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Tuberculous Epididymitis Treatement as Acute Scrotal Abscess

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Abstract **Original Research Article**

Objective: Tuberculous epididymis TB introduced as a colossal scrotal ulcer with scrotal sack inclusion is extraordinarily remarkable. The side effects of such ITE look like the epididymo-orchitis or dangerous tumor, which results in misdiagnosis or defer in conclusion. ***Methods:*** This study is a review information examination of 16 instances of histologically-affirmed epididymal tuberculosis in patients treated at IBN-SINA medical clinic from March 2015 to December 2022. ***Results:*** The age of the patients was normal around 42 years (range, 24-62 years); 5 patients (31.25%) had tuberculosis in the left epididymis, 7 patients (43.75%) had tuberculosis in the right epididymis and 4 patients (25%) had two-sided epididymal tuberculosis. Of the 16 patients, 3 patients (18.75%) had a past filled with tuberculosis, including 1 instance of pneumonic tuberculosis, 1 instances of renal tuberculosis and one instance of prostate tuberculosis. ***Conclusion:*** Epididymal tuberculosis is probably going to have attacked encompassing tissues when signs, for example, epididymal beaded changes and not well characterized epididymis-testis line are available. Careful treatment joined with preoperative and postoperative anti-tubercular treatment is a successful way to deal with treating this condition. Sperm retrieval and cryopreservation must be considered for potential intra-cytoplasmic sperm infusion.

Keywords: Tuberculous epididymis, symptoms, epididymo-orchitis, malignant, diagnosis.

PRESENTATION

Epididymal tuberculosis is an uncommon extrapulmonary type of tuberculosis that happens in youthful grown- ups patients with this sickness might have no undeniable clinical side effects or just gentle side effects. The illness ordinarily grows gradually and early determination is troublesome; postponed analysis and misdiagnosis are normal. As of late, because of the development of multi-drug safe microbes, hostile to tuberculosis drug obstruction, and the inescapable utilization of glucocorticoids, the rate of male genital tuberculosis, including epididymal tuberculosis, has been expanding around the world. Epididymal tuberculosis stays a significant medical issue in many agricultural nations, The obsessive elements of epididymal tuberculosis are broad tissue obliteration and fibrosis, in the long run prompting obliteration of the epididymis and encompassing genital tissues and organs and difficulties, for example, fruitlessness and other serious consequences for male regenerative framework function [1, 2] as of now, early determination and customary oral medication and infusion are the keys to fix male conceptive framework tuberculosis and to keep away from careful and chemotherapy therapy. In any case, because of its late beginning and vague clinical signs and side effects, and the absence of fast, touchy, and explicit demonstrative techniques, the sickness is frequently misdiagnosed or the determination is postponed. Be that as it may, for its treatment technique, we have prescript essentially taken some sort of medication orally and embed infusing the expected sum into the body [3-5]. This review, a review investigation of a progression of instances of epididymal tuberculosis, is planned to all the more completely describe the clinical elements and results of careful treatment of this sickness.

METHODS AND MATERIALS

From March 2015 to December 2022, we collected the medical records of 16 patients with histologically confirmed epididymal tuberculosis at IBN-SINA hospital. The final results were compared and analyzed after collecting age, clinical signs and

symptoms, diagnostic methods, and treatment effects from the patients' electronic medical records.

RESULTS

The patients' average age was 41.98 years old. Left-sided epididymal lesions were found in 5 patients (31.25%), right-sided lesions in 7 patients (43.75%), and bilateral lesions in 4 patients (25%). The most common symptoms were painless scrotal swelling in 7 cases (43.75%) and scrotal drop pain in 7 cases (44.7%). Scrotal physical examination revealed epididymal beaded enlargement in 4 (25.5%), testicular mass in one (6.25%), scrotal tenderness alone in two (12.5%), an ill-defined epididymal-testicular border in 7 (43.75%), and sinus formation in 2 (12.5%) patients. The patients underwent surgery after 2-4 weeks of anti-tuberculosis injection. We discovered that 3 (75%) of the 4 patients with epididymal beaded enlargement had simple epididymal special injecting treatment. 5 (71.42%) of the 7 patients with ill-defined testis-epididymis demarcation underwent epididymis-testicular treatment. For 3-6 months, all patients received postoperative injections and medications. [6] Postoperative evaluation revealed a positive response to treatment.

Epididymis Immune Characteristics

The Epididymis's Structure

The epididymis is primarily made up of the epididymal tube. The inner layer of the epididymal duct is lined by a pseudostratified columnar ciliated epithelium, and the outer layer is surrounded by a peritubular layer of smooth muscle cells, which contains the vasculature and lymphatics [7]. As shown in Image 1, epididymis epithelial cells (EECs) are made up of a variety of epithelial cells, including main cells, basal cells, lymphocyte or halo cells, clear cells, and monocyte phagocytes, which include dendritic cells and macrophages [8] as shown in Figure 1.

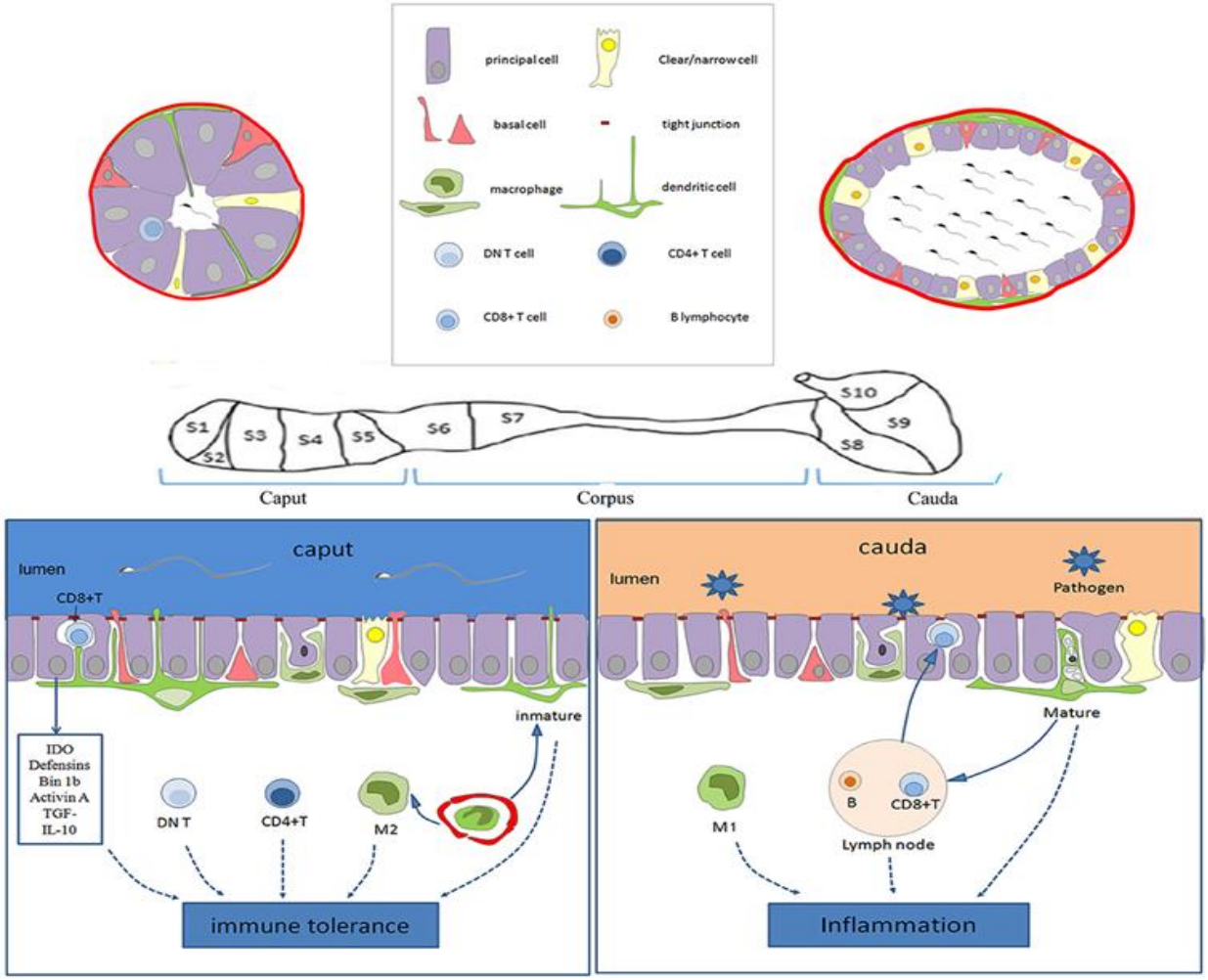

Figure 1: Schematic diagram of the immune characteristics of the epididymis in various regions.

The epididymis epithelium contains a variety of cell types such as main cells, basal cells, lymphocyte cells, clear cells, dendritic cells, and macrophages. Dendritic cells in the caput may extend to the tight junction between epithelial cells and be particularly active. The caput has more CD4+ T cells and DN T cells than the cauda. Furthermore, immune molecules (such as IDO, actin, defensins, and Bin 1b) are highly

expressed in the caput, which, in conjunction with immune cells, provides an environment of immune tolerance for spermatozoa neoantigens. Pathogens that enter the genital tract, on the other hand, always cause inflammation in the cauda epididymis. Pathogen clearance is aided by CD8+ T cells in EECs and M1 macrophages. Furthermore, B lymphocytes and lymphatics tend to accumulate in the caudal region, enhancing the ability to respond to ascending infections. IDO stands for tryptophan-catabolizing enzyme indoleamine 2, 3-dioxygenase; DN T stands for CD4-CD8- T; and EECs stand for Epididymis epithelial cells.

Epididymis-Blood Barrier

The epididymis has a barrier function known as the Blood-Epididymis Barrier (BEB). Anatomical, physiological, and immunological barriers make up the fully functional BEB [9]. The anatomical barrier is made up of tight junctions formed by the basolateral and apical membranes of the principal cells, which prevent molecules and cells from entering or leaving the lumen. The physiological barrier is made up of transporters and channels, whereas the immunological barrier is made up of various immune components both inside and outside of the tubule/duct [10].

Tight junctions and selective transport by the principal cells can result in a high concentration of some molecules, such as carnitine and inositol, in the epididymis, which is beneficial for sperm storage and maturation [11, 12]. The BEB provides an immune-privileged environment for sperm with neoantigens in addition to providing a suitable environment for sperm maturation [13].

EECs and TRLs

Toll-like receptors (TLRs) are innate immune pathogen pattern recognition receptors that can recognize proteins, nucleic acids, and lipids of invading pathogenic microorganisms [such as viruses, bacteria, fungi, and protozoa [14]. TLRs are expressed by both EECs and immune cells throughout the epididymis in rats, indicating that EECs play an immune role [15]. TLR1-TLR9 mRNA is abundant in the rat epididymis, whereas TLR10 and TLR11 are less abundant [16]. TLRs5-7 and TLR11 are not expressed by clear cells in the rat cauda epididymis [17]. TLRs 1-4 are expressed by principal cells throughout the rat duct [17]. TLR1-6 expression in the caput epididymis is similar to that in the testis, whereas TLR7, 9, and 11 expressions in the mouse epididymis are higher [18].

Table 1: The clinical manifestations and diagnosis in 16 patients with epididymal Tuberculosis

	Number	Percentage (%)
Location		
Left	5	31.25
Right	7	43.75
Bilateral	4	25
Symptoms		
Painless swelling	7	43.75
Scrotal drop pain	7	43.75
Urinary tract irritation	1	6.25
Scrotal skin ulceration	1	6.25
Systemic symptoms		
Yes	2	12.50
No	14	87.5
Physical examination		
Epididymal beaded enlargement	1	6.25
Testicular mass	1	6.25
Scrotal tenderness	7	43.75
Ill-defined epididymal testicular border	7	43.75
Sinus formation		12.50
History of tuberculosis		
Pulmonary tuberculosis	3	0.06
Renal tuberculosis	4	0.08
Prostate tuberculosis	1	0.02
No	8	0.84
Preoperative diagnosis		
Tuberculosis	14	87.20
Tumors	1	6.40
Masses	1	6.40

Painless scrotal swelling in 7 patients (43.75%); scrotal drop pain in 7 patients (43.75%); urinary tract irritation such as urinary frequency, dysuria, and hematuria in 4 patients (25%); and scrotal skin ulceration in one patient (6.25%). 2 patients (12.5%) experienced systemic symptoms such as low-grade fever, fatigue, and night sweats. All patients had a scrotal physical examination, which revealed epididymal beaded enlargement in 4 (25.5%), testicular mass in one (6.25%), scrotal tenderness alone in two (12.5%), an ill-defined epididymal testicular border in 7 (43.75%), and sinus formation in 2 (12.5%) (Table 1).

All patients underwent urinalysis and chest imaging. 4 patients 26.6%) had white blood cells in their urine, while 2 (13.35%) had red blood cells in their urine. 2 patients (12.75%) had positive chest imaging. Preoperative diagnoses included epididymal tuberculosis in 4 (27.2%), epididymal tumor in 2 (6.4%), and epididymal mass in 1 (6.4%). All patients had surgical treatment for the lesion [19].

The results of treating 16 patients with tuberculous epididymitis with rifampicin injection for orally administered rifampicin (600 mg), isoniazid (300 mg), and ethambutol (25 mg/kg body weight). Every 4 to 6 days, 600 mg of rifampicin was injected intratunically. Both groups received treatment for 6 months, with a 3-month follow-up. Periodic clinical evaluations, as well as semen and hydrocele fluid examinations, were carried out. Epididymal swellings in the intratunical injection group disappeared in 3 to 6 months, and semen and hydrocele fluid became sterile in 4 months. Only one patient in the oral group had a partial reduction in epididymal mass, and one developed a scrotal fistula. Semen remained tubercle bacilli positive, and hydrocele fluid became negative in only one patient. The good results with intratunical rifampicin administration appear to be due to the drug reaching high concentrations in the epididymis [20]. Furthermore, intratunical injection treatment uses a single drug, as opposed to oral therapy, which improves outcomes through multidrug administration.

14 (87.2%) of the 16 cases were initially diagnosed as epididymal tuberculosis and were treated pre-operatively with rifampicin, isoniazid, pyrazinamide, and ethambutol for 2-4 weeks. Eight patients (50.3%) underwent epididymectomy, and 7 patients (43.75%) underwent epididymectomy in conjunction with orchiectomy; all recovered well after the injection.

We discovered that 3 (75%) of the 4 patients with epididymal beaded enlargement had simple medicine and two (12.5%) had epididymis-testicular injection. There were 16 (72.2%) epididymis-testicular injections and five epididymal injections performed on the 7 patients whose main clinical manifestation was ill-defined testis-epididymis demarcation (Table 2).

Table 2: Association between surgical methods and physical examination

	Total	Epididymal resection	Epididymis-testicular resection
Ill-defined epididymal testicular border	7	6 (85.71%)	1 (14.29%)
Epididymal beaded enlargement	3	2 (66.66%)	1 (33.34%)
Scrotal tenderness	2	2 (100%)	0
Sinus formation	2	1 (50%)	1 (50%)
Testicular mass	1	1 (100%)	0

All specimens had solitary or confluent pale, grayish caseous necrotic nodules on the macroscopic level. Some lesions invaded the entire epididymis, while others involved the testis with adherence to the scrotum to form a cold abscess and formed ulcerated sinus tracts in the skin. The specimens' centers were red-stained with amorphous granular, irregularly sized foci of caseous necrosis surrounded by tuberculous granulation tissue (epithelioid cells, Langhans giant cells, and lymphocytes) under the microscope (Figs. 2 and 3).

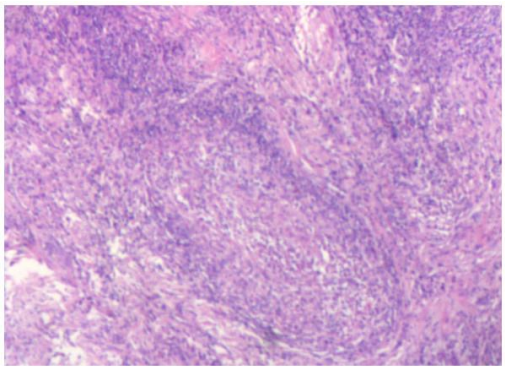

Figure 2: Microscopy images of caseous necrosis with amorphous granular

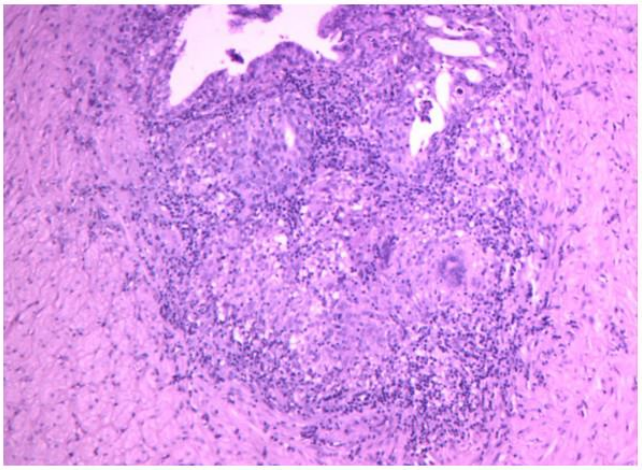

Figure 3

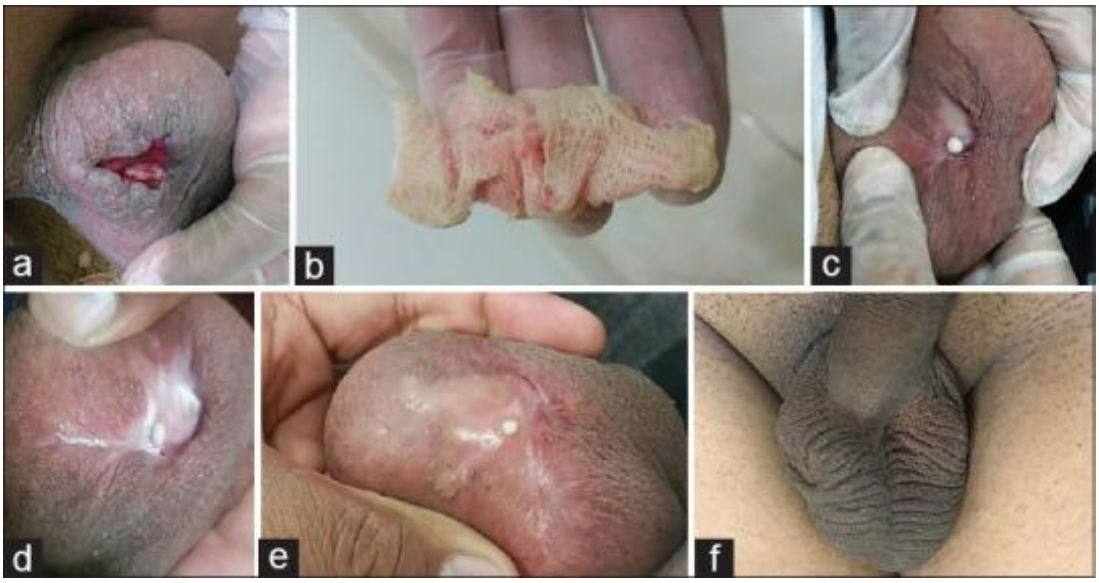

Figure 4: Raptured scrotum of a 32-year-old male with multiple pockets of intrascrotal abscess.

The arrow indicates abscess excretion at the time of diagnosis (a). Discharge or abscess from the scrotum on a cotton swap following scrotal skin rapture (b) Abuse discharge after 3 months of diagnosis during treatment (c). After 5 months of diagnosis, the discharge and orifice (d). (d) Shows the healed scrotum after 6 months of medication completion.

After treatment, all patients received 3-6 months of anti-tuberculosis treatment with rifampicin, isoniazid, pyrazinamide, or ethambutol. There was no recurrence reported.

DISCUSSION

To prevent Mtb infection from spreading from one person to another, health-care workers who care for patients with UG-TB must follow infection-control procedures. There are no clear guidelines or evidence base for reducing the risk of transmission to surgical staff from patients with UG-TB who require surgery. To reduce Mtb bacillary load, anti-TB treatment should be started at least 8 weeks before surgical intervention [22]. Nursing in patients with UG-TB follows standard infection control procedures.

The only available vaccine for tuberculosis prevention is the BCG vaccine, which has been around for 80 years and is routinely used in developing countries' neonates and infants [23]. In children, the BCG vaccine has been shown to protect against meningitis and disseminated tuberculosis. It does not protect against primary infection and, more importantly, it does not protect against reactivation of latent pulmonary infection. Over the last two decades, there has been an increase in efforts to develop new pre-exposure and post-exposure vaccines, with 15 new candidate vaccines currently under investigation [24]. Hopes for accelerated vaccine development and evaluation stem from renewed political and funding commitments made at the United Nations General Assembly High Level Meeting on Tuberculosis on September 28, 2018 (UNG-HLM-TB) [25].

Tuberculosis of the reproductive system can strike at any age, but it is most common in men aged 24-62. It is uncommon in children due to the lengthy incubation period. The epididymis is the most commonly involved organ, followed by the seminal vesicle, prostate, testis, and vas deferens. Isolated epididymal tuberculosis is extremely uncommon. According to one new study, isolated epididymal tuberculosis could be the first or only manifestation of early genitourinary tuberculosis. Similarly, there were 15 cases (92.75%) of isolated epididymal tuberculosis in our patient cohort.

The pathogenesis of epididymal tuberculosis includes Mycobacterium tuberculosis blood-borne transmission and transurethral reflux caused by trauma, alcohol abuse, and excessive sexual activity. Because of its rich blood supply and retrograde infection from the vas deferens, epididymal tuberculosis lesions first appear in the epididymal tail. Epididymal tuberculosis lesions spread from the body to the head, eventually affecting the entire epididymis. The testis may be involved in severe cases. In this group, 7 (43.75%) patients with epididymal tuberculosis invading the testis underwent radical testicular injection. The main reason for the patient's visit in our study was a painless mass of the epididymis, which is consistent with previous research. However, the proportion of patients with scrotal pain is higher, owing to the fact that all of the patients in this study had advanced epididymal tuberculosis or testicular or scrotal involvement.

The isolation and culture of M. tuberculosis is the gold standard for tuberculosis diagnosis. In cases of suspected Male genital tuberculosis, M. tuberculosis is usually found in the urine or tissue. Historically, the appearance of sterile pyuria on microscopic urinalysis has been thought to be a typical manifestation of urogenital involvement. According to some findings, leukocytes were present in urine microscopically or grossly in the majority of cases (50% and 10%, respectively). Hematuria is a common symptom of urinary tuberculosis, which is caused primarily by renal and bladder tuberculosis. Urinary tuberculosis has been linked to hematuria and acidic urine, but these are nonspecific findings. 18.75% of our patient cohort tested positive for red blood cells in urine, which is associated with renal tuberculosis. Leukocyte positivity in the urine helped to diagnose 9 (56.25%) of the patients, but its specificity was low. Color Doppler ultrasound is the imaging method of choice for epididymal tuberculosis. CT and MR scans have little value in diagnosing epididymal tuberculosis; they are primarily used to diagnose tuberculosis in the lung and kidney and provide support for epididymal tuberculosis diagnosis.

Tuberculous epididymitis is not always the only symptom of genitourinary tuberculosis. As a result, even in the absence of clinical and laboratory indicators of renal and urologic tuberculosis, all men with identified epididymal lesions should be injected with a fine needle. Kim *et al.,* (1993) proposed that B-ultrasound biopsy can often be used to diagnose epididymal tuberculosis, which supports the preceding conclusions. Polymerase chain reaction has been used extensively in diagnostics. In recent years, when combined with pathological biopsy, it has been shown to improve the diagnosis of epididymal tuberculosis (Chawla *et al.,* 2012). It has a high sensitivity, a high specificity, and a short turnaround time. However, diagnosing simple epididymal tuberculosis is difficult at the moment, and there is no preoperative diagnostic method with high sensitivity and specificity. It is not difficult to make a clinical diagnosis of scrotal abscess and ulceration. It is often possible to make a definitive diagnosis by looking for acid-fast bacilli in samples of ruptured tissue obtained via pus or secretion smears.

Bacterial epididymitis, epididymal sperm granuloma, epididymal tumor, and other diseases are included in the differential diagnosis of epididymal tuberculosis. 14 of the 16 patients had typical tuberculosis symptoms, signs, imaging findings, or a history of tuberculosis, and were diagnosed with epididymal tuberculosis. Three patients had no typical tuberculosis symptoms and were misdiagnosed as epididymal masses due to tumor characteristics (24-62) years, weight loss, solid epididymal mass). Because of the mass affecting life, three patients who did not have the above symptoms required surgery. Patients with bacterial epididymitis frequently experience testicular-epididymis pain, as well as scrotal swelling and heat (Banyra & Shulyak, 2012). Among the benefits are a shorter course of illness and symptoms that are generally relieved following antibiotic treatment. According to Carl and Stark (1997), epididymal tuberculosis should be suspected when patients have persistent or repeated epididymitis episodes and symptoms are not controlled after adequate antibiotic treatment. Antibiotics and anti-tuberculosis treatment are ineffective for epididymal sperm granuloma, which primarily occurs in the epididymal head and is characterized by a smooth solid mass. Epididymal tumors are uncommon, accounting for approximately 0.9% of all male reproductive system tumors. The majority of tumors in men between the ages of 20 and 40 occur during periods of sexual activity. Slow growth, large volume, and no tenderness characterize the disease. CT scans aid in the confirmation of the diagnosis.

Like other tuberculosis diseases, epididymal tuberculosis necessitates early, consistent, full-course, moderate, combined anti-tuberculosis treatment. For 6-9 months, three to four anti-tuberculosis drugs are administered. If there is no response to drug treatment or if an abscess forms, surgical treatment is required. Because the early symptoms of epididymal tuberculosis are not obvious, abscesses or involvement of

surrounding tissues such as the testicles have frequently developed during treatment, necessitating surgery for the majority of patients. When there is active tuberculosis, anti-tuberculosis treatment must come first, followed by medicine. In this study, eight patients (18.75%) had pulmonary tuberculosis that had developed calcification, proving that they had old tuberculosis. Fourteen patients (87.2%) were diagnosed with epididymal tuberculosis and received antituberculous therapy for 2-4 weeks prior to surgery. The epididymal-testis border was unclear or sinus formation was found in 10 of our patient cohort's (59.6%) cases presenting as a testicular painless mass, indicating that the surrounding tissues were invaded. Despite the fact that injection treatment is effective, patients still require regular anti-tuberculosis medication for 3-6 months with injection and close monitoring.

CONCLUSION

In patients with a history of tuberculosis, epididymal tuberculosis is easily diagnosed. Early symptoms of isolated epididymal tuberculosis, on the other hand, are not obvious, and cases are typically advanced at the time of diagnosis. Symptoms and signs include epididymal enlargement, falling pain, and bead-like changes. By the time epididymal tuberculosis is discovered, it has spread to surrounding tissue. Injection therapy combined with preoperative and postoperative injection is a successful treatment strategy. When epididymal tuberculosis causes bead-like changes, testicular involvement, or sinus formation, definitive epididymal-testicular surgery can produce good results. Even though it is a rare and difficult to diagnose disease, isolated epididymis TB should be considered as a differential diagnosis with a case presentation of testicular mass. For cases of epididymis TB, the Pharmacological approach should be used first. When a patient does not respond to pharmacological treatment, an injection should be considered. Only in cases where the diagnosis is unknown or where there is a strong clinical indication, such as abscesses, cutaneous fistulas, or extensive involvement of the epididymis and testis, should an oral medication and injecting procedure be considered. For an accurate diagnosis, a diagnostic algorithm should include minimally invasive diagnostic approaches such as FNA. The purpose of this article is to present this type of extrapulmonary tuberculosis and to elucidate and bring more insights to this rare diagnosis, as well as to conduct it appropriately.

REFERENCES

1. Alsultan, A., & Peloquin, C. A. (2014). Therapeutic drug monitoring in the treatment of tuberculosis: an update. *Drugs*, 74(8), 839-854.
2. Banyra, O., & Shulyak, A. (2012). Acute epididymo-orchitis: staging and treatment. *Central European Journal of Urology*, 65, 139-143.
3. Carl, P., & Stark, L. (1997). Indications for surgical management of genitourinary tuberculosis. *World Journal of Surgery*, 7(5), 505-510.
4. Chawla, A., Chawla, K., Reddy, S., Arora, N., Bairy, I., Rao, S., ... & Thomas, J. (2012). Can tissue PCR augment the diagnostic accuracy in genitourinary tract tuberculosis?. *Urologia internationalis*, *88*(1), 34-38.
5. Chung, J. J., Kim, M. J., Lee, T., Yoo, H. S., & Lee, J. T. (1997). Sonographic findings in tuberculous epididymitis and epididymo-orchitis. *Journal of clinical ultrasound*, *25*(7), 390-394.
6. Glaziou, P., Floyd, K., & Raviglione, M. C. (2018). Global epidemiology of tuberculosis. *Seminars in Respiratory and Critical Care Medicine*, 39(3), 271-285.
7. Da Silva, N., & Smith, T. B. (2015). Exploring the role of mononuclear phagocytes in the epididymis. *Asian journal of andrology*, *17*(4), 591-6. doi: 10.4103/1008-682X.153540
8. Wang, H., & Kumar, T. R. (2012). Segment-and cell-specific expression of D-type cyclins in the postnatal mouse epididymis. *Gene Expression Patterns*, *12*(3-4), 136-144. doi: 10.1016/j.gep.2012.01.003
9. Légaré, C., & Sullivan, R. (2020). Differential gene expression profiles of human efferent ducts and proximal epididymis. *Andrology*, *8*(3), 625-636. doi: 10.1111/andr.12745
10. Domeniconi, R. F., Souza, A. C. F., Xu, B., Washington, A. M., & Hinton, B. T. (2016). Is the epididymis a series of organs placed side by side?. *Biology of reproduction*, *95*(1), 10-1. doi: 10.1095/biolreprod.116.138768
11. Mital, P., Hinton, B. T., & Dufour, J. M. (2011). The blood-testis and blood-epididymis barriers are more than just their tight junctions. *Biology of reproduction*, *84*(5), 851-858. doi: 10.1095/biolreprod.110.087452
12. Johnston, D. S., Turner, T. T., Finger, J. N., Owtscharuk, T. L., Kopf, G. S., & Jelinsky, S. A. (2007). Identification of epididymis-specific transcripts in the mouse and rat by transcriptional profiling. *Asian journal of andrology*, *9*(4), 522-527. doi: 10.1111/j.1745-7262.2007.00317.x
13. Gregory, M., & Cyr, D. G. (2014). The blood-epididymis barrier and inflammation. *Spermatogenesis*, *4*(2), e979619. doi: 10.4161/21565562.2014.979619
14. Cyr, D. G., Dufresne, J., & Gregory, M. (2018). Cellular junctions in the epididymis, a critical parameter for understanding male reproductive toxicology. *Reproductive toxicology*, *81*, 207-219. doi: 10.1016/j.reprotox.2018.08.013
15. Hedger, M. P. (2011). Immunophysiology and pathology of inflammation in the testis and

epididymis. *Journal of andrology*, *32*(6), 625-640. doi: 10.2164/jandrol.111.012989

16. Itoh, M., Xie, Q., Miyamoto, K., & Takeuchi, Y. (1999). Major differences between the testis and epididymis in the induction of granulomas in response to extravasated germ cells. I. A light microscopical study in mice. *International journal of andrology*, *22*(5), 316-323. doi: 10.1046/j.1365-2605.1999.00186.x
17. Smith, T. B., Cortez-Retamozo, V., Grigoryeva, L. S., Hill, E., Pittet, M. J., & Da Silva, N. (2014). Mononuclear phagocytes rapidly clear apoptotic epithelial cells in the proximal epididymis. *Andrology*, *2*(5), 755-762. doi: 10.1111/j.2016-2927.2014.00251.x
18. Dubé, E., & Cyr, D. G. (2012). The blood-epididymis barrier and human male fertility. *Adv Exp Med Biol.*, 763, 218–36. doi: 10.1007/978-1-4614-1611-5_1
19. Fitzgerald, K. A., & Kagan, J. C. (2020). Toll-like receptors and the control of immunity. *Cell*, *180*(6), 1044-1066. doi: 10.1016/j.cell.2020.02.04
20. Palladino, M. A., Savarese, M. A., Chapman, J. L., Dughi, M. K., & Plaska, D. (2008). Localization of Toll-like receptors on epididymal epithelial cells and spermatozoa. *American journal of reproductive immunology*, *60*(6), 541-555. doi: 10.1111/j.1600-0897.2008.00654.x
21. Palladino, M. A., Johnson, T. A., Gupta, R., Chapman, J. L., & Ojha, P. (2007). Members of the Toll-like receptor family of innate immunity pattern-recognition receptors are abundant in the male rat reproductive tract. *Biology of reproduction*, *76*(6), 958-964. doi: 10.1095/biolreprod.106.059410
22. Zhu, W., Zhao, S., Liu, Z., Cheng, L., Wang, Q., Yan, K., ... & Han, D. (2015). Pattern recognition receptor–initiated innate antiviral responses in mouse epididymal epithelial cells. *The Journal of Immunology*, *194*(10), 4825-4835. doi: 10.4049/jimmunol.1402706
23. Kadhiravan, T., & Sharma, S. K. (2008). Medical management of genitourinary tuberculosis. *Indian journal of urology: IJU: journal of the Urological Society of India*, *24*(3), 362.
24. WHO. Guidelines on the management of latent tuberculosis infection. WHO https://www.who.int/tb/publications/latent-tuberculosis-infection/en/ (2019).
25. White, R. G., Hanekom, W. A., Vekemans, J., & Harris, R. C. (2019). The way forward for tuberculosis vaccines. *The Lancet Respiratory Medicine*, *7*(3), 204-206.
26. Zumla, A., & Petersen, E. (2018). The historic and unprecedented United Nations General Assembly High Level Meeting on Tuberculosis (UNGA-HLM-TB)—'United to End TB: an urgent global response to a global epidemic'. *International Journal of Infectious Diseases*, *75*, 118-120.
27. Kim, S. H., Pollack, H. M., Cho, K. S., Pollack, M. S., & Han, M. C. (1993). Tuberculous epididymitis and epididymo-orchitis: sonographic findings. *The Journal of urology*, *150*(1), 81-84.
28. Kulchavenya, E., Kim, C. S., Bulanova, O., & Zhukova, I. (2012). Male genital tuberculosis: epidemiology and diagnostic. *World journal of urology*, *30*(1), 15-21.
29. Lee, H. Y., Lee, J., Lee, Y. S., Kim, M. Y., Lee, H. K., Lee, Y. M., ... & Ko, Y. (2015). Drug-resistance pattern of Mycobacterium tuberculosis strains from patients with pulmonary and extrapulmonary tuberculosis during 2006 to 2013 in a Korean tertiary medical center. *The Korean Journal of Internal Medicine*, *30*(3), 325-334.
30. Surati, K. N., Suthar, K. D., & Shah, J. K. (2012). Isolated tuberculous epididymo-orchitis: a rare and instructive case report. *Southeast Asian Journal of Case Report & Review*, *1*, 46-50.
31. Tzvetkov, D., & Tzvetkova, P. (2006). Tuberculosis of male genital system–myth or reality in 21st century. *Archives of andrology*, *52*(5), 375-381.
32. Viswaroop, B. S., Kekre, N., & Gopalakrishnan, G. (2005). Isolated tuberculous epididymitis: A review of forty cases. *Journal of postgraduate medicine*, 51(2), 109.
33. Yadav, S., Singh, P., Hemal, A., & Kumar, R. (2017). Genital tuberculosis: current status of diagnosis and management. *Translational Andrology and Urology*, *6*(2), 222-233.
34. Zhang, S., Luo, Y., Wang, C., Xiong, H., Fu, S. J., & Yang, L. (2016). Open surgery versus retroperitoneal laparoscopic nephrectomy for renal tuberculosis: a retrospective study of 120 patients. *PeerJ*, *4*, e2708.