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Review Article

Tuberculosis of the Testis, Epididymis, Scrotum and Scrotal Contents and Tuberculosis of the Penis and Urethra: A Review and Update

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Abstract

Cases of tuberculosis of the testis, epididymis, scrotum and or the penis including the urethra are very rare even though pulmonary tuberculosis is common globally. In view of the fact that tuberculosis of the scrotum and scrotal contents and penis is rare, it would be envisaged that majority of clinicians would not have encountered a case of this infection during their training and professional practices. Tuberculosis which has afflicted either the scrotum, testis, epididymis and penis does manifest with non-specific symptoms that simulate symptoms of more common conditions of the scrotum, scrotal contents and penis and hence a high index of suspicion is required in order to establish a prompt correct diagnosis in order to initiate the correct treatment. Tuberculosis of the testis and tuberculosis of the scrotal contents as well as the penis usually manifests as is as painful or painless testicular swelling with or without scrotal ulceration or discharging sinus. Infertility may occur. Epididymal involvement is usually seen in testicular TB. In most cases, genital TB is associated with TB involvement of kidneys or lower urinary tract. Ultrasound (USG) and USG-guided fine needle aspiration cytology of testicular swelling confirm the diagnosis. Anti-TB chemotherapy is the mainstay of treatment to ensure the complete resolution of the lesion. However, in very few cases, orchidectomy is required for both diagnosis and treatment. Tuberculosis of the scrotum would tend to present as a nodule, ulceration, mass or bleeding or rash on the scrotum. Tuberculosis of the penis would tend to manifest as a nodule, ulceration, a mass or masses on the penis, a urethral fistula or voiding problems. Tuberculosis of the scrotal contents, scrotum or penis may occur alone or there may be a history of contemporaneous pulmonary tuberculosis or tuberculosis elsewhere in the body or there may be a history of an antecedent tuberculosis elsewhere in the body which had been treated before. Isolation and culture of M. tuberculosis, fine needle aspiration cytology (FNAC) and polymerase chain reaction (PCR) may provide an accurate diagnosis of tuberculosis of the scrotum and scrotal contents as well as the penis even though in some cases histology may be the only confirmatory diagnostic modality. Anti-TB chemotherapy is the mainstay of treatment, however, in few cases, orchidectomy is required for both diagnosis and treatment of tuberculosis of the testis and epididymis. Also, on rare occasions when tuberculosis of the penis is misdiagnosed initially as possibly malignancy of the penis, partial amputation of the penis may be undertaken before the diagnosis of tuberculosis of penis is finally confirmed. Nevertheless, if a high index of suspicion for the possible diagnosis of tuberculosis of the scrotum and scrotal contents is maintained then early biopsy of the scrotal and intra-scrotal lesion or penile lesion for pathology examination would help establish the diagnosis of tuberculosis so that mutilating surgery would be avoided. The association between infertility and testicular and epididymis mass should alert the clinician to have a high index of suspicion for tuberculosis. Diagnosis of tuberculosis of the scrotum, testis, epididymis, and or penis can be confirmed by the histopathology examination finding of caseating Granuloma with multi-nucleated Langhan's giant cell upon pathology examination of biopsy specimen of the lesion.

Conclusions:

- Tuberculosis of the testis, epididymis, scrotum, penis, and urethra are rare clinical entities which all clinicians should have a high index of suspicion for in order to ensure they establish a prompt diagnosis for in order to avoid misdiagnosis as well as delay in the provision of appropriate early treatment of their patients who have the condition.

- Cases of tuberculosis of the testis, epididymis, scrotum, penis, and urethra do simulate many common clinical conditions of the testis, epididymis, scrotum, penis as well as urethra.
- Biopsy of lesions of the testis, epididymis, scrotum, penis, and urethra for pathology examination is very useful for the diagnosis of tuberculosis of the testis, epididymis, scrotum, penis, and urethra in order to treat patients who have the disease appropriately and to avoid the undertaking of mutilating surgery and patients who have been treated for this disease should be followed-up carefully over a long time period to ensure the patients do not develop recurrence and to identify quickly patients who develop recurrence early in order to quickly effective and appropriate treatment for the early recurrent disease so ss to achieve satiety of all patients who are treated for the disease.
- Tuberculosis of the testis, epididymis, scrotum, penis, and urethra, could manifest as de novo disease or they may manifest contemporaneously (synchronously) with pulmonary tuberculosis or tuberculosis elsewhere of at times pursuant to previous treatment of patients who had undergone treatment for pulmonary tuberculosis or tuberculosis elsewhere in the body.
- Tuberculosis of the testis and epididymis may on rare occasions manifest as infertility as well as pursuant to treatment of tuberculosis of the testis and epididymis, some patients may manifest with infertility subsequent to complete and appropriate treatment of the disease related to scarring and obliteration of the lumen of the epididymis and perhaps obliteration of the ejaculatory duct as well as scarring within the testes of the disease is bilateral.

Keywords: tuberculosis; testis; epididymis; scrotum; penis; urethra; biopsy; histopathology; langhan's giant cell; caseating granuloma; chemotherapy; pulmonary; recurrence; follow-up. high index of suspicion; rare

Introduction

It has been iterated that testicular tuberculosis (TB) is an uncommon rare form of genitourinary TB and that testicular TB usually does tend to manifests as painful or painless testicular swelling with or without scrotal ulceration or discharging sinus. [1] The ensuing statements had also been made about cases of tuberculosis (TB) of the testis. [1]

- Infertility might occur in cases of TB of the testis.
- Epididymis involvement is usually encountered in cases of testicular TB.
- In majority of cases, genital TB had tended to be associated with TB involvement of kidneys or lower urinary tract.
- Ultrasound (USG) scan and USG-guided fine needle aspiration cytology of testicular swelling for pathology examination would confirm the diagnosis if the condition is suspected and the biopsy is undertaken.
- It has been pointed out that anti-TB chemotherapy is the mainstay of treatment to ensure the complete resolution of the lesion. Nevertheless, in very few cases, the undertaking of orchidectomy had been required for both the diagnosis and treatment of the lesion.

Considering the fact that Tuberculosis (TB) of the testis and epididymis does tend to simulate other more common lesions of the testis and epididymis and the fact that TB of the testis and epididymis is not common, it would be envisaged that a number of clinicians may not be familiar with the manifestations of the lesion and hence there could be delay in the diagnosis of the lesion. A high-index of suspicion is required in order to establish a quick diagnosis of TB of the testis and epididymis. Additionally, TB of the scrotum and penis is very rare and hence majority of clinicians would not have encountered a case of TB of the scrotum and penis during their training as well as their clinical practices and they may not be familiar with the manifestations of TB of the scrotal contents and penis. The ensuing review and update of the literature on TB of testis and epididymis and TB of the scrotum has been divided into two parts: (A) Overview which has discussed general aspects of TB and TB of the testis and epididymis, penis and scrotum and (B) Miscellaneous Narrations Related to Some Case Reports, Case Series and Studies Related to TB of the testis and epididymis with few discussions related to TB of the scrotum and penis.

Aims

To review and update the literature on Tuberculosis of the testis, epididymis, scrotum, penis, and urethra.

Methods

Internet data bases were searched including: Google; Google Scholar; PUBMED and Yahoo. The search words that were used included Tuberculosis of the testis, tuberculosis of epididymis, tuberculosis of the scrotum, tuberculosis of the penis, and tuberculosis of the urethra. Sixty-five (65) references were identified which were used to write the article that was divided into two parts: (A) Overview which has discussed various general as aspects of tuberculosis and Tuberculosis of the testis, epididymis, scrotum, penis, and urethra, and (B) Miscellaneous Narrations From Some Case Reports, Case Series and Studies related to Tuberculosis of the testis, epididymis, scrotum, penis, and urethra.

[A} Overview

Definition / general statements [2]

- It has been pointed out that tuberculosis of the testis is not common and that tuberculosis orchitis usually does affect men who are aged between 40 years and 59 years and who develop sudden onset of tender testicular mass, that is associated with variable fever
- It has also been iterated that tuberculosis of the testis might develop as a response to acid fast products of disintegrated sperm, postinfectious or due to trauma or sarcoidosis
- It has additionally been stated that tuberculosis of the testis does simulate pyogenic epididymo-orchitis.
- It has also been pointed out that tuberculosis of the testis is a benign disease, even though granulomatous inflammation may be associated with seminoma
- It has been advised that cultures should be undertaken to exclude infectious process of the testis and epididymis including: brucellosis, leprosy, sarcoidosis, syphilis, and tuberculosis (TB)

- It has been pointed out that tuberculosis of the testis and epididymis is a granulomatous ischemic lesion:
    - Which usually tends to affect the head of epididymis
    - And that tuberculosis of the testis and epididymis could be due to ischemia with secondary granulomatous reaction and scarring [3]

Gross description [2]

- It has been iterated that tuberculosis of the testis and epididymis is a solid, unilateral nodular enlargement of testis which simulates lymphoma of the testis and epididymis.

Microscopic (histologic) description [2]

- It has been documented that in cases of tuberculosis of the testis and epididymis microscopy examination of the testis and epididymis does tend to demonstrate lymphocytes and plasma cells infiltrating the interstitium and they surround the seminiferous tubules
- It has also been pointed out that microscopy examination of the testis and epididymis in cases of tuberculosis of the testis and epididymis does tend to show Giant cells and histiocytes that simulate actual granulomas but which are not actual granulomas
- It has been pointed out that tuberculosis of the testis and epididymis is a Granulomatous ischemic lesion which has tended to be associated with the following features:
    - Zone of necrosis involving efferent ducts and interstitial connective tissue, with adjacent lymphocytes and macrophages tend to be visualized upon microscopy examination of the specimen of the testis and epididymis
    - Microscopy examination of the testis and epididymis also does tend to demonstrate macrophages which form large clusters with cholesterol crystals and foreign body type giant cells in duct lumen
    - Microscopy examination of the testis and epididymis also does show intratubular epithelial regeneration and proliferation of small ducts showing epithelial regeneration and numerous spermatozoa in their lumen
    - Microscopy examination of the testis and epididymis specimen also does demonstrate associated with the aforementioned features ceroid granuloma, spermatic granuloma and epidermoid metaplasia of the efferent ducts

Differential diagnosis [2]

Some of the conditions that need to be considered as differential diagnoses to be excluded from tuberculosis of the testis and epididymis include the following: [2]

- Granulomatous inflammation associated with seminoma.
- Infection or inflammation [4]
- Lymphoma of the testis.

Laboratory tests

Haematology blood tests.

Routine haematology blood tests including full blood count INR and coagulation screen tend to be undertaken in the initial assessment of patients who manifest with non-specific symptoms related to the penis, testis, epididymis and scrotum. The results may be normal but the white cell count and lymphocyte count levels would tend to be raised but these results would tend not to be specific for the establishment of a specific diagnosis but in the scenario of anaemia, the anaemia would be investigated and treated appropriately to improve upon the general health the patient.

Biochemistry blood tests.

Routine biochemistry blood tests including: CRP, serum urea and electrolytes, liver function tests, bone profile, and random blood glucose tests tend to be undertaken in all cases of tuberculosis of the penis, scrotum, and intra-scrotal contents as part of the general assessment of all patients but generally the results tend to be non-specific and non-diagnostic of tuberculosis of the penis and intra-scrotal contents; nevertheless, if there is evidence of an abnormality in the results of any of the aforementioned tests, it would be investigated and treated appropriately to improve upon the general health of the patient.

Radiology imaging

Chest Radiograph

Majority of cases of tuberculosis tend to afflict the lungs and in cases of tuberculosis of the penis and intra-scrotal contents that are contemporaneous with pulmonary tuberculosis or disseminated tuberculosis, chest radiograph would demonstrate radiology image features of tuberculosis pneumonitis that should alert the clinician to be aware of the possibility of tuberculosis of the penis or scrotal contents.

Ultrasound scan

Ultrasound scan of the scrotum and scrotal contents and the penis would tend to demonstrate features of various types of hypoechoic lesions as well as at times calcification(s) within the testis or and extra-testicular areas of the scrotum, and the calcifications as well as evidence of pulmonary radiograph features of contemporaneous tuberculosis should alert the clinician to suspect the possibility of tuberculosis of the penis, scrotum, or scrotal contests so that biopsy of the lesion can be taken for histopathology examination confirmation of tuberculosis can be confirmed so as to enable commencement of anti-tuberculosis combination therapy and to avoid the undertaking of mutilating excision surgery in many cases.

Computed tomography scan

Computed Tomography (CT scan) of the testes, penis, and scrotal contents would demonstrate various types of hypo-dense areas that could be targeted for biopsy for histopathology examination that would confirm the diagnosis of tuberculosis which would enable commencement of anti-tuberculosis treatment as well as avoidance of the undertaking of mutilating excision surgery including orchidectomy for testicular tumour.

Magnetic Resonance Imaging Scan

Magnetic Resonance Imaging (MRI) CT scan of the testes, penis, and scrotal contents would demonstrate various types of hypo-dense areas that could be targeted for biopsy for histopathology examination that would confirm the diagnosis of tuberculosis which would enable commencement of anti-tuberculosis treatment as well as avoidance of the undertaking of mutilating excision surgery including orchidectomy for testicular tumour.

Diagnosis

- Diagnosis entails the undertaking of detailed clinical history including current and past medical history, immunizations as

well as current or previous treatment for tuberculosis. History of contemporaneous tuberculosis elsewhere should alert the clinician of contemporaneous tuberculosis of the penis or scrotal contents.

- The confirmation of the diagnosis of tuberculosis of the penis, and intra-scrotal contents tend to be confirmed based upon pathology examination of biopsy specimens of orchidectomy specimens containing the lesion and when the specimens are sent for culture in the microbiology department, there could be a growth of a tuberculosis organism. By confirming the diagnosis of tuberculosis of the penis and intra-scrotal contents, the undertaking of mutilating excision surgery including radical orchidectomy which would not be necessary.
- The undertaking of radical orchidectomy for intra-scrotal lesions of the testis that had inadvertently been misdiagnosed as malignant tumours had been utilized as treatment of lesions of the testis and intra-scrotal contents which had confirmed the diagnosis of treatable benign tuberculosis lesions for which radical excision of the lesions would not have been undertaken if a high index of suspicion for tuberculosis had been exercised and a biopsy had been undertaken instead of extirpative surgery.

Treatment

- Treatments for tuberculosis of the penis and intra-scrotal contents should entail anti-tuberculosis treatment following pathology and microbiology examination confirmation of tuberculosis.
- On rare occasions the undertaking of radical extirpative surgery including orchidectomy had been done and following confirmation of the diagnosis of tuberculosis, anti-tuberculosis treatment had been provided
- After the diagnosis of Tuberculosis of the testis, epididymis, scrotum, penis, and urethra, a combination of chemotherapy and local excision of the lesions had been successful in the treatment of various cases effectively, but on very rare occasions, as a results of provisional misdiagnosis, some cases had been treated by extirpative surgery before the corrective definite diagnosis had been establishes based upon pathology examination of the excised lesions and some these operations had included orchidectomy based upon a presumptive diagnosis of a testicular tumour and partial penectomy pursuant to a provisional diagnosis of malignant penile tumour and after the correct diagnosis was made, then chemotherapy was next provided to these rare patients.

Outcome

- The outcome following anti-tuberculosis-treated has tended to be good with resolution of the lesions.
- Nevertheless, some cases of tuberculosis of the epididymis and testes had been ensued by the subsequent development of infertility following ant-tuberculosis treatment.

[B] Miscellaneous Narrations and Discussions From Some Case Reports, Case Series, and Studies Related to Tuberculosis of the Testis and Epididymis As Well As Some Cases Of The Scrotum And Penis.

Scrotal tuberculosis

El-Keky et al. [5] iterated that Scrotal tuberculosis (TB) is a rare presentation of extra-pulmonary tuberculosis and that intra-scrotal tuberculosis includes tuberculous orchitis and epididymitis. It has also been stated that scrotal tuberculosis is uncommon and it does represent only about 3% of cases of genitourinary tuberculosis. [5] [6] The ensuing summations had been made about scrotal tuberculosis:

- Scrotal TB does manifest as a painless or slightly painful scrotal mass and so it tends to be difficult to differentiate from typical epididymoorchitis or other conditions such as testicular tumours or infarction of the testis [5] [7].
- Intra-scrotal TB infection usually tends to affect the epididymis first and then TB can affect the testis if it is not treated.
- It has been postulated that TB does occur due to a retrograde extension of TB from the prostate gland and seminal vesicles as well as hematogenous spread [5] [7].
- Scrotal tuberculous infection typically commences within the tail of the epididymis and the ductus deferens. [5].
- Tuberculous epididymitis does tend to appear as a diffuse heterogeneous predominantly hypoechoic enlarged epididymis or an intrinsic focal nodular hypoechoic lesion.
- TB epididymitis usually shows increased colour Doppler flow, differentiating it from infarction.
- Bilateral involvement of the epididymis by tuberculosis is common, unlike other non-tuberculous infections.

With regard to tuberculous orchitis, it had been stated that tuberculous orchitis is usually preceded or associated with epididymitis and that different ultrasound scan patterns of tuberculous orchitis had been described as follows [5] [7]:

- Diffusely enlarged heterogeneously hypoechoic testis tends to be found in some cases
- Diffusely enlarged homogeneously hypoechoic testis also does tend to be found in some cases of tuberculous orchitis.
- Nodular enlarged heterogeneously hypoechoic testis has tended to be visualized in some cases of tuberculous orchitis
- Multiple small hypoechoic nodules within an enlarged testis (miliary type) had been encountered in some cases of tuberculous orchitis

Other associated findings in tuberculous orchitis had been summated as follows: [5]:

- thickened scrotal skin had been found in some cases of tuberculous orchitis [5]
- Scrotal sinus tract had been found in some cases of tuberculous orchitis
- Scrotal hydrocoele
- Scrotal abscess
- Intra-scrotal extra-testicular calcification: at epididymis and tunica vaginalis
- evidence of tuberculosis infection elsewhere

With regard to treatment and prognosis of tuberculous orchitis, the treatment has tended to entail the following:

- Anti-tuberculous chemotherapy which has remained the mainstay of treatment.

- Orchiectomy has been on rare occasionally been required for the diagnosis or treatment of tuberculous orchitis bur this may result in the development of infertility [**8**].

Some of the differential diagnoses of tuberculous orchitis had been stated to include the ensuing clinical entities:

- Bacterial epididymoorchitis
- Sarcoidosis of the testis
- Lymphoma of the testis
- Primary tumours of the testis
- Metastases to the testis
- Haematoma of the testis
- Infarction of the testis

Salient points related to tuberculous epidydimo-orchitis had been summated by el-faky et al. [5] as follows:

- A heterogeneous, enlarged epididymis tends to be more commonly encountered with tuberculous rather than non-tuberculous epididymitis, which usually does tend appear homogeneous in appearance.
- Bilateral involvement is more commonly encountered in cases of tuberculous epididymo-orchitis
- Failure of antibiotic treatment for epididymo-orchitis should raise suspicion for the possibility of a tuberculous aetiology
- The presence of pulmonary or extrapulmonary tuberculosis infection elsewhere does make scrotal presentations more likely to be of tuberculous origin
- The associated features which are unusual in non-tuberculous epididymo-orchitis (such as intra-scrotal, extra-testicular scrotal calcifications, scrotal abscess, and sinus tracts) are helpful clues to establish the diagnosis

Das et al. [1] stated the following:

- Pulmonary tuberculosis (TB) is the most common form of TB disease.
- Extra-pulmonary TB (EP-TB) is seen only in 10% to 15% cases and lymph nodes are the most common site for EP-TB in India. Genital TB is uncommon, and testicular TB is further rare, comprising only 3% of genital TB. [6]
- Commonly, it occurs during disseminated TB, but isolated testicular TB is extremely rare.
- In majority of cases, it clinically simulates other testicular lesions, such as testicular tumour, infarction, or even testicular torsion.
- Middle-aged males, especially who are 20 years to 40 years of age are most commonly affected, and presented with painful or painless scrotal swelling with or without discharging sinus. Infertility may occur.
- In the elderly age group, diagnostic dilemma develops between testicular malignancy and testicular TB, as the first one is more common than the latter.
- Ultrasound scan (USG) of testes and USG-guided fine needle aspiration cytology (FNAC) do confirm the diagnosis.
- Sometimes, testicular biopsy is necessitated, especially in the elderly age group as exclusion of testicular malignancy, in this age group is main concern.
- Anti-TB chemotherapy comprising rifampicin, isoniazid, pyrazinamide, and ethambutol is the mainstay of treatment.
- They were reporting a rare case of isolated testicular TB in a 20-year-old male patient after getting the written informed consent from him.

Das et al. [1] reported a 20-year-old man who had presented with a painful, left-sided testicular swelling without any discharging sinus or scrotal ulceration over the preceding 2 months. He did not have any history of any respiratory symptom, fever, anorexia, and significant weight loss. He was a non-smoker and non-alcoholic. His clinical examination was generally normal, except for the finding of multiple, matted, nontender, firm enlarged inguinal lymph nodes on the left side. His pulse rate was documented to be 80 beats/minute, regular, respiratory rate, 20 breaths/minute, temperature, 97°F, and his blood pressure was 120/80 mmHg. His systemic examination did not demonstrate any abnormality. His right scrotum was normal; on the other hand, his left sided testicular swelling that measured 3 cm × 2.5 cm in size which was noted to be gradually increasing. The testicular swelling was tender, hard, elliptical in shape, and not fixed with the overlying scrotal skin, and the clinician was able to go above the mass. There was no discharging sinus or scrotal ulceration found. The results of his routine haematology and biochemistry blood tests with the inclusion of his fasting blood glucose were normal. Blood for anti-HIV types 1 and 2 antibodies was documented to be nonreactive. His chest radiograph on the posteroanterior view was noted to be normal. Mantoux test (5 TU) was undertaken which was reported to be positive (16 mm induration after 72 h). He underwent ultrasound scan (USG) of his testes which demonstrated that his left testis was enlarged and it had measured 4.8 cm × 2.6 cm. Furthermore, the ultrasound scan demonstrated one 3.2 cm × 2.4 cm × 2.7 cm sized hetero-echoic space occupying lesion with hypoechoic components and small cystic areas which were visualized within the lower pole of his left testis [See figure 1]. The testicular margin was found to appear ill-defined within the lower pole. Upon Doppler ultrasound scanning, increased blood flow was found within and periphery of the lesion. There was no evidence of hydrocele. His left epididymis, spermatic cord, and scrotal skin were noted to be normal. His right testis was found to be normal. Multiple, enlarged lymph nodes were observed within his left inguinal region upon his ultrasound scan (USG). He had USG of his abdomen which did not reveal any abnormality. He underwent USG-guided fine needle aspiration cytology (FNAC) biopsy of his left testicular swelling, and pathology examination of the specimen showed occasional ill-formed epithelioid cell granulomas in a background of large amount necrosis and mixed inflammatory cells. Ziehl-Neelsen staining of pus and blood mixed particulate that was obtained by fine needle aspiration revealed acid-fast bacilli (AFB) [see figure 2]. FNAC of the enlarged inguinal lymph nodes on left side demonstrated granulomatous inflammation with caseation. Microscopy and biochemical examination of his urine was found to be normal. He underwent endoscopy examination of the lower urinary tract which was normal. Hence, the diagnosis was left sided isolated testicular tuberculosis (TB) with ipsilateral inguinal lymphadenopathy. As the patient did not have any history of anti-TB chemotherapy, category I anti-TB treatment regimen (thrice-weekly regimen which comprised of rifampicin: 450 mg/day, isoniazid: 600 mg/day, pyrazinamide: 1500 mg/day, and ethambutol: 1200 mg/day for first 2 months, followed by rifampicin and isoniazid for next 4 months) was provided as given therapy. Complete resolution of left testicular swelling and pain was observed and documented at the end of 6 months of his treatment.

Figure 1

Ultrasound of left testis showing a heteroechoic space occupying lesion. Reproduced from: [1]

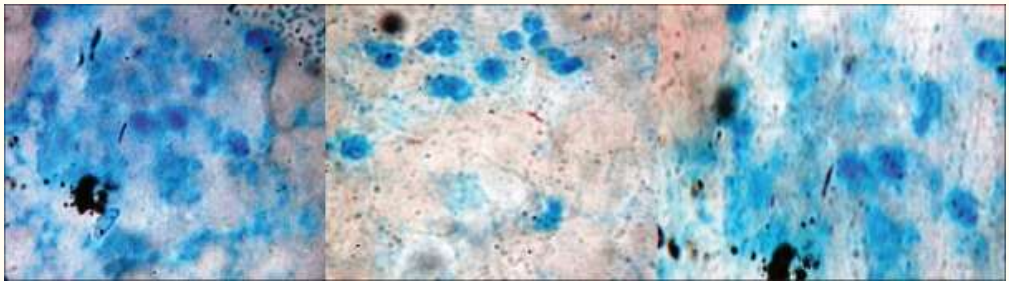


Figure 2: Ziehl-Neelson staining of fine needle aspiration cytology materials obtained from the left testicular swelling showing two acid fast bacilli (x 100). Reproduced from [1]

Das et al. [1] made the ensuing summating discussions:

- TB represents a leading cause of death globally, especially within the developing countries which are TB endemic zones, like India.
- Emergence of drug resistance TB as well as rapid increase in the incidence of HIV infection has made the world's scenario further critical. Genitourinary
- It has been iterated that TB is an unusual manifestation of TB and comprises 8% to 15% of EP-TB. [7]
- It had also been pointed out that isolated genital involvement is seen in 28% patients of genitourinary TB. [9]
- It has also been stated that tuberculosis is more common in males.
- It has been pointed out that the commonest site of genital TB is the epididymis in men, followed by the seminal vesicles, prostate, testis, and the vas deferens. [10]
- The mechanism of dissemination of tubercle bacilli into the scrotal sac structures is considered to be controversial. It is believed that, in majority of cases, TB epididymo-orchitis does tend to develop from retrograde spread of tubercle bacilli from the affected urinary tract into the prostate via reflux, followed by canalicular spread to the seminal vesicle, deferent duct, and epididymis. [11] [12]
- Nevertheless, TB bacilli might also gain entry via the haematogenous as well as lymphatic spread. In most cases, testicular involvement is due to local spread or retrograde seeding from the epididymis, and rarely by hematogenous spread. [11] [12] Hence, TB orchitis without epididymal involvement is extremely uncommon, which we present in this case report.
- TB orchitis does tend to occur common with TB involvement of the lower urinary tract, even of the kidneys. Hence, TB orchitis does manifest with lower urinary tract symptoms, especially irritative voiding symptoms and haematuria. Epididymo-orchitis, prostatitis, scrotal swelling with or without discharging sinus are other presentations. Garbyal et al. and Shugaba et al. had reported cases of isolated TB orchitis manifesting with scrotal ulceration. [13] [14]
- With regard to their reported case, the initial manifestation was only the left sided hard, painful testicular swelling without any discharging sinus, scrotal involvement, or urinary tract symptoms.
- Ultrasound scan (USG) of testis is a very useful investigation for the diagnosis of TB orchitis.
- TB involvement of the epididymis and testis may be classified into four types depending upon the USG finding as follows:
    - (1) Diffusely enlarged, heterogeneously hypoechoic;
    - (2) diffusely enlarged, homogenously hypoechoic;
    - (3) nodular enlargement, heterogeneously hypoechoic;

  - and (4) miliary TB. [15]

- Seminoma and lymphoma had tended to be mostly homogenous while non-seminomatous tumours tend to be heterogeneous. [16]
- Colour Doppler USG is useful for the differentiation of testicular TB from testicular torsion, as blood flow within the testis is reduced or absent, whereas blood flow tends to be increased in subjects who have inflamed testis. [17]
- The finding of the epithelioid granulomas and AFB on Ziehl-Neelsen staining in the ultrasound scan-guided (USG-guided) FNAC materials obtained from the testicular swelling does confirm the diagnosis of TB orchitis.
- Nevertheless, the presence of AFB is again extremely uncommon, especially in an isolated TB orchitis in an immunocompetent male, which they had reported in their case.
- On the contrary, FNAC should be the first investigation where TB orchitis is suspected, especially in the scenario of young individuals, as it is possible to confirm the diagnosis of TB orchitis without testicular biopsy or orchidectomy.
- Six-month regimen of anti-TB chemotherapy comprising of rifampicin, isoniazid, pyrazinamide, and ethambutol for the first 2 months, followed by rifampicin, and isoniazid for next 4 months has tended to be very much effective to ensure the complete resolution of the TB lesion of the testis.
- Sometimes, the undertaking of surgery could be required. [10]

Badmos et al. [18] stated that isolated tuberculous epididymo-orchitis may closely simulate testicular tumour particularly in patients who have no history of systemic tuberculosis (TB) thereby presenting a diagnostic and therapy challenges. Badmos et al. [18] reported a 44-year-old man who had manifested with 4 months history of left scrotal mass for which he had undergone left orchidectomy following a presumptive diagnosis of testicular tumour. Histopathology diagnosis of tuberculosis of testis was subsequently made. Even though the patient was thereafter referred for antituberculosis treatment at the local tuberculosis treatment centre, he defaulted after commencing treatment. Badmos et al. [18] concluded that adequate evaluation of patients who have testicular mass by means of abdominal and scrotal ultrasound coupled with fine needle aspiration cytology is critical for the establishment of diagnostic accuracy, optimal treatment and possibility of avoiding surgery in those who have testicular tuberculosis.

Chiu et al. [19] stated that tuberculous epididymo-orchitis is an uncommon complication of intravesical bacillus Calmette–Guérin (BCG) immunotherapy for bladder cancer. Chiu et al. [19] reported a patient who had urinary bladder cancer and a history of intravesical BCG immunotherapy who had manifested with right scrotal pain for 1 week. A heterogeneous, hypoechoic, and solid mass encompassed by increased blood flow in the right testis was visualized upon scrotal echogram. His urine ordinary and tuberculosis culture yielded negative results. After failure of antibiotic therapy and the inability to exclude tumour, the diagnosis was confirmed by radical orchiectomy. Acid-fast staining of pus in the tumour and tumour tissue was positive, and a pus culture was positive for Mycobacteria tuberculosis complex. Right radical orchiectomy was undertaken, and anti-tuberculosis treatment with rifampicin, isoniazid, ethambutol, and pyrazinamide was provided. The patient was at the time of publication of the article under anti-tuberculosis treatment, and no significant adverse effects had been identified. Chiu et al. [19] advised that BCG-related epididymo-orchitis should be suspected in patients who have a history of intravesical BCG immunotherapy if the empiric antibiotic treatment typically used to treat common epididymo-orchitis has failed. Chiu et al. [19] made the following conclusions:

- Intravesical BCG immunotherapy is a useful treatment for NMIBC after TURBT; nevertheless, BCG-related tuberculosis epididymo-orchitis should be kept in mind.
- Even though the symptoms and signs of tuberculosis epididymo-orchitis often tend to be non-specific, ultrasound and urine-based tuberculosis screening before empiric antibiotic treatment could be used to make the diagnosis.
- It could be difficult to differentiate BCG-related epididymo-orchitis from malignancy based upon the clinical manifestation and image findings.
- Orchiectomy could be undertaken as a diagnostic and therapeutic procedure.

Sadeghi et al. [20] stated that Tuberculous epididymo-orchitis is a rare complication after intravesical bacilli Calmette-Guerin therapy for non-muscle invasive urinary bladder cancer and that spread of granulomatous disease via the genitourinary tract specifically to the testes does occur in 0.4% of treated patients. Sadeghi et al. [20] stated the following:

- It has pointed out that the earliest microbiological confirmation of tuberculosis (TB) dates back to the Neolithic Period approximately 9000 years ago [21]
- TB is known as the great mimicker and could evade diagnosis due to clinical and radiologic overlap with several disease processes.
- TB reached epidemic proportions in the 18th and 19th centuries.
- In 1882, Robert Koch isolated the tubercular bacillus.
- Nearly a century later, a Canadian urologist used bacille Calmette-Guerin (BCG) to treat recurrent non-invasive urinary bladder cancer via weekly intravesical instillation for 6 weeks. [22]
- Intravesical BCG was approved by the Food and Drug Administration in 1990 for the treatment of carcinoma in situ of the urinary the bladder and had currently also been approved for the treatment of stage TaT1 tumours that are at high risk for the development of recurrence. [23]
- Adjuvant treatment with BCG was currently the most effective strategy in non-muscle invasive urinary bladder cancer following trans-urethral resection [24]
- Intravesical BCG is effective in prophylaxis against both recurrence and progression of intermediate or high-risk non–muscle invasive bladder cancer.
- A standard dose of BCG is administered by diluting a powdered vial of BCG vaccine. After a urethral catheter is inserted, the urinary bladder is drained and the BCG solution is infused into the bladder where it remains for 1 to 2 hours.
- The solution is drained through the catheter prior to removal of the urinary catheter.
- Infusion is undertaken once weekly for 4 to 6 weeks and may commence 2 to 4 weeks after resection of the urinary bladder tumour.

- Subsequent maintenance intravesical therapy may be given once per week for 3 weeks 3, 6, and 12 months after initial treatment and can be extended for up to 3 years.
- Clinical surveillance takes place by the undertaking of cystoscopy and urine cytology every 3 months to 6 months for four years then once yearly.
- Radiology imaging surveillance with computed tomography (CT) scan is often undertaken on a yearly basis

Sadeghi et al. [20] reported a 77-year-old man who had a history of benign prostatic hyperplasia as well as urothelial carcinoma of the urinary bladder who had manifested with testicular discomfort and a palpable mass two years ensuing his undergoing of intravesical instillations of BCG treatment, The patient initially had manifested with haematuria in 2017 and he underwent computed tomography (CT) (see figure 3a)) and post-CT abdominal radiograph in the excretory phase (see figure 3b), which had shown a soft tissue mass within the urinary bladder that was suspicious for urothelial carcinoma. This was confirmed visually during his cystoscopy procedure at which time the patient had undergone excision of the mass as well as transurethral resection of the urinary bladder tumour. Pathology examination of the surgical specimen demonstrated non-invasive high grade papillary urothelial carcinoma, stage Ta. In view of this, the patient was reported to be determined to be a candidate for BCG therapy and he was successfully treated with subsequent intravesical BCG instillations for 6 weeks followed by maintenance BCG instillation for 1 year.

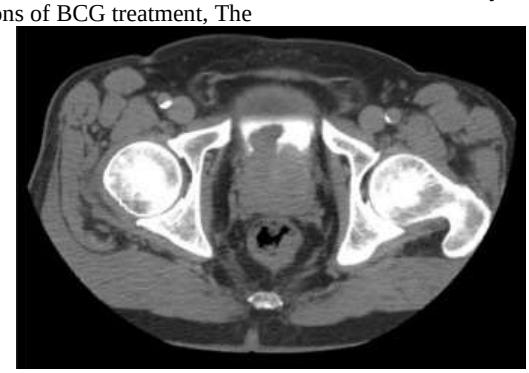


Figure. 3a. Urogram phase CT performed on initial presentation for hematuria outlines an eccentric tissue mass at the base of the bladder suspicious for neoplasm. There is no lymphadenopathy in the pelvis. Reproduced from: [20]

Figure. 3b. Frontal abdominal radiograph obtained on initial presentation after intravenous contrast administration demonstrates filling defect at the base of the bladder. Trabeculation in the bladder wall is identified due to longstanding history of benign prostate prostatic hyperplasia and bladder outlet obstruction. Reproduced from [20]

Two years following his initiation of intravesical BCG therapy, the patient had complained of mild left testicular pain and a palpable mass. He had ultrasound scan of the testis which had demonstrated multiple vague hypoechoic lesions within his left epididymis (see figure 3a) and testis (see figures 3b to 4d) and fluid within his scrotal sac containing septations which were interpreted to be consistent in appearance with a complex hydrocoele (see figures 4a to 4d). His left testis was noted to be mildly hyperaemic in comparison with his right (see figures 4e to 4f) that was indicative of underlying infectious process. He had urinalysis which revealed small leukocyte esterase and urine culture which was negative. He was treated with routine antibiotic treatment for epididymyo-orchitis without significant improvement.

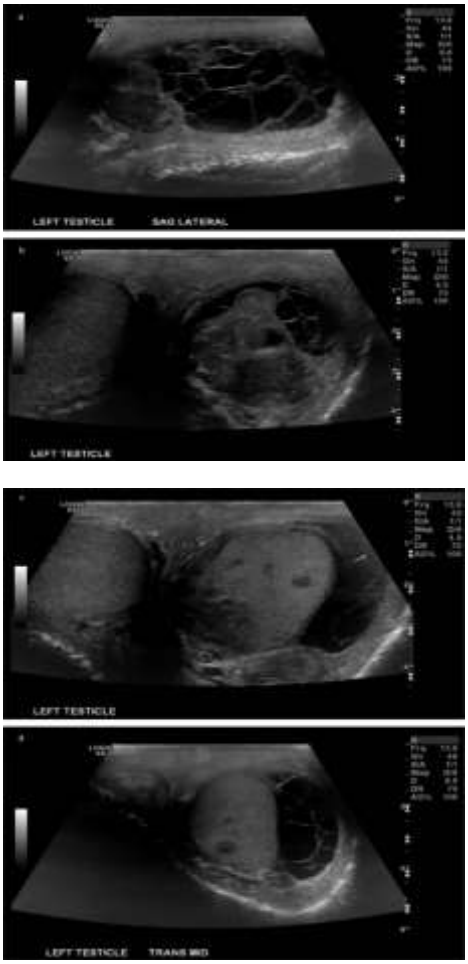
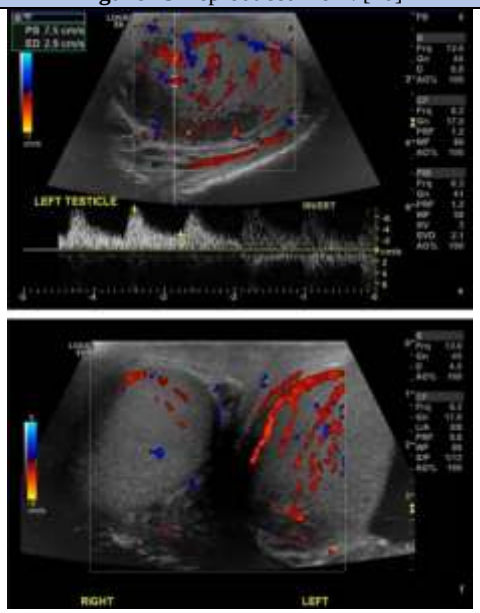
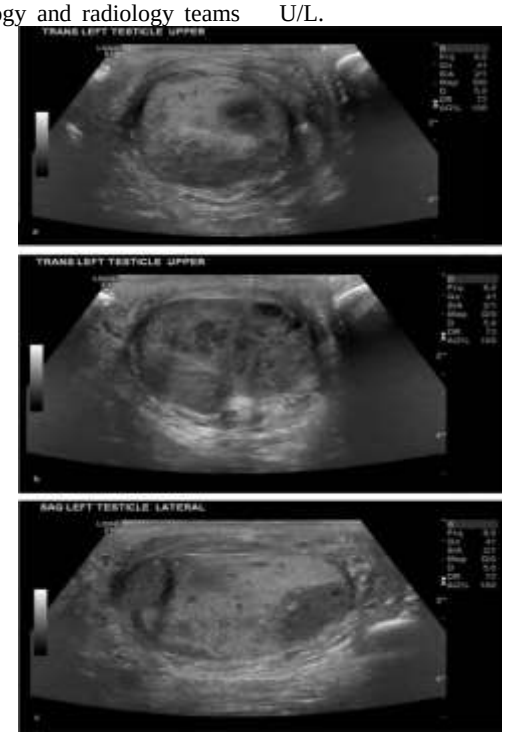


Figure 15 Reproduced from: [20]



Figures 4: Two years after TURBT and subsequent initiation intravesical BCG therapy, the patient presented with testicular pain and palpable abnormality. Sonographic image of the left testicle shows hypoechoic areas within the testicular parenchyma and a complex hydrocele (a-d). There is asymmetric hyperemia of the left testicle (e-f).Reproduced from: [20]

He underwent follow-up ultrasound scan imaging after his antibiotic therapy which demonstrated interval resolution of the complex hydrocele but increase in size and number of hypoechoic testicular lesions (see figures 5b and figure 5c). His urinalysis was again shown to be positive for leukocyte esterase and his urine culture was again negative. Discussion was undertaken between the urology and radiology teams regarding the patient's history and imaging findings which led to a differential diagnosis including sequalae of chronic infection such as testicular TB in light of prior intravesical BCG treatment. The results of his Serology tests were within normal limits including alpha feto-protein at 2.0 ng/mL, b-HCG at 1.0 mIU/mL, and lactate dehydrogenase at 162 U/L.



Figures 5. (a-c) Follow-up sonography 4 weeks later after antibiotic therapy shows resolution of complex hydrocele but increasing size and number of hypoechoic lesions in the left testicle. Reproduced from: [20]

Possibility of tuberculosis of the testis was raised after his initial failed antibiotic therapy.

Discussion with the patient regarding his treatment options led to the decision for him to undergo orchidectomy. Pathology examination of the radical orchiectomy specimen showed necrotizing and non-necrotizing granulomatous inflammation which had involved the testis, epididymis, and rete testis, with rare acid-fast bacilli forming a 4.5-cm dominant mass which was consistent with tuberculous epididymo-orchitis. Staining for acid fast bacilli demonstrated rare acid-fast bacilli (see figure 6a, figure 6b, and figure 6c).

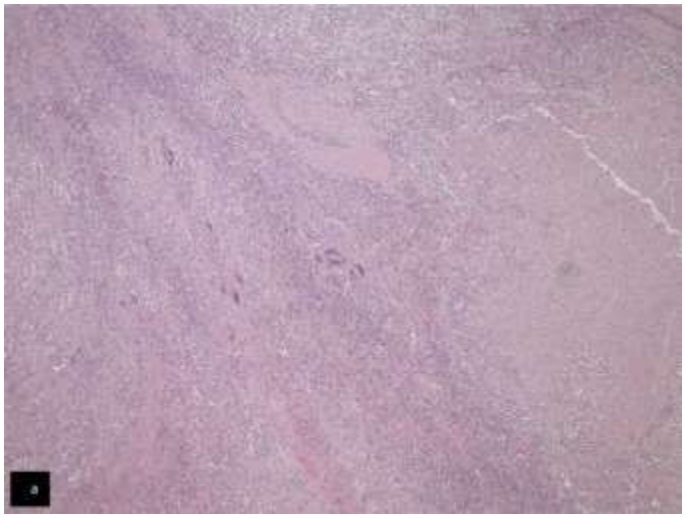


Figure. 6a. Low power photomicrograph of orchiectomy specimen demonstrates areas of granulomatous and nongranulomatous inflammatory change and displacement of testicular parenchyma. Reproduced from: [20]

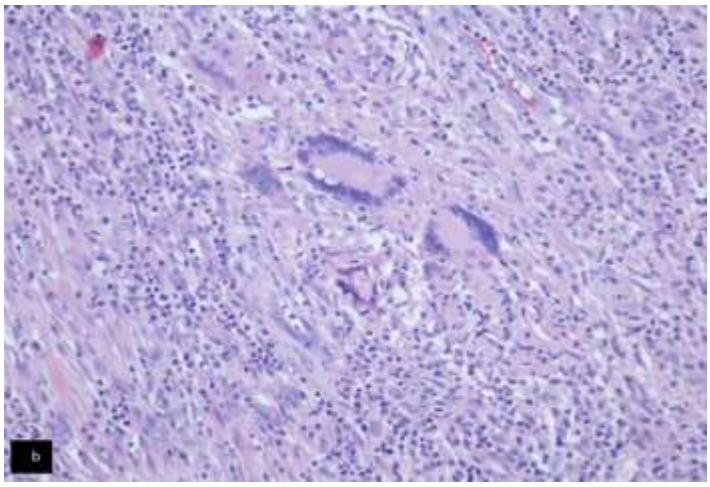


Figure. 6b. High power photomicrograph of orchiectomy specimen demonstrating giant cells suggestive of tuberculosis. Reproduced from: [20]

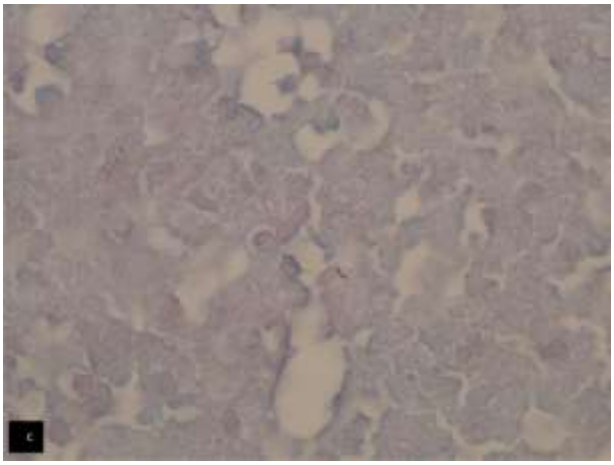


Figure. 6c. Acid fast stain showing sparse acid-fast bacilli. Reproduced from [20]

He underwent subsequent surveillance cystoscopy and biopsy of the urinary bladder tumour scar and pathology examination of the biopsy specimens showed predominantly denuded urothelial mucosa with mild chronic inflammation and reactive changes which were adjudged to be consistent with successful treatment of the tumour. He had follow-up urinalysis which was negative for leukocyte esterase suggesting successful treatment of testicular TB.

Sadeghi et al. [20] made the ensuing summative discussions:

- TB involving the genitourinary tract is most commonly encountered following primary pulmonary tuberculosis.
- The kidneys, ureters, and urinary bladder are commonly affected up to 15% of the time in the setting of extrapulmonary tuberculosis.
- Urinary tract TB could also occur in isolation and it comprises 25% of cases of genitourinary.
- Spread of TB to the testis and epididymis is considered to occur through retrograde spread of tubercular bacilli from the affected urinary tract into the prostate by means of reflux, followed by canalicular spread to the seminal vesicle, ductus deferens, and epididymis [1]
- Disseminated spread might occur due to poor healing following transurethral resection of urinary bladder tumour.
- Intravesical BCG therapy is not without risk as it uses an active but weakened strain of bovine TB bacillus, Mycobacterium bovis.
- Most common side effects tend to be related to inflammatory response within the urinary bladder leading to chemical cystitis including dysuria, urinary frequency, and haematuria.
- Direct contact of the BCG solution could lead to anterograde or retrograde spread of M. bovis and associated granulomatous inflammation to involve to the remainder of the genitourinary tract including the penis, epididymis, testis, prostate gland, and kidney. [25]
- In their reported case, spread of live attenuated *M. bovis* from the prostatic urethra via the vas deferens and ductus deferens into the epididymis and testes and caused epididymal and testicular TB.
- Prostatitis and associated elevation of serum prostate-specific antigen levels is common following intravesical BCG therapy and might occur with an incidence of up to 10%.
- Tuberculous epididymo-orchitis is relatively uncommon and does occur in about 0.4% of patients. [25]
- Pyelonephritis and kidney abscess are also less common at 0.3%.
- Systemic complications also do occur infrequently at a rate of about 3% and include military TB, mycotic aneurysms,

granulomatous hepatitis, tuberculous spondylitis, and BCG-related sepsis. [25] [26]

- Ultrasound scan findings of testicular TB do include diffuse enlargement of the testicle, heterogeneous or homogeneous hypoechoic echotexture, and hypoechoic nodules. [15] [27] [28]
- Tuberculous epididymoorchitis is similar with regard to appearance with diffuse enlargement and hypoechoic areas of heterogeneity.
- Tuberculous orchitis usually tends to be the result of contiguous extension from tuberculous epididymitis [1] [27] [28].
- Extension of TB to the scrotum does include scrotal skin thickening, blurred separation between the testis and the epididymis, hydrocoele, and calcification of the epididymis as well as the tunica vaginalis. [27] [28]
- Testicular TB could be confirmed with fine needle aspiration, and cytology or biopsy of the testis. [13]
- Fine needle aspiration might show epithelioid granulomas and acid-fast bacilli staining might be positive for occasional acid-fast bacilli.
- Treatment options for testicular TB does include anti-TB antibiotic therapy and the undertaking of orchidectomy.
- While their patient had elected to undergo orchidectomy for his suspected testicular TB, an anti-TB antibiotic regimen could include rifampicin, isoniazid, pyrazinamide, and ethambutol with follow-up radiology imaging to document resolution [29] Ultimately, orchidectomy was the best current treatment option particularly in resistant cases [9]

.

Huang et al. [30] stated that nowadays, majority of studies of tuberculous epididymo-orchitis (TBEO) have been case reports or small sample cohort series. Huang et al. [30] undertook a study which was aimed to present the largest series of TBEO with their management experiences and long-term follow-up outcomes. With regard to the methods of their study, Huang et al. [36] reported that patients who were diagnosed as having TBEO after surgical procedures at Department of Urology, West China Hospital from 2008 to 2019 were included in their study. Huang et al. [30] extracted all clinical features, auxiliary examination results, treatment and histopathological findings if they were available. Huang et al. [30] summarized their results as follows:

- They had included in their study eighty-one patients (mean age 50.77 ± 16.1 years).
- Scrotal swelling ($N = 47$, 58.0%) and pain ($N = 29$, 35.8%) were the commonest manifesting complaint.
- Pyuria and non-visible haematuria were observed in twenty-two (27.2%) and eight patients (9.9%), respectively.
- Urine acid fast bacilli cultures were available in 16 patients and all were noted to be negative.
- The mean duration between the commencement of symptoms and the definite diagnosis was 6.42 ± 7.0 months.
- TBEO was considered in 30 (37.0%), tumours in 28 (34.6%) and non-specific bacterial epididymo-orchitis in 23 (28.4%) patients.
- All of the patients had received triple therapy of chemotherapy-surgery-pharmacotherapy and definite diagnosis was confirmed through histopathology examination of surgical specimens.
- Fifty-five patients had been followed up regularly (mean follow-up 82.35 ± 36.6 months). One patient (1.2%) died from liver cirrhosis and no recurrence was observed.
- Postoperative complications of the patients included erectile dysfunction in 4 patients which amounted to 4.9% of the patients, premature ejaculation in 5 patients which amounted to 6.2% of the patients and sterility in 7 patients (which amounted to 8.6% of the patients.

Huang et al. [30] made the following conclusions:

- They had recommended that patients who have advanced TBEO should receive triple therapy of chemotherapy-surgery-pharmacotherapy.
- Physicians should pay more attention to patients' sexual function as well as fertility during follow up after treatment had been completed.

E Sousa et al. [31] reported a 42-year-old immunocompetent male patient who had manifested with a 4-day history of unilateral right testicular pain. The patient had also complained of dry cough, asthenia and weight loss (9 kg) during the preceding 5 months. His laboratory test results revealed an elevated serum C-reactive protein (75mg/L) without leucocytosis/neutrophilia and mild anaemia (11.6g/dL). He underwent Doppler ultrasound scanning of the testis, which revealed that the right testicle was slightly enlarged with multiple small ill-defined hypoechoic parenchymal nodules (3 to 5mm) and the epididymis (body and tail) was diffusely enlarged and markedly hypoechoic with increased vascularization. The left testicle was unremarkable. He underwent Chest CT scan based upon his symptoms (long-standing dry cough and weight loss) and an abnormal chest x-ray, which had revealed multiple bilateral tree-in-bud parenchymal infiltrates within the upper lobes and upper segments of the lower lobes, as well as peri-bronchial consolidation areas and cylindrical bronchiectasis, which had suggested an endobronchial spread of pulmonary infection. Right pleural effusion and multiple enlarged paratracheal lymph nodes were also noted. E Sousa et al. [31] reported that pulmonary tuberculosis was confirmed with positive culture for Mycobacterium tuberculosis in bronchoalveolar lavage sample.

E Sousa et al. [31] made the following summations:

- Tuberculosis (TB) is a multisystemic disease with a high morbidity/mortality rate, caused by the bacillus *Mycobacterium tuberculosis*.
- It typically affects the lungs (pulmonary TB), although, in about 15% of cases, it can also affect other sites (extrapulmonary TB).
- It had been stated that the latter often presents a challenging diagnosis in which the radiologist can play a decisive role [1]

Clinical Perspective

With regard to clinical perspective, e Sousa et al. [31] made the ensuing iterations:

- Even though genitourinary TB is a common site of extrapulmonary TB which accounts for 20% of cases, testicular involvement is rare and represents only up to 3% of cases. [8] Concurrent pulmonary and renal TB is seen in 50% and 80–85% of cases, respectively [32].
- TB epididymo-orchitis may develop from retrograde spread of tubercle bacilli from the urinary tract via reflux to deferent duct, epididymis and testicles or by hematogenous spread [33] [34]

- Testicular pain and/or swelling are the most common symptoms, haematospermia and urinary tract irritation have also been reported [15] [34]

Imaging Perspective

With regard to imaging perspective, e Sousa et al. [31] stated the following:

- The sonographic appearances tend to be non-specific and overlap with those from other more common pathologies such as tumour, infection, inflammation and infarction.
- There are two main sonographic appearances of TB epididymitis [12] [32] [35] Diffuse heterogeneous predominantly hypoechoic enlarged epididymis;
- Focal nodular hypoechoic lesion within the epididymis.
- These findings are usually associated with increased colour flow on Doppler images, which differentiates this condition from infarction.
- Tuberculosis orchitis usually occurs as a result of contiguous extension from the epididymis and is considered to reflect a later stage of the disease process [32] [36]
- The main sonographic patterns include [12] [32]:
    - Testicular enlargement (which may be diffuse or nodular);
    - Multiple small hypoechoic nodules (miliary type).
- Other associated sonographic findings include thickened scrotal skin, septated hydrocele, scrotal abscesses, scrotal sinus tract and intra-scrotal extra-testicular calcification (affecting the epididymis and the tunica vaginalis in the later stages of disease) [32] [34] [36]

Outcome

With regard to outcome e Sousa et al. [31] made the ensuing iterations:

- Isolation and culture of M. tuberculosis, fine needle aspiration cytology (FNAC) and polymerase chain reaction (PCR) may provide an accurate diagnosis, even though in some cases histology might be the only confirmatory diagnostic modality [11] [15] [31] [34]
- Anti-TB chemotherapy is the mainstay of treatment, however, in few cases, orchidectomy is required for both diagnosis and treatment [8]

Take-Home Message / Teaching Points

With regard to teaching points and take-home message, e-Sousa et al. [31] made the ensuing iteration:

- In a patient manifesting with scrotal swelling/pain, ultrasound scan signs of epididymo-orchitis should raise suspicion for tuberculosis in the presence of miliary nodularity of the testis and markedly hypoechoic epididymis enlargement, especially when there is evidence of TB infection elsewhere or failure of conventional antibiotic therapy

Differential Diagnosis List

e-Sousa et al. [31] summated the differential diagnoses of tuberculous epididymoorchitis include the following:

- Tuberculous epididymo-orchitis and pulmonary tuberculosis
- Bacterial epididymo-orchitis
- Sarcoidosis
- Lymphoma
- Testicular tumour (primary and metastasis)
- Testicular hematoma or infarction

e-Sousa et al. [31] stated that the final diagnosis of their patient was tuberculous epididymo-orchitis and pulmonary tuberculosis

Nepal et al. [35] made the ensuing relevant iterations related to Genitourinary tuberculosis (TB):

- Genitourinary tuberculosis (TB) is the commonest form of extrapulmonary TB, which accounts for to 20% of cases. [1]
- Nevertheless, testicular TB is rare and does account for only up to 3% of the cases of genitourinary TB. [1] [16].
- Genitourinary TB may occur at any age, but more common between the third and fifth decade of life. [27]
- It has been iterated that concurrent pulmonary and kidney TB is seen in 50% and 80% to 85% of the cases of genitourinary TB. [38]
- The incidence of extrapulmonary TB has been increasing not only in endemic regions but also all across the entire world due to immigration, immunosuppression, and HIV infection.
- Radiology imaging features of testicular TB are non- specific and they are often impossible to differentiate from other more common pathologies such as tumor, infection, inflammation, and infarction.
- Testicular radiology imaging has been limited to the use of magnetic resonance imaging (MRI) and ultrasound.
- Computed tomography (CT) scan is not reliable with regard to the diagnosis and characterizing of testicular pathology.
- Ancillary tests such as positive chest radiograph or tuberculin test do support the diagnosis. Nevertheless, it has been pointed out that negative results cannot reliably exclude the diagnosis. [16] [27]
- It has also been iterated that unfortunately, only half of the patients have evidence of active TB at manifestation. [16].
- Antitubercular medicaments are the mainstay of treatment; nevertheless, orchidectomy may be required for both the diagnosis as well as the treatment.
- Differential diagnoses of testicular TB are summarized in the ensuing section with specific teaching points which may help in differentiating with its close simulators.

Nepal et al. [35] made the ensuing summative discussions:

- Ultrasound scan is the investigation of choice for diagnosis of testicular TB.
- Various sonographic patterns had been described for testicular TB[5] [Table 1 and Figure 7]. [15]
- The sonographic appearances of testes could be explained by various pathology stages of tubercular infection which do include caseous necrosis, granulomas, and healing by fibrosis and calcification [Figure 8].

- Due to vague sonographic patterns, imaging features had often been non-specific and difficult to distinguish TB from other inflammatory causes, tumor, or infarction.
- The disease may progress to involve entire epididymis and testis or might heal with fibrocalcific changes. Calcification is seen in 10% of cases [Figure 9]. [39]

Diffusely enlarged heterogeneously hypoechoic testis
Diffusely enlarged homogeneously hypoechoic testis
Nodular enlarged heterogeneously hypoechoic testis
Multiple small hypoechoic nodules in the enlarged testis (miliary type)

TB: Tuberculosis

Table 1: Gray scale sonographic patterns of testicular TB.

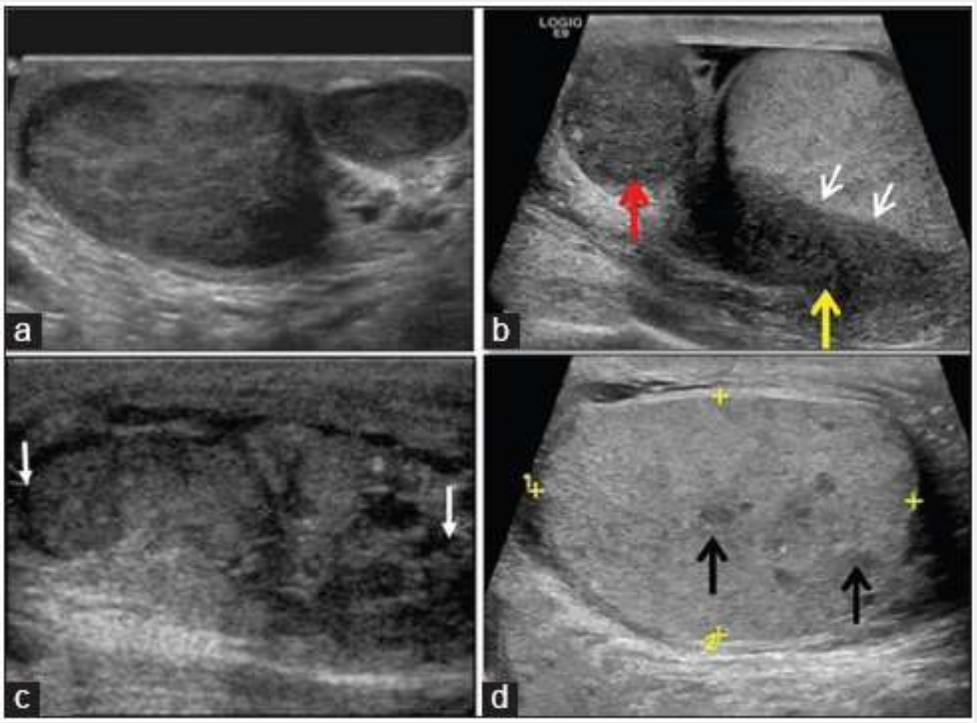


Figure 7: Various examples of gray scale sonographic patterns of testicular tuberculosis. (a) Diffusely enlarged right testis with heterogeneous hypoechoic pattern, (b) diffusely enlarged head (red arrow) and body (yellow arrow) of epididymis with infiltration of adjacent testes parenchyma (white arrows) showing homogenous hypoechoic pattern, (c) nodular enlarged heterogeneously hypoechoic testes, with ill-defined nodules (small white arrows) virtually indistinguishable from tumor, (d) ill-defined tiny hypoechoic nodules (black arrows) in testicular parenchyma. Reproduced from: [35]

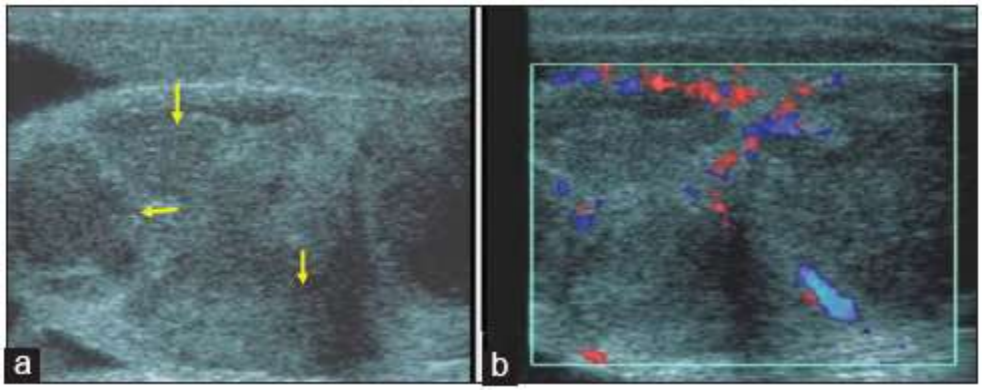


Figure 8: A 44-year-old man with testicular tuberculosis who presented with 6 months history of testicular pain. (a) Gray scale sonographic image demonstrates an enlarged and heterogeneous testis with the presence of multiple ill-defined focal hypoechoic lesions (small yellow arrows). (b) Color Doppler shows increased vascularity along the periphery of the hypoechoic lesions. These imaging findings are non-specific and may be seen in both inflammatory and neoplastic conditions. A diagnosis of testicular tuberculosis was made the following orchiectomy. Reproduced from: [35]

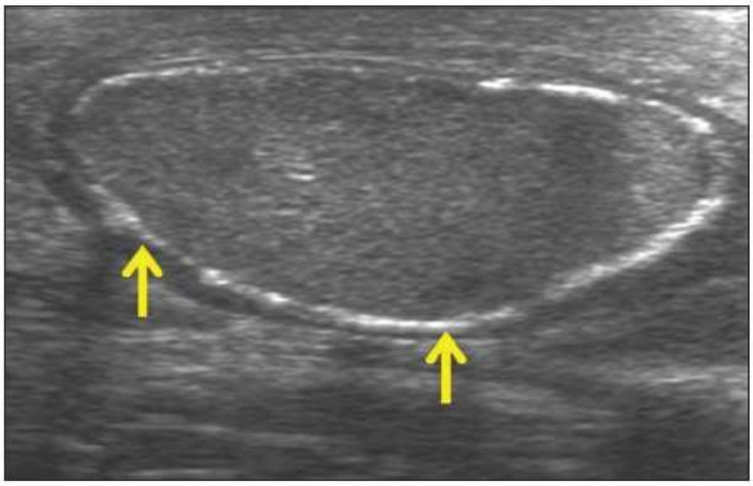


Figure 9: A 42-year-old man with healed testicular tuberculosis: Gray scale sonographic image demonstrates smooth peripheral calcification along the tunica vaginalis (yellow arrows). The patient had a remote history of pulmonary tuberculosis, which was treated with antitubercular drugs.

Reproduced from: [35]

- The epididymis is the commonest site of tubercular infection in scrotum.
- Tubercular orchitis usually emanates from contiguous extension from the epididymis.
- Isolated orchitis in the absence of epididymal involvement is not common; nevertheless, possible with hematogenous spread. [10] [34]
- Tubercular epididymitis occurs first due to early involvement from retrograde spread of mycobacteria through urinary reflux. Again, the tail of the epididymis has greater blood supply and might be another reason for early involvement.
- Concurrent presence of epididymis involvement and testic ular lesion favors the diagnosis of infection. [12]
- Complications of testicular TB do include: scrotal abscess, scrotal sinus tract, and extra-testicular calcification.
- Intra-scrotal extra-testicular calcification does affect the epididymis and the tunica vaginalis covering the testes.
- Scrotal fistula formation has a poor prognosis.

Specific ultrasound imaging features of testicular TB

[35] stated that with regard to specific ultrasound scan imaging features of TB of the testis, the following:

- Concurrent involvement of the epididymis along with testes, scrotal wall thickening, and septated or infected hydrocele does favor infection rather than tumor [Figure 10]. Nevertheless, the testicular tumours at advanced stages might also involve the epididymis. [1] [38]
- Miliary nodules within testes should alert a radiologist toward tubercular etiology. Smooth peripheral calcification of tunica vaginalis is also a specific feature of testicular TB in contrast to intratesticular coarse calcifications seen in malignancy. It has been pointed out that Colour Doppler ultrasound scan is also helpful in differentiating TB from infarcts and tumours. TB orchitis commonly tends to occur together with the involvement of lower urinary tract and sometimes with concurrent renal involvement. [15]

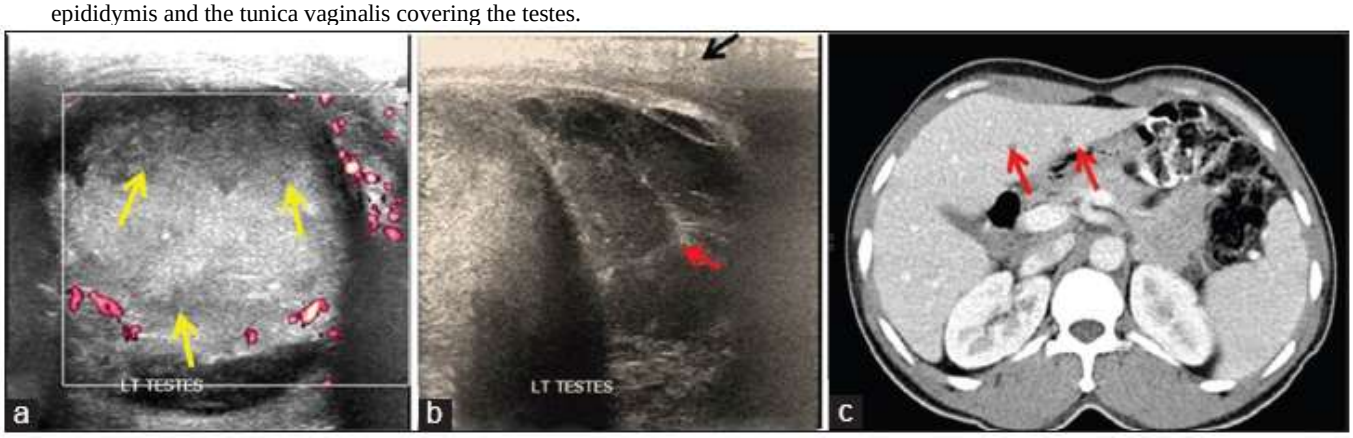


Figure 10: A 43-year-old male with complicated testicular tuberculosis presenting with scrotal pain and swelling. (a) Color Doppler sonographic image demonstrates diffuse, ill-defined heterogeneous hypoechoic area with increased peripheral vascularity but lack of central vascularity (yellow arrows). (b) Gray scale ultrasound image showing scrotal wall edema (black arrow) and multiseptated hydrocoele and debris (red arrow). (c) Contrast-enhanced axial computed image of abdomen in same patient shows hypoechoic lesions in the left lobe of live (red arrows) likely representing tubercular granulomas. Reproduced from [35]

[35] iterated the following:

- Upon Magnetic Resonance Imaging (MRI) Scan, the tubercular granulomas usually tend to appear hypo-intense in T2-weighted (T2W) images and they do show variable contrast enhancement.
- Rarely, acute involvement by TB may demonstrate T2 hyperintense signal mimicking bacterial orchitis.

Testicular TB simulators

With regard to the testicular TB simulators, Nepal et al. [35] iterated that imaging appearance of testicular TB is non-specific and it masquerades non-specific infection, inflammation, tumor, trauma, and infarct.

Sarcoidosis

[35] stated the following with regard to sarcoidosis of testis and epididymis:

- Sarcoidosis is a chronic granulomatous disease with multisystem involvement which could rarely involve the testes.
- The commonest manifestation of genitourinary sarcoidosis is epididymitis, which is often bilateral.
- Most often, the epididymitis is asymptomatic, but patients may present with pain or scrotal mass. In most cases, sarcoidosis is diagnosed before genitourinary involvement occurs.
- Like TB, isolated involvement of the testis without inflammation of epididymis is very rare.
- Upon ultrasound, sarcoid granulomas appear as single or multiple hypoechoic nodules within the testes, simulating TB. [40] [41]
- The sarcoid granulomas are similar to tubercular granulomas and are hypointense on T2W MRI and usually exhibit contrast enhancement.
- Management of sarcoidosis is completely different as steroid therapy is beneficial.
- Multiple bilateral granulomas with simultaneous involvement of the epididymis and testes had tended to be indistinguishable from TB; nevertheless; in conjunction, other systemic presentations such as pulmonary involvement should raise the suspicion of sarcoidosis.
- Similar to testicular TB, in sarcoidosis (a) testicular involvement without epididymitis has tended to be rare or uncommon, (b) the granulomas do appear hypoechoic upon ultrasound scan, and (c) granulomas show T2 hypo-intensity and enhancement [Figure 11]. Nevertheless, concurrent systemic presentations of sarcoidosis should provide clue to the diagnosis of sarcoidosis.

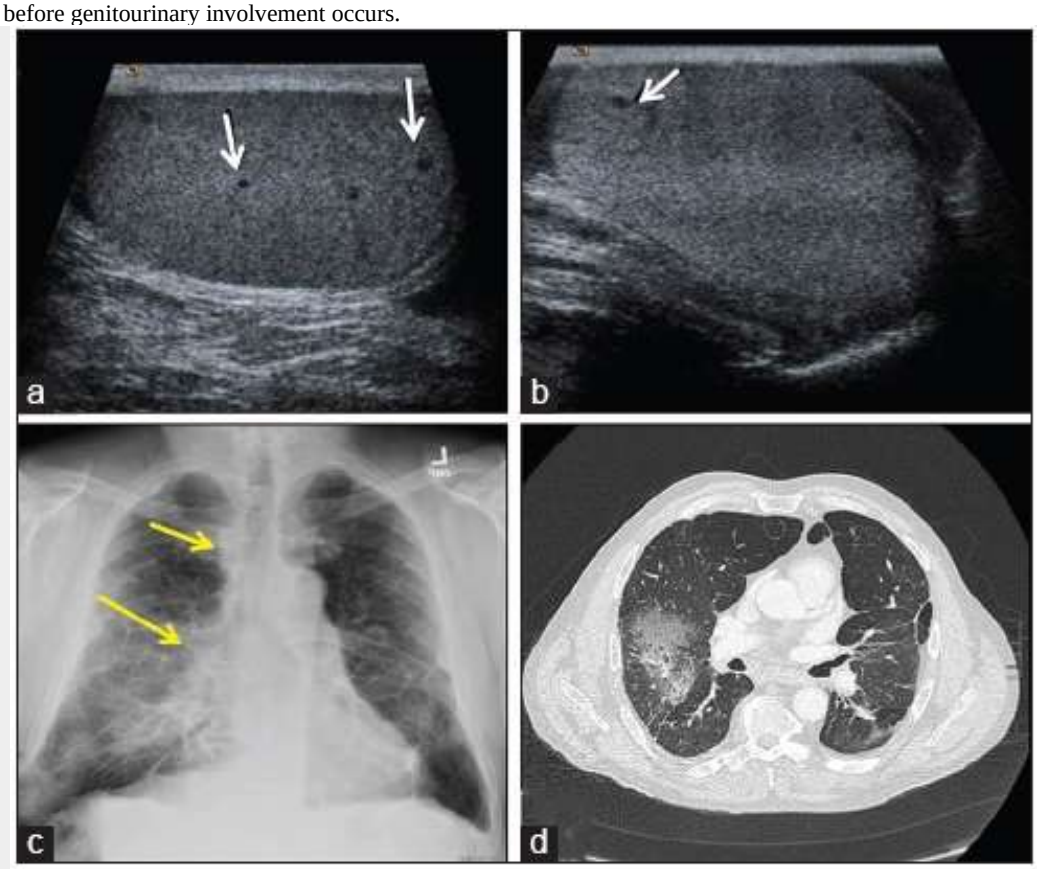


Figure 11: A 55-year-old male with sarcoidosis who presented with the right testicular pain. (a and b) Gray scale sonographic image of testis revealed several, tiny bilateral hypoechoic lesions (white arrows) on both testes (A-right, B-left testis). (c) Frontal chest radiograph shows the right hilar and paratracheal lymphadenopathy (yellow arrows) and bilateral interstitial and airspace opacities more on the right side. (d) Axial computed tomography chest image on lung window demonstrates asymmetric ground-glass opacities with surrounding pulmonary fibrosis and architecture distortion more prominent on the right. Reproduced from [35]

Lymphoma

[35] made the ensuing iterations related to Lymphoma of the testis / epididymis and TB of testis / epididymis:

- Testicular lymphoma does constitute about 5% of all testicular tumors. Nevertheless, it is the most common testicular tumor in elderly men who are older than 60 years. [42] [43]
- Lymphoma of the testis is the most common bilateral testicular tumor.
- Lymphoma could involve the testes either as primary site of extra-nodal disease or as secondary involvement of systemic disease.
- Lymphoma in testes had most often been secondary and Lymphoma of testis is usually seen in disseminated lymphoma – which makes the diagnosis of the testicular lymphoma easier to make. Most of them are diffuse large B-cell non-Hodgkin's lymphoma.
- Most common radiology imaging feature in ultrasound scan of testis is diffuse enlargement of testes with large hypoechoic infiltrative area replacing the testes but characteristically maintaining normal testicular shape. Less commonly, Lymphoma of the testis may manifest as discrete hypoechoic intratesticular mass which might be solitary or multiple. Upon color Doppler ultrasound scan, increased color flow is noted resembling diffuse inflammation, but without pain or tenderness [Figure 12] [42]
- Imaging features on ultrasound are non-specific and they tend to be similar to TB and sarcoidosis, epididymis may be involved which appears enlarged and hypoechoic. On MRI scan, the soft tissue does appear hypointense both in T1W and T2W images with subtle enhancement. [43]
- Testicular lymphoma should be considered in an elderly male who has infiltrative hypoechoic mass within enlarged testes yet maintaining the shape of the testes or multiple bilateral non-tender testicular masses with increased vascularity upon color Doppler.
- Diagnosis has been made with orchidectomy, and pathology examination of the testicular specimen which is also therapeutic.

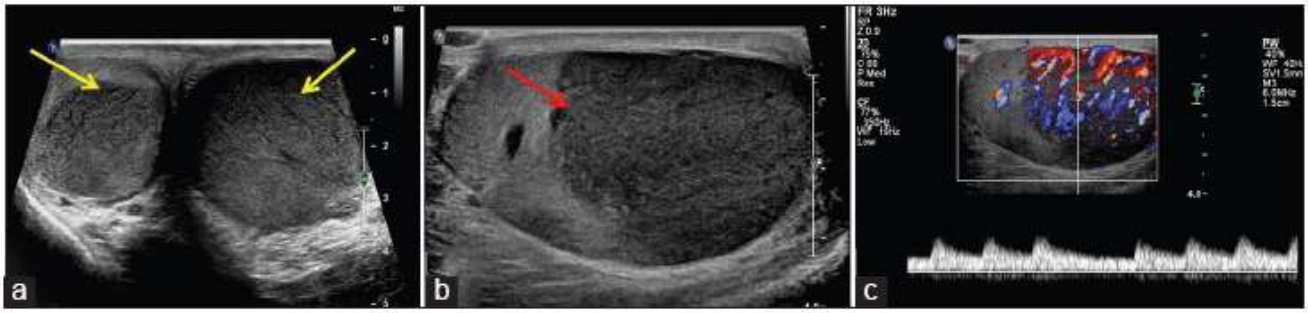


Figure 12: A 70-year-old elderly male with lymphoma who presented with scrotal swelling (a) Gray scale ultrasound shows bilateral enlarged testes with bilateral hypoechoic masses (yellow arrows). (b) Note the diffuse involvement of the left testis by hypoechoic mass (annotated with red arrow). (c) color Doppler image showing profound vascularity concerning for tumor. A presumptive diagnosis of testicular tumor was made based on the patients age, clinical presentation, and sonographic findings. Histopathological examination of the left orchiectomy specimen revealed non-Hodgkin's lymphoma. Reproduced from: [35]

Primary testicular tumors

[35] made the ensuing iterating summations related to Primary testicular tumours and TB of testis / epididymis:

- Testicular tumours are the commonest neoplasms in men of the second and third decade of life.
- The most common manifesting symptoms of tumors are scrotal swelling and lump.
- Testicular tumors and other non-tumorous conditions such as focal infarct, hematoma, and infection have overlapping radiology imaging appearances, i.e., hypoechoic areas with variable color flow [Figure 25]. Hence, a solid testicular mass which contains internal vascularity should be considered as testicular tumor until proven otherwise.
- Ultrasound scan can distinguish between intratesticular versus extra-testicular mass; intratesticular mass is more commonly malignant. Seminomatous tumours are more homogenous in contrast to non-seminomatous tumours.

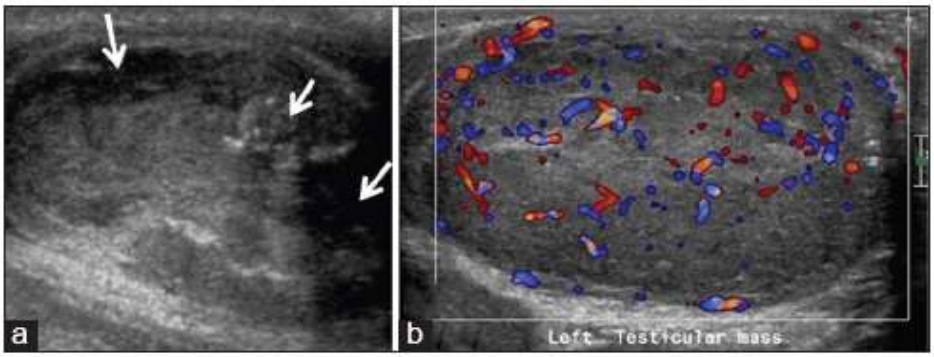


Figure 13: A 30-year-old male with testicular tumor who presented with progressive right scrotal pain and swelling for a month. (a) Gray scale sonographic image demonstrates heterogeneous testis with multiple focal hypoechoic lesions with punctate calcifications (white arrows). The imaging features are simulating malignancy. (b) On color Doppler, peripheral and central vascularity is seen. This was found to be testicular undifferentiated sarcoma. Reproduced from: [35]

[35] also stated the following:

- Color Doppler could help differentiate infarction, tumor, and inflammation. Upon color Doppler ultrasound scan, tubercular epididymitis and orchitis does demonstrate peripheral vascularity due to granulomas and lack of central flow due to caseation necrosis which is in contrast to tumor which usually shows central vascularity. [44]
- Concurrent epididymis enlargement with a testicular involvement does favour infection rather than tumour because orchitis is preceded by the development of epididymitis. [45]
- Testicular tumours might also infiltrate the epididymis; however, in the advanced stages, when we also expect extra-testicular systemic findings.
- Calcification can also be observed in testicular tumours which usually tend to be intratesticular, coarse, and inhomogeneous distinct from the pattern of calcification in testicular TB.
- Calcification which is typical for TB is smooth peripheral and it involves the tunica.

Testicular metastasis

[35] made the following summating iterations related to testicular metastases and TB of testis / epididymis:

- Metastasis to the testes is not common.
- The commonest primary tumours that metastasize to the testicle are carcinoma of prostate, lung, kidney, and colon.
- Leukemia and metastasis from melanoma can also manifest in the testes.
- Neuroblastoma, Wilms tumor and sarcoma can metastasize to the testis in children.
- It has been pointed out that most often, the metastasis is unilateral but can be bilateral in up to 15% of cases. [45] [46]
- The mean age at presentation is the 5th decade of life which is much older than the age for primary testicular tumor.
- Testicular metastasis is rare, probably in view of the low temperature of scrotum where malignant cells find it difficult to proliferate as well as due to blood-testicular barrier. [46] [51]

Hematoma and infarcts

[35] made the ensuing iterations related to haematoma and infarcts of the testis as well as Tuberculosis of the testis / epididymis:

- Even though upon radiology imaging testicular hematoma and infarcts mimic testicular TB and tumors, hematoma and infarcts could be differentiated clinically.
- Testicular infarct manifests with acute scrotal pain, color flow tends to be absent or reduced.
- An area of infarct is avascular and will become more hypoechoic upon follow-up ultrasound scan.
- Testicular hematoma is suspected pursuant to trauma which appears hypoechoic and shows reduced or absent vascularity upon color Doppler.
- Chronic hematoma may mimic mass, which must be correlated with the history and color Doppler scan findings [Figure 14].
- In uncertain cases, if it seems as an incidental finding associated with trauma, short-term follow-up imaging in 2–4 weeks might be helpful because hematoma will regress in size with time. [37]

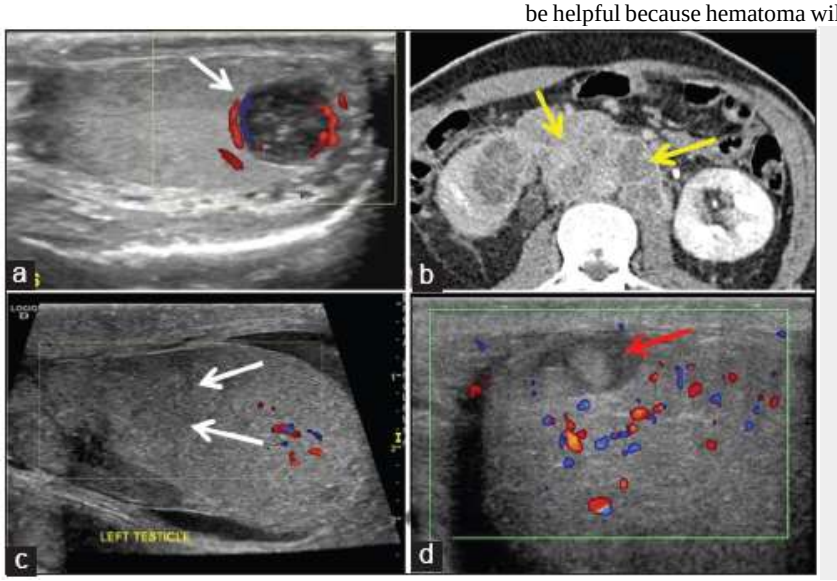


Figure 14: Tuberculosis mimics. A 20-year-old male with scrotal pain. (a) A well-defined heterogeneous hypoechoic lesion in lower pole of testes (white arrow) with peripheral flow on color Doppler. (b) Axial contrast-enhanced computed tomography abdomen of same patient revealed bulky conglomerate lymphadenopathy (yellow arrows) diagnosed as germ cell tumor. (c) A 16-year-old male with trauma. Irregular hypoechoic area in upper pole of testis (white arrows) with minimal hydrocoele. (d) A 35-year-old male for follow-up of testicular trauma. Avascular heterogeneous lesion in upper pole of testis (red arrow) diagnosed as hematoma. Reproduced from: [35]

Other infectious orchitis

[35] stated the following about other infectious orchitis and TB orchitis/epididymitis:

- Bacterial orchitis might have similar findings upon ultrasound scan; nevertheless, the clinical manifestation is different and manifests with fever, acute scrotal pain, urinary tract infection, and leukocytosis.
- Upon color Doppler, pyogenic orchitis does tend to demonstrate markedly increased vascularity opposed to spotty peripheral flow along the tubercular abscess. [47].
- Progression of abscess to fibrosis or calcification is favorable in tubercular aetiology.
- Upon MRI scan, tubercular orchitis usually depicts T2 hypointense signal in contrast to pyogenic orchitis which shows hyperintense signal upon T2W imaging.

Adrenal rests

[35] made the ensuing summating iterations related to testicular adrenal rests and tuberculosis of the testis / epididymis:

- Adrenal rest tumors of the testis are benign masses that are found in patients who have congenital adrenal hyperplasia with the prevalence of 94%.
- Adrenal rest tumors are present in childhood; and hence, baseline ultrasound scan screening has been recommended to preserve testicular function.
- Adrenal rest tumors typically tend to be bilateral and located near the mediastinum of testes.
- Most often, the lesions appear hypoechoic with well-defined margins and they do demonstrate vascularity upon color Doppler scanning, [48]

Importance of extra-testicular ancillary findings

With regard to the importance of extra-testicular, Nepal et al. [35] stated the following:

- It is important to correlate the testicular ultrasound findings with extra-testicular ancillary findings.
- From the above discussion, it is clear that testicular TB simulates a wide range of differential diagnoses.
- Extra-testicular findings can guide us to the correct diagnosis [Figure 15].

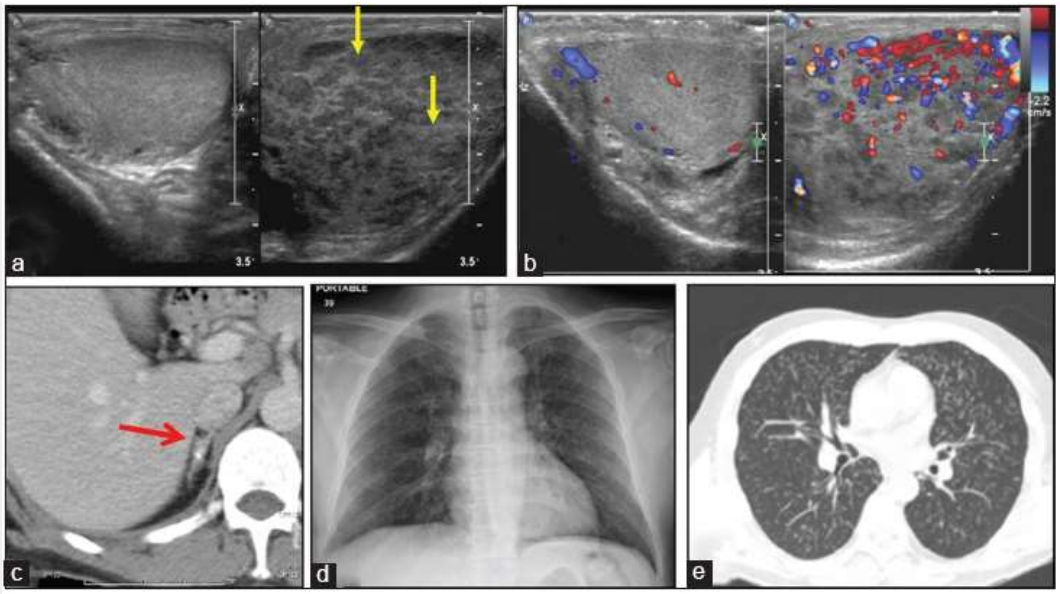


Figure 15: Testicular tuberculosis mimicking tumor, importance of extra-testicular ancillary findings: (a) Gray scale sonography image of scrotum showing enlarged left testis with multi-focal ill-defined hypoechoic nodularity (yellow arrows). (b) Color Doppler shows increased vascularity. The left radical orchiectomy revealed caseous granulomatous orchitis and epididymitis. (c) Retrospective analysis of contrast-enhanced computed tomography (CT) abdomen shows calcified right adrenal gland (red arrow). (d) Chest-Xray was normal and (e) CT chest revealed bilateral lung parenchyma studded with multiple miliary tubercles. Reproduced from: [35] made the ensuing additional summating iterations:

- Both TB and sarcoidosis are granulomatous diseases that are associated with overlapping radiology imaging findings.
- Hilar and mediastinal lymphadenopathy with occasional calcification of affected nodes might be found in both TB and sarcoidosis.
- Interstitial lung disease with characteristic thickening of broncho-vascular bundles in high-resolution CT does favour the diagnosis of sarcoidosis.
- On the other hand, cavity formation does favour TB which is seen in less than 3% of the cases of sarcoidosis.
- TB should be suspected in patients who have testicular lesions and concurrent lower urinary tract symptoms such as voiding difficulty and hematuria.
- Multiple nodules within the testes could be confused with sarcoidosis, but systemic evaluation in difficult cases is useful.
- Testicular TB is common in the 3rd–4th decade of life. [44]

Half of the cases of testicular TB will have active disease presentation, thus systemic evaluation and correlation could establish the diagnosis.

- In the elderly age group, diagnostic dilemma develops between testicular malignancy and testicular TB. After the sixth decade, malignancy such as lymphoma is more common.
- Testicular malignancy might manifest with bulky retroperitoneal lymphadenopathy which could be an important extra-testicular ancillary finding.
- TB could also involve abdominal lymph nodes which are necrotic, hypoechoic/attenuating, calcified with mesenteric predominance.
- It is in addition important to search for evidence of trauma to differentiate chronic hematoma from testicular pathology.

Nepal et al. [35] made the ensuing conclusions:

- Testicular TB is a great masquerader and may simulate a wide range of infectious, inflammatory, and neoplastic processes.
- Even though the ultrasound scan findings of testicular TB are overlapping, knowledge of extra-testicular ancillary findings and history is useful in most cases.
- It is important to accurately diagnose testicular TB and differentiate it from other differentials, especially testicular malignancy in view of the fact that the management is totally different.

Kharbach et al. [49] stated the following:

- Tuberculosis (TB) is an infectious disease which is caused by bacilli of the Mycobacterium tuberculosis (Mtb) complex [50] [51]
- Tb has been considered a serious global public health emergency for the past 25 years [50]
- It has been pointed out that Urogenital tuberculosis is the second most common form of extrapulmonary TB; [52] nevertheless, isolated testicular TB, as presented in their patient, is extremely uncommon. [52] [53] Moreover, the mechanism of spread of TB bacilli to the testis has still been controversial.]53]
- In view of the non-specific manifestation of testicular TB, diagnosis of testicular TB is challenging and is often discovered on pathology examination after orchiectomy [51]
- They had reported the case of an isolated testicular TB simulating malignancy who had undergone radical orchidectomy.
- The aim of their presentation was to argue if orchidectomy was avoidable. It also illustrated the probable hematogenous or lymphatic spread of Mtb to the testicle.

[49] reported a 73-year-old Moroccan man who had manifested to their tertiary referral hospital after one week of left scrotal swelling. The patient did not have any history of tuberculosis or tubercular contact, and he did not have any significant medical history, he denied trauma and other symptoms. His clinical examination demonstrated a left testicular firm mass which measured about 3 cm, with irregular surface; scrotal skin and epididymis were normal on palpation. There was no palpable inguinal lymphadenopathy found during his examination. The results of his Serum tumour markers were within normal limits, AFP: 3.3 ng/mL; HCG: < 2 mUI/mL; LDH: 203 U/L. Serology for human immunodeficiency virus (HIV) was negative. He had chest radiograph which was within normal limits. He had scrotal ultrasound scan of the left testis which showed a heterogeneous, hypoechoic anterolateral mass that measured 28.9 mm × 14.7 mm in diameter (Figure 16), with internal vascularity upon colour Doppler imaging which had suggested testicular tumour (Figure 17). His right testis and both epididymes were normal upon his ultrasound scan of testes.

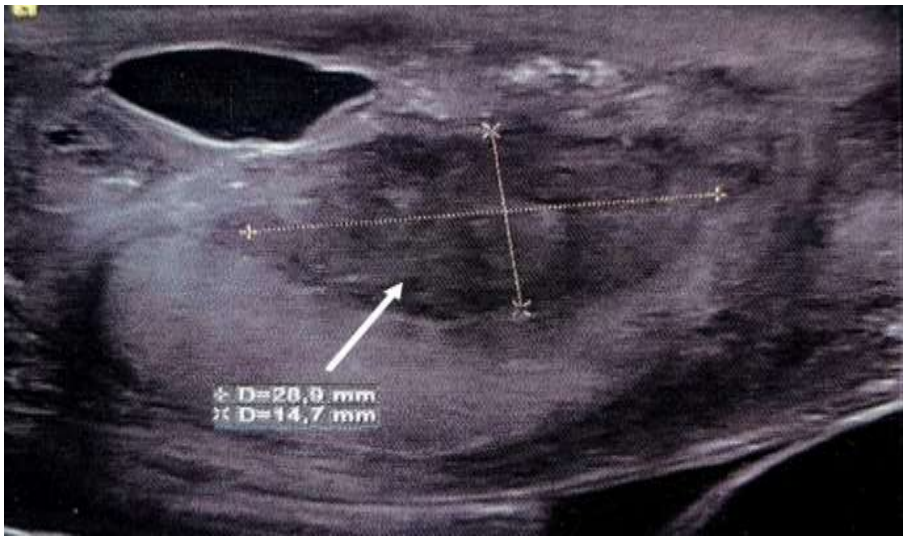


Figure 16

Ultrasonography of left testis showing a heterogeneous and hypoechoic mass measuring 28.9 × 14.7 mm in diameter. Reproduced from [49]

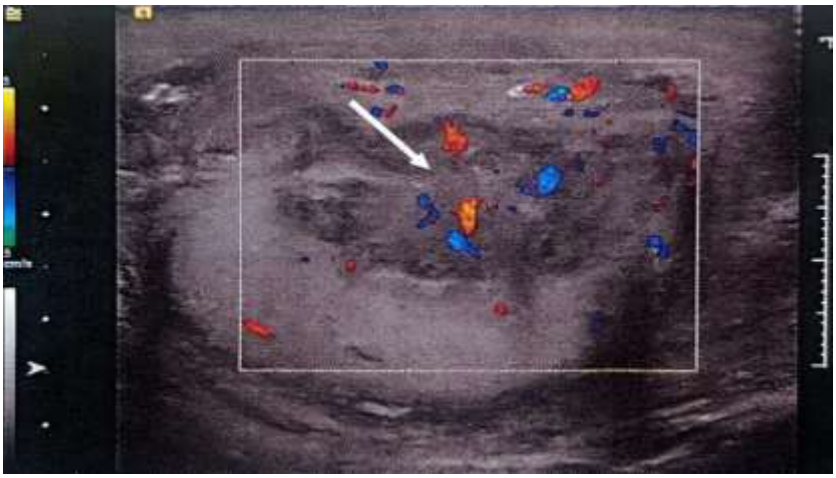


Figure 17

Color Doppler image showing internal vascularity of the testicular mass. Reproduced from: [49]

In light of these findings, left-sided high inguinal orchiectomy was undertaken (Figure 18) after an informed consent was obtained in view of the preliminary diagnosis of testicular tumour. **Figure 18** Reproduced from: [54]

Figure. 18

Postoperative picture of orchiectomy. Reproduced from: [49]

Histopathological examination of testicular tissue revealed the presence of large areas of tuberculotic granuloma caseous necrosis ((Figure 19), multinucleated Langhans giant cells were present in the center of granuloma (Figure 20), and the epididymis was histologically normal. There was no evidence of malignancy.

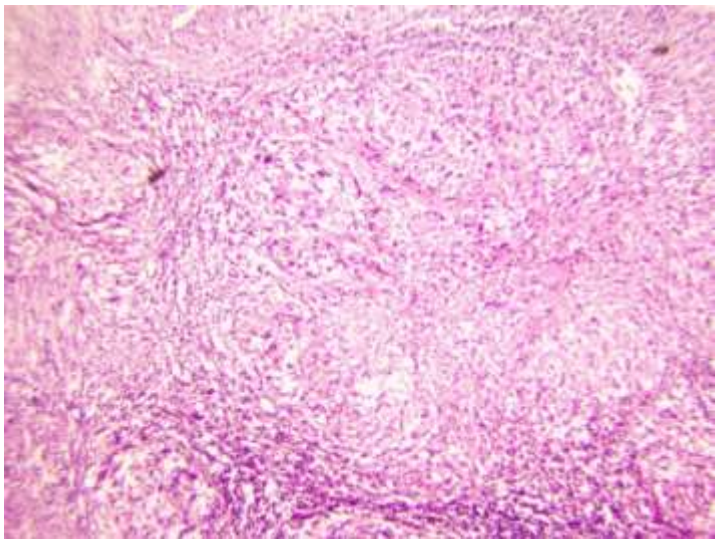


Figure. 19

Photomicrograph showing granulomatous inflammation in testicular tissue, featuring caseous necrosis (H&E stain, × 100). Reproduced from: [49]

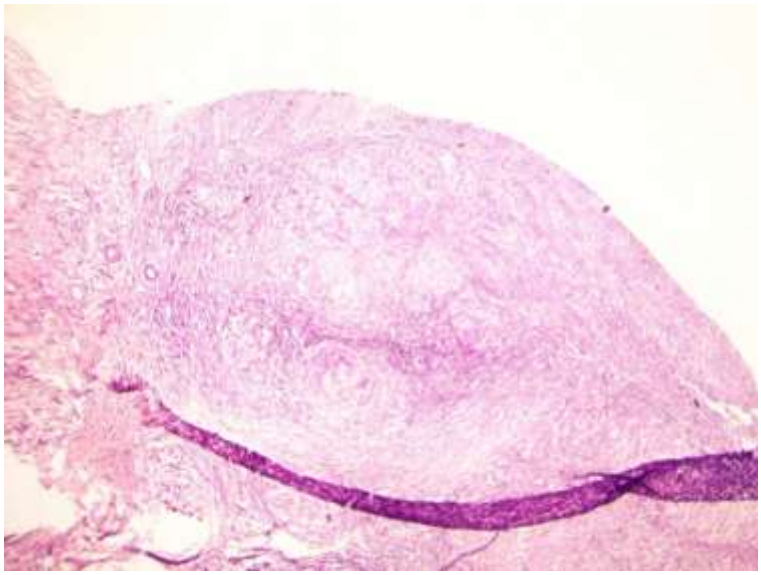


Figure 20

Photomicrograph showing epitheloid granuloma with multinucleated Langhans-type giant cells (H&E stain, × 40). Reproduced from: [49]

The results of his Acid-fast bacilli (AFB) sputum smear and cultures were negative. His Urine smear for AFB was negative, and his uroscan did not find any evidence of abnormality or urinary disorder, which had excluded an active site of genitourinary tuberculosis. Based upon the aforementioned findings, the patient was diagnosed as having isolated testicular TB.

The patient was referred at the local tuberculosis treatment centre. Anti-tuberculosis chemotherapy was then commenced for 6 months.

Kharbach et al. [49] made the ensuing summating discussions:

- Tuberculosis does continue to cause considerable morbidity and mortality globally and TB is considered as a disease of poverty [50].
- Risk factors for the development of TB do include malnutrition, HIV infection, diabetes, substance abuse, poor housing, smoking, immunosuppressive drugs, and chronic renal disease. [50] [51]
- TB does generally tend to afflict the entire male genital tract [52].
- Prostate and epididymis tuberculosis does emanate through hematogenous spread [52]
- Genital TB could also occur via the urinary system to the prostate gland, and then, it spreads from the ejaculatory ducts to the seminal vesicles, vas deferens, and epididymis [52].
- The testicles are affected by TB by contiguity with the epididymis, because the blood-testicles barrier plays a protective role [53] Nevertheless, this mechanism of spread of TB bacilli to the testis is considered to be controversial. Some

reported cases of isolated testicular tuberculosis and their reported case had suggested that patients might develop isolated testicular TB via the haematogenous or/and lymphatic spread [53]. In view of this, isolated testicular TB with no epididymal involvement is very rare, which they had present in their case report.

- The diagnosis of urogenital tuberculosis is presumptive and tends to be based upon a patchwork of suggestive clinical, biological and radiological arguments, without microbiological or histological confirmation in approximately 10.4% of patients [52].[54] Subsequently diagnosis of epididymo-testicular tuberculosis has tended to be challenging and it is discovered upon pathology examination after the undertaking of orchidectomy in up to one fifth of cases [51]
- Non-specific constitutional symptoms of TB such as fever, weight loss, and night sweats are not common in testicular TB [51]
- It has been pointed out that a patient who has TB of the testis could present with acute or chronic, painful, or painless scrotal swellings. [51] It had also been documented that physical examination can find a non-tender testicular mass [51] Associated scrotal skin inflammation and fistulae discharging pus are suggestive of TB [51].
- It has been iterated that ultrasound examination is useful, but it is non-specific [53]. It has also been stated that ultrasound scan could show various patterns, depending upon the pathological stage of tubercular infection, including diffusely enlarged heterogeneously hypoechoic testis, diffusely enlarged homogeneously hypoechoic testis, and nodular enlarged heterogeneously hypoechoic testis [15].
- It has been documented that smooth peripheral calcification of tunica vaginalis (typical of TB), concurrent involvement of the epididymis and scrotal wall thickening are highly suggestive of testicular TB. [35]
- It has also been iterated that Colour Doppler ultrasound scan could help differentiate testicular TB from tumour which generally tends to show central vascularity, whereas TB demonstrates peripheral vascularity due to granulomas and lack of central flow due to caseation necrosis. [35] [44].
- Microbiological diagnostic method for TB is usually not helpful in testicular TB.
- Smear microscopy diagnostic yields using urine tend to be below 40%. [51]
- Culture in Lowenstein-Jensen medium is the diagnostic gold standard for urogenital tuberculosis; [52] nevertheless, it is not contributory in isolated testicular TB.
- PCR for Mtb identification in the urine is highly sensitive and specific and may contribute to the diagnosis. [52]
- In their reported case, the patient's manifestation with only painful scrotal swelling and ultrasound findings prompted the diagnosis of testicular cancer even with the normal level of serum his serum tumour markers suggesting non-seminomatous germ cell tumour of the testis for example.
- Fine-needle aspiration biopsy (FNAB) was not undertaken to avoid causing local spread of tumour cells or to the inguinal lymph nodes.
- Actually, FNAB has usually tended to be prohibited in testicles masses in view of scrotal violation that could lead to neoplastic cell dissemination [55] [56].
- FNAB is especially helpful in young patients who have testicular swelling and normal serum testicular tumour markers, [56] especially if epidemiology risk factors for TB are present. [57]
- The treatment does tend to consist of four medications (isoniazid, rifampicin, pyrazinamide, and ethambutol) which are given for a total of 2 months followed by two medications (isoniazid and rifampicin) which are given for an additional 4 months [54]

[49] made the ensuing conclusions:

- Testicular TB is a curable disease; however, its diagnosis has remained challenging.
- TB of the testis is often missed owing to its non-specific manifestations. Thus, testicular TB should be suspected in patients with a notion of contagion or history of tuberculosis.
- Some ultrasound scan of testes features, are highly suggestive of TB.
- FNAB could prevent unnecessary orchiectomy, but there is a lack of consensus on its use.
- In their reported case, the presentation was typically simulating to a testicular cancer with no evocative evidence of TB. It seemed to them that the undertaking of orchidectomy was not avoidable in their reported patient.

Shugaba et al. [14] reported a 45-year-old man who had attended their visited their clinic with a painless swelling of his left scrotum and an ulcer as his chief complaints. A hard and indurated mass was found palpable with ulcerating foci which were proximal and distal, and which had measured 3 cm× 2 cm and 2 cm × 1 cm respectively and which were about 2 cm apart. The results of his laboratory data were normal except for an elevated erythrocyte sedimentation rate (ESR), and white blood cell (WBC) differential which had shown neutropenia and lymphocytosis. A diagnosis of left testicular tumour was made and the patient had undergone a left orchidectomy with fistulectomy. Histopathology examination of the left orchidectomy specimen showed a stratified squamous epithelium with tuberculous granuloma and necrotic caseation. At the time of the report of the case the patient was undertaking anti-tubercular medication. Shugaba et al. [14] pointed out that the rarity of this condition does make these findings important to report, so that clinicians could have a high index of suspicion for tuberculosis of the testis.

[58] stated the following:

- Genitourinary tuberculosis represents a form of extra-pulmonary tuberculosis which occurs within the kidneys, ureters, seminal vesicles, prostate, testis, vas deferens, and epididymis.
- Isolated testicular involvement of tuberculosis is unusual, and differential diagnosis of tuberculosis of the testis does include testicular tumour, acute infection, infarction, as well as granulomatous infection.

Abraham et al. [58] reported the case of a 36-year-old Ecuadorian man who was residing in New York, New York, and who had manifested with a painful scrotal mass, weight loss, and purulent discharge from ulcerated lesion within his scrotal area 10 years following his immigration into the United States of America. The did not present with any other systemic

symptoms. Positive QuantiFERON-TB Gold and radio imaging results had led to the diagnosis. After extensive workup, acid fast bacilli positive cultures which were obtained by computed tomography guided fine needle aspiration grew Mycobacterium tuberculosis complex. Anti-tuberculosis chemotherapy was commenced after sensitivity tests were confirmed. Significant recovery after 3 months of directly observed therapy was achieved.

[2022] [59] made the ensuing summations related to scrotal tuberculosis:

- Scrotal Tuberculosis (ST) has tended to be an uncommon presentation of extra-pulmonary tuberculosis and scrotal tuberculosis includes tuberculous orchitis and epididymitis.
- With regard to epidemiology of ST, it is an uncommon manifestation presentation which does account for 3% of cases of genitourinary tuberculosis as was documented by Das et al. [1]
- With regard to clinical presentation, ST does tend to manifest as a painless or slightly painful mass within the scrotum and in view of this Scrotal TB has been stated to be difficult to differentiate from typical epididymoorchitis or other scrotal conditions such as tumours or infarction. [15]
- With regard to the pathology of scrotal TB, the infection has usually tended to afflict the epididymis first and then it can affect the testis if it is not treated and scrotal TB has been postulated to occur due to a retrograde extension from the prostate gland and the seminal vesicles as well as by haematogenous spread. [15]

With regard to the radiography features of scrotal TB, Knipe et al. [59] had made the ensuing summating iterations:

Ultrasound

- In cases of scrotal TB, ultrasound scan does tend to depict or indicate that scrotal tuberculosis typically commences within the tail of the epididymis and the ductus deferens.

Tuberculous epididymitis.

- Tuberculous epididymitis does manifest as a diffuse heterogeneous predominantly hypo-echoic enlarged epididymis or an intrinsic focal nodular hypoechoic lesion.
- TB epididymitis usually does tend to demonstrate increased colour Doppler flow, which does tend to differentiate scrotal TB from infarction.
- Bilateral involvement of the epididymis does tend to be commonly encountered, unlike as is found in other nun-tuberculous infections.

Tuberculous orchitis

It is known that tuberculous orchitis does usually tend to be preceded or associated with epididymitis as well as different ultrasound scan patterns had been described including the ensuing: [15]

- Ultrasound scan of the scrotum and testes does tend to depict diffusely enlarged heterogeneously hypo-echoic testis.
- Ultrasound scan of the scrotum and scrotal contents does tend to illustrate diffusely enlarged homogeneously hypoechoic testis.
- Ultrasound scan of the scrotal contents does also tend to demonstrate nodular enlarged heterogeneously hypoechoic testis.
- Ultrasound scan of the scrotal contents in some cases of tuberculous orchitis does tend to demonstrate multiple small hypoechoic nodules within an enlarged testis (the milliary type).

Other documented ultrasound scan of scrotal contents features

Other documented ultrasound scan of scrotal contents features that had been reported in cases of tuberculous epididymitis had been summated by Knipe et al. [59] to include the ensuing:

- Ultrasound scan demonstrated features of thickened scrotal skin.
- Ultrasound scan demonstration of scrotal sinus tract.
- Ultrasound scan demonstration of scrotal hydrocoele.
- Ultrasound scan demonstration of intra-scrotal abscesses.
- Ultrasound scan demonstration of intra-scrotal extra-testicular calcification: at the epididymis and tunica vaginalis.
- Evidence of tuberculosis infection elsewhere within the body of the patient.

Treatment and prognosis associated with treatment of scrotal TB.

- It has been iterated that anti-tuberculous chemotherapy has remained the mainstay of treatment of intra-scrotal tuberculosis.
- Or on rare occasions, the undertaking of orchidectomy had been necessitated for the diagnosis or treatment of intra-scrotal tuberculosis.[8]
- With regard to prognosis pursuant to treatment of intra-scrotal tuberculosis, infertility could be a subsequent emanation.

Differential diagnoses

Some of the documented differential diagnosis of intra-scrotal TB include the following:

- Bacterial epididymo-orchitis.
- Sarcoidosis of the testis.
- Lymphoma of the testis
- Primary tumours of the testis
- Testicular metastasis tumours
- Haematoma of the testis.
- Infarction of the testis**.**

Practical points to learn from

Some of the practical points related to scrotal tuberculosis which should be known and reflected upon include the ensuing:

- A heterogeneous, enlarged epididymis has tended to be more commonly encountered in cases of tuberculous rather than non-tuberculous epididymitis which usually does appear to be homogeneous.
- Bilateral involvement of the scrotal contents tends to be more commonly encountered with tuberculous epididymo-orchitis.
- Failure of antibiotic treatment for epididymo-orchitis should enable clinicians and patients to raise the suspicion for tuberculous aetiology.

- The presence of pulmonary or extra-pulmonary tuberculosis infection elsewhere in the body should make scrotal manifestations to be more likely that of tuberculosis.
- Associated features which tend to be unusual in non-tuberculous epididymo-orchitis including; intra-scrotal and extra-scrotal calcifications, scrotal abscess, and sinus tracts should be helpful clues for the diagnosis of scrotal TB.

Cherif et al. [60] stated the following:

- Globally, it has been estimated that 14.8% of all new tuberculosis cases in adults are attributable to HIV infection.
- Genitourinary tuberculosis is a known complication of HIV infection, which is regarded as a severe form of extrapulmonary tuberculosis. Isolated tuberculous epididymo-orchitis is rare.

Cherif et al. [60] reported a Caucasian HIV-positive heterosexual male with a clinical diagnosis of testicular tumour for which he had undergone a right orchidectomy. Tuberculous epididymo-orchitis was confirmed based upon histology examination of the orchidectomy specimen. Cherif et al. [60] iterated that in this case, all Immune Reconstitution Inflammatory Syndrome (IRIS) criteria were met. Cherif et al. [60] stated that they wanted to convey the message that in HIV-positive patients presenting with testicular swelling, an infective aetiology should be considered and that this will increase the possibility of early diagnosis and proper management.

El-Hamrouni et al. [61] described an unusual case of miliary tuberculous epididymo-orchitis following his undergoing a BCG-therapy, that simulated malignancy at his initial manifestation. They stated that genitourinary tuberculosis in a miliary pattern is rare, and their reported case report had emphasized the importance of meticulous analysis of the patient's clinical history combined with imaging findings in order to ensure an adequate diagnosis and treatment.

Khan et al. [62] stated the following:

- Tuberculosis (TB) is a world-wide disease and if it is not adequately treated could lead to morbidity and mortality.
- Even though genitourinary TB is common and only next to pulmonary TB, cutaneous 'ulcerative' tuberculosis of the scrotum had not been reported so far at the time of publication of their article in the literature.

Khan et al. [62] reported a 32-year-old man who had a non-healing scrotal ulcer for which he underwent excision. Histopathology examination of specimens of the excised ulcer was consistent with features of tuberculosis (TB). Antitubercular therapy was administered and at the end of a year's follow-up, there had been no evidence of recurrence. Khan et al. [62] made the ensuing conclusions:

- TB of the scrotum need to be considered in the differential diagnosis of scrotal ulcers.
- Proper diagnosis and adequate treatment of TB of the scrotum would offer a cure to such patients.

Gangalakshmi et al. [63] stated the following:

- Tuberculosis (TB) of penis is a very rare clinical entity, even within developing countries.
- It might manifest as primary or secondary to Pulmonary TB (PTB).
- Penile TB simulates carcinoma of the penis, granulomatous penile ulcer, genital herpes simplex, granuloma inguinale and HIV infection.

Gangalakshmi et al. [63] reported the case of a 57-year-old male patient who had presented with ulcerative growth over his glans penis and who was clinically diagnosed as carcinoma penis; nevertheless, biopsy of the lesion upon pathology examination showed evidence of tuberculosis which was supported by chest X-ray. This narration has pointed out that even though rare, tuberculosis of the penis could be encountered on rare occasions.

Venyo [64] stated that tuberculosis of the penis (TBP) is rare. Venyo reviewed the literature related to tuberculosis of the penis in 2015 utilizing various internet data bases. Venyo [64] summarized aspects of tuberculosis of the penis as follows:

- TBP could be primary or secondary, may develop following circumcision performed by a person who had pulmonary Tb, and may be transmitted to the penis from ejaculation, contamination from clothing, or from contact with endometrial secretions, following an earlier pulmonary Tb or Tb elsewhere.
- TBP manifests with a painless/painful small nodule, ulcer, mass on penis which gradually enlarges, and induration/swelling of penis, with or without erectile dysfunction.
- Inguinal lymph nodes may or may not be palpable.
- The patient's voiding tends to be normal.
- There may or may not be history of circumcision, pulmonary Tb, and BCG immunization.
- TBP simulates penile carcinoma, granulomatous syphilis penile ulcer, genital herpes simplex, granuloma inguinale, and HIV infection.
- Diagnosis of TBP is established by microscopic examination finding of granulomas +/−AFB in penile discharge or biopsy of lesion or culture of Tb organism from discharge or biopsy specimens or positive Elisa serology/PCR for Tb.
- PTBs do respond to first- or 2nd-line anti-Tb 6-month treatment.

Venyo [64] iterated that close contacts of TBP patients should be screened and that extrapulmonary Tb should be excluded. Venyo [64] concluded that clinicians should consider the possibility of PTB in cases of penile lesions and erectile failure.

Rujaba et al. [65] iterated the following:

- Extrapulmonary tuberculosis accounts for only 15% of new cases of tuberculosis.
- In extrapulmonary tuberculosis, some of the usually affected areas include bone, pleura, lymph nodes, genitourinary system, joints, peritoneum and meninges.
- Tuberculosis epididymo-orchitis is not a common type of extrapulmonary tuberculosis.

Rujaba et al. [65] reported a case of tuberculosis epididymo-orchitis and involvement of the left testis in a 37-year-old male patient. His left testicle had a heterogeneous parenchymal echo, and multiple hypo-echo and ill-defined areas were found within the left testis. In the colour Doppler ultrasound scan, the left testis with the epididymis on both sides was found to be completely hyperaemic. The findings were adjudged to be primarily in favour of extrapulmonary tuberculosis. Therefore, after a 2-month first-stage

treatment with four-drug therapy of anti-TB drugs such as rifampin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg and ethambutol 275 mg, considering the weight of the patient (56 kg), 4 pills per day and the second phase of treatment with two-drug therapy, rifampin 150 mg and 75 mg of isoniazid, 4 pills per day for 4 months, and the extrapulmonary tuberculosis symptoms improved to a large extent. Rujaba et al. [65] concluded that in order to prevent epididymectomy and the effects that the disease might have on fertility, it should be tried to quickly diagnose and treat the disease at the same early stage of the disease.

Conclusions

- Even though pulmonary tuberculosis is the most common type of tuberculosis that afflicts people globally that most people in the world know about, it is important that clinicians and all individuals globally need to be aware that other tuberculosis can affect other organs of the body contemporaneously or subsequent to treatment of pulmonary tuberculosis or tuberculosis afflicting other organs could be de novo tuberculosis affecting extra-pulmonary organs.
- Tuberculosis of testis, epididymis, scrotum and scrotal contents, as well as tuberculosis of the penis and urethra does occur or rare occasions and manifestations of intra-scrotal tuberculosis, tuberculosis of the penis and urethra tend to be non-specific and the manifestations tend to simulate the manifestations of more common diseases and if clinicians do not have a high index of suspicion for tuberculosis, then the diagnosis would be delayed or there would tend to be misdiagnosis of the disease which would prolong the symptoms of these patients as well as impair the quality of life of many patients.
- It is important for clinicians and individuals globally to be aware that tuberculosis of the testis and epididymis could be the cause of a number of cases of unexplained infertility.
- Diagnosis of tuberculosis of the scrotal contents, penis and urethra can be confirmed based upon pathology examination of the lesions of the scrotal contents, penis and urethra.

Conflict of Interest - None

Acknowledgements

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