medicine and urology specialists. Subsequently, diagnostic tests were performed. Hematology showed a hemoglobin level of 8.8 g/dL, leukocyte count of 2,060 /mm^3, hematocrit of 26 mm, platelet count of 190,000 /mm3, neutrophils of 76%, lymphocytes of 12%, and albumin level of 2.67 g/dL. Acid-fast bacilli (AFB) were detected in the urine with a positive 1+ result. Complete urine analysis indicated positive protein (100 mg/dL), positive blood (50 ery/UL), sedimentation rate of 4-5 for erythrocytes, full sedimentation rate for leukocytes, squamous epithelium of 3-4, and bacteria +2. Repeat ultrasound examination of the testes revealed increased vascularity observed in both the right and left epididymis and testes, along with a hypoechoic

mass with internal echoes seen in the right epididymis with a diameter of 1.82 cm. The medications administered during the hospital stay included pantoprazole injection 2x1, vitamin K injection 1x1, tranexamic acid injection 3x1, neurosanbe injection 1x1, 25% albumin infusion due to hypoalbuminemia, codeine 2x10 mg, and ATD three tablets every 24 hours as a single dose.

On the fifth day of treatment, the patient's eyes appeared jaundiced, prompting an examination of serum glutamic-oxaloacetic transaminase (SGOT), with results indicating 249.3 U/L, serum glutamic pyruvic transaminase (SGTP) 125.0 U/L, total bilirubin 3.58 mg/dl, and direct bilirubin 2.02 mg/dl. The pulmonary specialist postponed the ATD and replaced it with Norphagen injection, 2 ampoules, in 0.9% NaCl infusion. The urology specialist postponed the exploration and drainage due to elevated SGOT and SGPT levels. After three days, the patient's SGPT/SGOT levels were rechecked, with results of 30.2 U/L and 32.8 U/L respectively.

On the ninth day, the urology specialist took the patient to the operating room for scrotal exploration with drainage. Subsequently, hydrocele fluid was aspirated and sent for culture. On the 11th day, the patient was discharged while awaiting the results of AFB. The culture results indicated the presence of MTB, and the full treatment was handed over to the pulmonary specialist for the management of pulmonary TB and tuberculosis epididymo-orchitis. The pulmonary specialist prescribed Category 1 ATT.

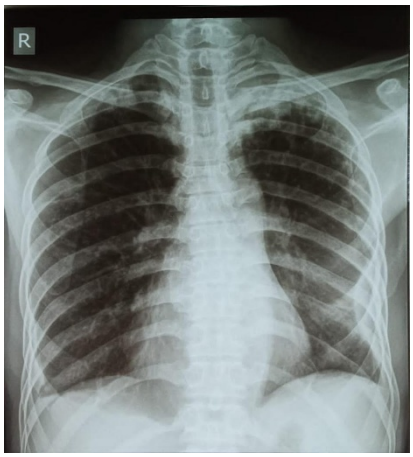

Figure 1. Revealed basal left-sided pulmonary TB with no enlargement of the heart

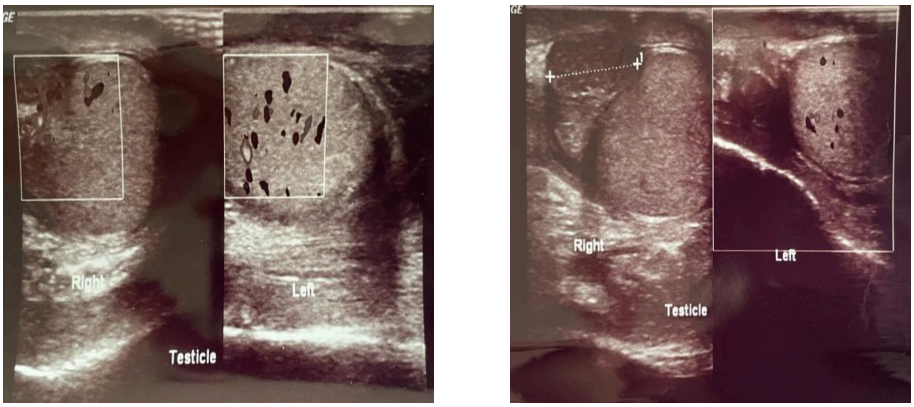

Figure 2. Doppler examination showed an increase of vascularity observed in the epididymis and right and left testes (left). A hypoechoic mass with internal echoes was seen in the right epididymis with a diameter of 1.82 cm (right).

DISCUSSION

MTB enters the lungs through airborne transmission, as it can survive in the air for several hours depending on environmental conditions. Subsequently, it traverses the respiratory tract through inspiration, reaching the bronchioles and alveoli. When a small number of TB bacteria are inhaled, they are promptly engulfed and digested by the macrophages of the immune system. However, if the TB bacteria are numerous and surpass the macrophages' capacity to engulf and digest them, they exit the macrophages upon the macrophages' death. The surviving TB bacteria then lodge in lung tissue and form a primary focus. This focus can emerge anywhere in the lungs, leading to inflammation in the lymphatic vessels toward the hilum.

This process leads to the formation of a primary complex, during which hematogenous spread can occur, potentially causing TB in other organs such as the kidneys and genitals.[2,4] In extrapulmonary TB, affected areas typically include the bones, pleura, lymph nodes, genitourinary system, peritoneal joints, and meninges.[5,6] Genital TB in men is part of UGTB, contributing to almost 8-15% of all types of TB outside the lungs.[6,7] From various literature sources, it has been found that the average age of patients with UGTB is around 20-40 years old, rarely occurring in children due to a long latent period.[8–10] The demographic characteristics of the patients in this case report resemble existing literature or studies, being male and aged 31 years old.

Genital TB in men is a rare occurrence and more commonly involves renal TB.[7] UGTB typically affects the prostate, seminal vesicles, vas deferens, testes, epididymis, or penis.[5,13] According to various literature sources, the spread of TB to the genital area often occurs through hematogenous dissemination.[7,13,14] The most commonly affected areas of genital TB are the epididymis and prostate.[15] TB can present as a highly painful scrotal mass known as epididymo-orchitis. Several articles state that 80% of patients with TB epididymo-orchitis experience severe scrotal pain, typically ranging from 40-44%, often caused by the complex and sensitive nature of the epididymis.[10] Clinically, it is challenging to differentiate scrotal TB from tumors or infarctions. Symptoms such as epididymal or testicular swelling associated with groin pain, fever, dysuria, and localized pain often lead to a diagnosis of either cancer or inflammation.[11] However, in this patient's case, there was no involvement of renal or prostatic TB. Instead, the testes and epididymis were affected. TB affecting the testes is extremely rare, occurring in only 3% of male genital TB cases.[16]

Diagnosis of pulmonary TB can be confirmed based on clinical symptoms, which are categorized into two groups, 1) Respiratory symptoms that include coughing up phlegm for more than 2 weeks, and 2) Additional symptoms such as coughing up blood, shortness of breath, fatigue, unintentional weight loss, malaise, night sweats without physical exertion, subfebrile fever for more than one month, and chest pain.[4] Typically, testicular TB is caused by TB epididymitis.[6] Many doctors experience delays in diagnosis due to the absence of typical clinical features. Furthermore, manifestations have varied presentations, with most cases presenting with pelvic pain, dysuria, and subsequent fever. Scrotal swelling without pain or tenderness occurs in about ⅓ of cases, often bilaterally. There may also be symptoms of irritation in the lower urinary tract, such as increased frequency of urination (initially during the day and then at night as the disease progresses) and suprapubic pain with pus in the urine.[9,11,12] In this case, the patient presented with complaints of productive cough and decreased appetite without coughing up blood, shortness of breath, fatigue, unintentional weight loss, malaise, night sweats, or chest pain. Regarding urogenital symptoms, the patient complained of pain in both testicles and swelling in the scrotal area, without fever, increased frequency of urination, pus in the urine, suprapubic pain, or dysuria. Clinical examination of patients with UGTB requires further investigation, such as ultrasound and biopsy.[6]

Chest radiography should be performed in all suspected cases. Although it may show active or old pulmonary TB lesions, typically, 50% of patients have negative chest radiographs. Rapid molecular bacteriological testing can identify MTB and simultaneously perform drug sensitivity testing, usually using GeneXpert MTB/RIF (rifampicin sensitivity testing).[11] Literature mentions that culturing urine samples obtained in the morning has been used as a test and standard to confirm UGTB, and repeating the collection three to six times can increase sensitivity to 80-90%.[10] However, urine cultures may yield negative results.[17] USG is the best step in diagnosing scrotal pathology and distinguishing potential malignancy, testicular torsion, and epididymitis.[18,19] USG can also detect complications such as abscesses and infarctions, especially with Doppler examination.

Findings from USG in TB epididymo-orchitis depend on the pathological stage of disease development and are classified as follows, 1) Diffuse enlargement, heterogeneous hypoechoic; 2) Diffuse enlargement, homogeneous hypoechoic; 3) Nodular enlargement, heterogeneous hypoechoic; and 4) Miliary.[15,20] USG examination is useful but not highly specific, unlike Doppler, which can help differentiate testicular TB from tumors, typically showing central vascularization. TB exhibits peripheral vascularization due to granulomas and reduced flow to the center.[7]

A biopsy is an important diagnostic procedure. Fine-needle aspiration biopsy (FNAB) and cytology can show epithelioid granulomas, and AFB can be detected with acid-fast staining, which is crucial for diagnostic accuracy and treatment.[16,21] Subsequently, various literature suggests performing a computed tomography (CT) scan, which is recommended when the margins of the mass are unclear on USG examination. However, in this case, a CT scan was not performed.

On the first day, the patient underwent a radiological examination, revealing findings suggestive of basal left lung TB without hilar shadow enlargement. Furthermore, the result of the molecular biomolecular testing (GeneXpert) was positive for rifampicin sensitivity. Subsequently, to support the diagnosis of TB epididymo-orchitis, a USG examination was conducted on the patient, showing a hypoechoic mass with internal

echoes within the right epididymis, measuring 1.82 cm in diameter. Additionally, on conducting USG and Doppler examinations of the testes, increased vascularity was observed in both the right and left epididymis and testes. Testicular exploration and fine-needle aspiration were then performed, initially delayed due to the patient's elevated SGPT and SGOT levels. Bacterial culture for AFB revealed MTB and all supportive investigations conducted were consistent with existing literature.

According to various urological literature, there has been a change in the treatment approach. It had initially spanned 18-24 months but has now been reduced to six months, which has become the current standard of treatment. For newly diagnosed patients, a two-month *intensive phase* of treatment is administered, consisting of rifampicin (8-12 mg/kg), isoniazid (4-6 mg/kg), pyrazinamide (20-30 mg/kg), and ethambutol (15-20 mg/kg). This is followed by a four-month *continuation phase* with a regimen of rifampicin (8-12 mg/kg) and isoniazid (8-12 mg/kg). Conversely, patients with low immune resistance or co-infection with HIV/AIDS (acquired immunodeficiency syndrome) require a longer duration of treatment, typically 9-12 months. Similarly, in line with the TB 2021 guidelines, the treatment regimen includes both an intensive phase and a continuation phase for patients with drug-sensitive TB.[4,10] This corresponds to the management provided by pulmonary specialists using a fixed-dose combination (FDC) based on the patient's body weight.

The patient, in this case, weighs 50 kg. The medication during the intensive phase consisted of three tablets every 24 hours as a single dose, with each tablet containing rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol 275 mg, taken for two months. Subsequently, during the continuation phase, the patient was given three tablets every 24 hours as a single dose, with the regimen containing rifampicin 150 mg and isoniazid 57 mg, taken for 16 weeks. Surgical intervention in cases of epididymo-orchitis is indicated when there is a visible abscess or unresponsive sepsis despite therapy, urinary tract obstruction, and tissue damage. Surgical procedures may include urinary diversion, abscess drainage, or even removal of the infected organ (orchidectomy).[10]

What about the prognosis of patients with TB epididymo-orchitis? Actually, favorable outcomes can be achieved in patients who adhere to treatment, are young, have no comorbidities, and, most importantly, have good social support.[11] After more than two months of treatment, the patient returned for a follow-up and showed clinical improvement in both pulmonary and urogenital symptoms.

CONCLUSION

Tuberculous epididymo-orchitis is a rare condition, often overlooked by many physicians due to its non-specific symptoms. Therefore, meticulous attention and comprehensive evaluation from taking the history, physical examination, and diagnostic tests are crucial. Early diagnosis and medical management can help prevent unnecessary surgical interventions and complications associated with the disease.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Data collection and manuscript writing: YAP. Review and revision: YAP, LLP, BL, CH, SHA. All authors contributed and approved the final version of the manuscript.

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