Tuberculosis of the prostate and urethra: A review

Nitin Gupta, A. K. Mandal, S. K. Singh
Department of Urology, PGIMER (Post Graduate Institute of Medical Education and Research), Chandigarh, India

ABSTRACT

Genitourinary tuberculosis contributes to 10-14% of extrapulmonary tuberculosis and is a major health problem in India. Prostate tuberculosis is uncommon and is usually found incidentally following transurethral resection. The most common mode of involvement is hematogenous, though descending infection and direct intracanalicular extension is known. Predisposing factors include prior tuberculous infection, immuno-compromised status, previous BCG therapy. The presentation is diffuse caseating epitheloid cell granulomas, which can be confirmed by prostate biopsy. Urine PCR has good sensitivity (95.5%) and specificity (98.12%) in diagnosis. Imaging techniques like TRUS and CT/MRI also allow good visualization of the lesion and its extension. Urethral tuberculosis is very rare and is usually secondary to upper tract or genital tuberculosis. The presentation may be acute urethritis or chronic stricture or fistulae. The treatment of choice is chemotherapy with 3-4 anti tubercular drugs for initial 6-12 weeks and later 2 drugs for additional 3-6 months. Surgery is usually reserved for cases where chemotherapy fails and is done after 4-6 weeks of ATT. With a high index of suspicion it may be possible to diagnose a larger number of cases of prostatic and urethral tuberculosis especially in this country where tuberculosis is almost endemic.

Key words: Genitourinary, granulomatous, infection, prostate, rare, tuberculosis, urethra

INTRODUCTION

Tuberculosis (TB) is a major public health problem in developing countries. Worldwide also, TB continues to be an important clinical problem, mainly because of its nonspecific clinical presentation and variable radiographic appearance. Genitourinary tuberculosis (GUTB) has been reported to contribute 10-14% of the extrapulmonary tuberculosis with involvement of any part from kidney to urethra.[1] With an estimated over 10 million sufferers of TB, GUTB constitutes a major urological problem in India. It is a form of secondary TB, the symptoms and signs of which are often vague and insidious. A high index of suspicion helps in early diagnosis.

PROSTATE TUBERCULOSIS

Prostate TB is much less common than renal, vesiculoseminal and epididymal TB. Thus many urologists are unfamiliar with the diagnosis and management of prostatic TB with many cases found incidentally following transurethral resection.[2]

The possible modes of involvement include a descending infection from the urinary organs, direct intracanalicular extension from a neighboring tuberculous focus in the genital tract or a hematogenous spread. On the basis of clinical observations and animal experiments, Sporer et al.,[3] suggested that TB of the prostate is almost always the result of one or perhaps successive hematogenous seedings. Direct extension may occur; however, descending infection of the prostate has never been encountered.[3] It is well established that the predisposing factors associated with the development of TB include prolonged steroid use, immunosuppressive therapy, diseases that impair cell-mediated immunity, and diseases with poor immune mechanisms.[2] Extrapulmonary TB has been reported to be steadily increasing in patients with acquired immunodeficiency syndrome (AIDS).[4]

Tuberculosis of the prostate gland presents with diffuse caseating epithelioid cell granulomas which are not confined to the periglandular/periductal region, as seen in cases of nonspecific granulomatous prostatitis (NSGnP). Other infectious agents, such as Treponema pallidum, [Figure 1] viruses[5] and various fungi,[6] are rare causes of granulomatous prostatitis. Histochemical stains like PAS, Gomori’s stain and Ziehl-Nielson stain are helpful in confirming infectious etiology.

In most cases the cause of granulomatous prostatitis (GnP) is unknown,[5] but GnP can occur after various predisposing/precipitating events, e.g. urinary tract infections(71%)[8], transurethral resection of prostate/ open prostatectomy[9] and needle biopsy.[10] Recently, a higher incidence of GnP

For correspondence: Dr. A K Mandal, Department of Urology, PGIMER, Chandigarh, India.
E-mail: drarupkumar@yahoo.co.in
was found in patients who had been treated with intravesical bacille Calmette-Güézin.11-13 Nonspecific granulomatous prostatitis is usually an incidental finding, with an incidence of <3.4% in unselected series of patients;14 it is detected in 0.44% of routine prostatectomy specimens and in 0.29% to 3.3%15 of needle prostate biopsies. It is important to differentiate NSGnP from specific granulomatous prostatitis, as this type is a self-limiting benign condition, while the latter requires specific treatment.16

URETHRAL TUBERCULOSIS

Urethral TB is very rare despite the constant exposure of the urethra to the infected urine. Most often it has been reported to occur in association with upper tract involvement or female genital involvement.17 Isolated urethral involvement is extremely uncommon. Tuberculosis of the urethra is usually due to the spread from another focus in the genitourinary tract, the prostate being the common source.18 The exact incidence of urethral involvement in TB is not known. Female urethral TB is probably still rarer as compared to male urethral involvement with the spread from uterus and cervix being the important source in them. Symes and Blandy18 have reported five cases of urethral TB out of 112 male patients having urethral stricture. Ross19 reported nine cases of urethral involvement out of 469 patients with GUTB. Indudhara et al.,20 have reported their experience with two cases; one was a male patient who presented with urethral stricture and perineal fistulae, wherein histopathology of the excised scar tissue revealed TB. The other one was a female who presented with a urethral caruncle which was excised and histopathology revealed features of TB.

DIAGNOSIS

Diagnosing prostatic TB can be challenging. The most critical step in attempting to elucidate a diagnosis of genitourinary TB is from the patient’s clinical history.21 Prior TB infection as a child, immunocompromised states, such as human immunodeficiency virus/acquired immunodeficiency syndrome, immunosuppression with organ transplantation, travel to endemic areas, and immigration are important considerations when obtaining the medical history.4 The latency between pulmonary TB and manifestations seen in the genitourinary tract can be lengthy, with some reports showing a period of 30 years before the disease making an appearance. Tubercular prostatitis should also be suspected in patients with lower urinary tract symptoms and prostatic tenderness or nodularity after undergoing bacille Calmette-Güézin therapy for bladder cancer.22

a) TRUS: The tuberculous lesions are typically located in the peripheral part of the posterior and lateral lobes of the prostate.23 The TRUS findings of diffuse hypoechoic lesions within the peripheral zone of the prostate makes it frequently difficult to differentiate between prostatic TB and adenocarcinoma of the prostate. The diagnosis can only be confirmed by prostate biopsy. However, TRUS is one of the tools useful for the diagnosis of prostatic abscess, TRUS allows excellent visualization of the prostatic anatomy and the relationship of the abscess to the prostatic lobes, and permits appropriate transurethral unroofing.24

b) Computed Tomography/ Magnetic Resonance Imaging scan: CT findings have also been shown to be consistent with the findings of previous reports that the round areas of decreased attenuation within the prostate suggest a tuberculous abscess.25 CT can also demonstrate the extension of the abscess and the involvement of the adjacent organ.24 Prostatic tuberculous cavities or abscesses may discharge into the surrounding tissues, forming sinuses or fistulae to the perineum or rectum and eventually resulting in a watering-can perineum. These changes are demonstrated best on MRI scans.

c) Immunological tests: Positive Siebert purified protein derivative of tuberculin test (PPD) supports TB infection, but a negative test does not rule it out.26 A definitive diagnosis is made by positive cultures, Ziehl-Nielsen staining, and/or histological examination Figure 1.14,26 However, staining has a low sensitivity (52.7% in one study), especially in nonpulmonary TB, and cultures require up to eight weeks for maximal sensitivity to be reached.4,26,27

d) Molecular diagnosis: Polymerase chain reaction (PCR) is becoming a useful clinical diagnostic tool because of its rapid detection and high sensitivity and specificity. Moussa et al.,27 reported the sensitivity and specificity of PCR of urine to be 95.59% and 98.12%, respectively. However, one of the disadvantages of PCR is its inability to detect whether the TB infection is biologically active or in its latent phase.4 Most investigators suggest using PCR in combination with cultures and Ziehl-Nielsen staining when making a diagnosis and developing a treatment plan.4,26,27
Urethral TB may present as acute urethritis with urethral discharge and associated affection of the prostate, seminal vesicles, and other parts of the urinary tract or as the chronic variant with stricture formation.[28] Confirmation of the diagnosis in acute variant is probably not difficult while in the later it is difficult. The chronic form may present in bizarre and unexpected forms with fistulae of unusual types and difficult strictures not responding to conventional urethroplasty. Biopsy of the scar tissue may suggest tubercular affection.

TREATMENT

Since 1982, the American Thoracic Society and the Centers for Disease Control have recommended a nine–month course of isoniazid and rifampin for the routine treatment of TB in the United States.[29] However, a shorter course of four or six months of chemotherapy has been recommended for the treatment of tuberculosis.[30] Lee et al.[35] reported results of a triple-drug regimen of a second-line intervention when chemotherapy fails. Biopsy of the prostate in patients with acquired immunodeficiency syndrome were mostly prostatic abscesses.[24,40,41] Moreover, the outbreaks of multidrug-resistant tuberculosis (MDR-TB) in persons with or without HIV infection are associated with higher mortality.[42,43] Thus, a different strategy should be applied in patients with MDR-TB or HIV or other severely immunocompromised status. Histological follow-up is a good method for monitoring the efficacy of treatment. Periodic transrectal biopsies to evaluate the efficacy of antituberculosis treatment have been successfully used for follow-up.[35] Consistent with this notion is the report indicating that after an appropriate course of chemotherapy, residual induration can be biopsied percutaneously.[44] Fine needle aspiration cytology is a suitable alternative for the diagnosis and follow-up of prostatic TB.[45,46]

Antitubercular therapy (ATT) is highly effective, and in most cases curable. Surgical intervention is required only in a minority of cases.

Patients diagnosed to have urethral TB should be given ATT for at least six weeks before any surgical intervention in order to prevent reactivation of a latent focus in the dense scar tissue. The strictures can be treated on conventional lines similar to any urethral stricture. However, urethroplasty may be preferred in the presence of dense fibrous scar involving the urethra and periurethral tissue. The timing of urethroplasty is not clearly defined. However, all reconstructive procedures on the genitourinary tract are done after an initial four to six weeks of ATT.

CONCLUSION

Prostatic and urethral involvement by *Mycobacterium tuberculosis* is rather uncommon. Its rarity is difficult to understand in view of the almost constant exposure of the urethra to the infected urine. A complete understanding of the cause and optimal treatment of prostatic TB and periodic histological follow-up to determine the efficacy of chemotherapy are especially beneficial for patients with MDR-TB or HIV or other severely immunocompromised conditions.

The diagnosis of the tuberculous etiology of the stricture urethra is not easily proven and this makes one think that urethral tuberculosis may be more common than one observes from a study of the literature. With a high index of suspicion and availability of sophisticated and reliable tests for molecular diagnosis like PCR, RT-PCR etc. it may be possible to diagnose a larger number of cases of urethral and prostatic tuberculosis especially in this country where tuberculosis is almost endemic.
REFERENCES

1. Coabawalla BB. Reflections on urogenital tuberculosis. Indian J Urol 1990;6:51-9.
2. Gow JG. Genitourinary tuberculosis. In: Walsh PC, Retik AB, Vaughan ED, et al, editors. Campbell’s Urology 7th ed. Philadelphia: WB Saunders; 1998. p. 817-8.
3. Sporer A, Auerback MD. Tuberculosis of the prostate. Urology 1978;11:362-5.
4. Lenk S, Schroeder J. Genitourinary tuberculosis. Curr Opin Urol 2001;11:93-8.
5. Clason AE, McGeorge A, Garland C, Abel BJ. Urinary retention and granulomatous prostatitis following sacral herpes zoster infection: A report of 2 cases and review of literature. Br J Urol 1982;54:166-7.
6. Hinchee WW, Someren A. Cryptococcal prostatitis. Am J Clin Pathol 1981;75:257.
7. Alexander RB, Mann DL, Borkowski AA, Fernandez-Vina M, Klyushnenkova EN, Kodak J, et al. Granulomatous prostatitis linked to HLA-DRB1*1501. J Urol 2004;171:2236-9.
8. Stillwell TJ, Engen DE, Farrow GM. The clinical spectrum of granulomatous prostatitis: A report of 200 cases. J Urol 1987;138:320-3.
9. Val-Bernal JF, Zaldumbide L, Garjio FM, Gonzalez-Vela MC. Nonspecific (idiopathic) granulomatous prostatitis associated with low-grade prostatic adenocarcinoma. Ann Diagn Pathol 2004;8:242-6.
10. Bahnon RR. Elevation of prostate specific antigen from bacillus Calmette Guerin-induced granulomatous prostatitis. J Urol 1991;146:1368-9.
11. Lamm DL, Stodgill VD, Stodgill BJ, Crispin RG. Complications of bacillus Calmette-Guerin immunotherapy in 1,278 patients with bladder cancer. J Urol 1986;135:272-4.
12. Oates RD, Stilhunt MM, Freedlund MC, Siroky MB. Granulomatous prostatitis following bacillus Calmette-Guerin immunotherapy in 1,278 patients with bladder cancer. J Urol 1988;140:751-4.
13. Sunderam G, Mangurah BT, Lombardo JM, Reichman LB. Failure of “optimal” four-drug short course tuberculosis chemotherapy in a compliant patient with HIV. Am Rev Respir Dis 1987;136:1475-8.
14. Small PM, Schecter GF, Goodman PC, Sande MA, Chaisson RE. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. N Engl J Med 1993;328:527-32.
15. Mebust WK, Noble MJ. Renal tuberculosis. In: Resnick MI, Kursh BC, editors. Current therapy in genitourinary surgery. Toronto: BC Decker; 1987. p. 326-9.
16. Shafer RW, Jones WD. Relapse of tuberculosis in a patient with the acquired immunodeficiency syndrome despite twelve months of anti-tuberculous therapy and continuation of isoniazid. Tubercle 1991;72:149-51, tuberculosis and AIDS. Nati Med J India 1994;7:166-7.
17. Iseman MD. Is standard chemotherapy adequate in tuberculosis patients infected with the HIV? Am Rev Respir Dis 1987;136:1326.
18. Lanjewar DN, Maheshwari MB. Prostatic tuberculosis and AIDS. Nati Med J India 1994;7:166-7.
19. Golbe M, Isemann MD, Madsen LA, Waiwa D, Ackerson L, Horsburgh CR Jr. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. N Engl J Med 1993;328:527-32.
20. Nolan CM. Nosocomial multidrug-resistant tuberculosis: Global spread of the third epidemic. J Infect Dis 1997;176:748-51.
21. Mobust WK, Noble MJ. Renal tuberculosis. In: Resnick MI, Kurosh BC, editors. Current therapy in genitourinary surgery. Toronto: BC Decker; 1987. p. 326-9.
22. Iseman MD. Is standard chemotherapy adequate in tuberculosis patients infected with the HIV? Am Rev Respir Dis 1987;136:1326.
23. Lanjewar DN, Maheshwari MB. Prostatic tuberculosis and AIDS. Nati Med J India 1994;7:166-7.
24. Golbe M, Isemann MD, Madsen LA, Waiwa D, Ackerson L, Horsburgh CR Jr. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. N Engl J Med 1993;328:527-32.
25. Nolan CM. Nosocomial multidrug-resistant tuberculosis: Global spread of the third epidemic. J Infect Dis 1997;176:748-51.
26. Buchholz N, Salahuddin R, Haque R. Genitourinary tuberculosis: A profile of 55 in-patients. J Pak Med Assoc 2000;50:269-9.
27. Moussa OM, Eraky EI, El-Far MA, Osman HG, Ghoneim MA. Rapid diagnosis of genitourinary tuberculosis by polymerase chain reaction and non-radioactive DNA hybridization. J Urol 2000;164:584-8.
28. McAlister SJ, Johnson CW, Johnson WD. Tuberculosis and parasitic and fungal infections of the genitourinary system. In: Campbell-Walsh Urology, Wein AJ, Novick AC, et al, editors. Campbell’s urology, 9th ed. Philadelphia: WB Saunders; 2007. p. 436-70.
29. Bailey WC, Albert RK, Davidson PT. Treatment of tuberculosis and other mycobacterial diseases: An Official Joint Statement of the American Thoracic Society and the Centers for Disease Control. Am Rev Respir Dis 1983;127:790-6.
30. Fox W. Whitner short course chemotherapy? Br J Dis Chest 1981;73:331-7.
31. Gow JG. Genitourinary tuberculosis: A 7-year review. Br J Urol 1979;51:239-44.
32. Gow JG, Barbosa S. Genitourinary tuberculosis: A study of 1117 cases over a period of 34 years. Br J Urol 1984;56:449-55.
33. Porter MP, Eubank WB, Kriel GN. Genitourinary tuberculosis: A focused update for the practicing urologist. Contemp Urol 2001;13:34-48.
34. Carl P, Stark L. Indications for surgical management of genitourinary tuberculosis. World J Surg 1997;21:505-10.
35. Lee YH, Huang WC, Huang JS, Wang J, Yu C, Jiaan B, et al. Efficacy of chemotherapy for prostatic tuberculosis: A clinical and histologic follow-up study. Urology 2001;57:872-7.
36. Sunderam G, Mangurah BT, Lombardo JM, Reichman LB. Failure of “optimal” four-drug short course tuberculosis chemotherapy in a compliant patient with HIV. Am Rev Respir Dis 1987;136:1475-8.
37. Small PM, Schecter GF, Goodman PC, Sande MA, Chaissen RE, Hopperwell PW. Treatment of tuberculosis in patients with advanced human immunodeficiency virus. N Engl J Med 1991;324:289-94.
38. Shafer RW, Jones WD. Relapse of tuberculosis in a patient with the acquired immunodeficiency syndrome despite twelve months of anti-tuberculous therapy and continuation of isoniazid. Tubercle 1991;72:149-51, tuberculosis and AIDS. Nati Med J India 1994;7:166-7.
39. Iseman MD. Is standard chemotherapy adequate in tuberculosis patients infected with the HIV? Am Rev Respir Dis 1987;136:1326.
40. Lanjewar DN, Maheshwari MB. Prostatic tuberculosis and AIDS. Nati Med J India 1994;7:166-7.
41. Wolf LE. Tuberculosis abscess of the prostate in AIDS. Ann Intern Med 1996;125:156.
42. Goble M, Isemann MD, Madsen LA, Waiwa D, Ackerson L, Horsburgh CR Jr. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. N Engl J Med 1993;328:527-32.
43. Nolan CM. Nosocomial multidrug-resistant tuberculosis: Global spread of the third epidemic. J Infect Dis 1997;176:748-51.
44. Mebust WK, Noble MJ. Renal tuberculosis. In: Resnick MI, Kurosh BC, editors. Current therapy in genitourinary surgery. Toronto: BC Decker; 1987. p. 326-9.
45. Kaufman JJ, Ljung BM, Walther P, Waisman J. Aspiration biopsy of prostate. Urology 1982;19:587-91.
46. Miralles TG, Gosalbez F, Menendez P, Perez-Rodriguez A, Folgueras V, Cabanilles DL. Fine needle aspiration cytology of granulomatous prostatitis. Acta Cytol 1990;34:57-62.

How to cite this article: Gupta N, Mandal AK, Singh SK. Tuberculosis of the prostate and urethra: a review. Indian J Urol 2008;24:388-391. Source of Support: Nil, Conflict of Interest: None declared.