

Prolonged Fever due to Tuberculous Prostatitis: A Case Report

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There are various causes of prolonged fever. The most common causes are infection, malignancy, and inflammatory diseases. Primary tuberculous prostatitis is one of the unrecognized causes of prolonged fever. The present study of tuberculous prostatitis have been documented, and most of them occurred in immunocompromised patients. The present study described an unusual cause of prolonged fever due to primary tuberculous prostatitis in a 68-year-old immunocompetent man. He was response well to anti-tuberculosis therapy. No surgical intervention was required.

Keywords: Tuberculosis; Prostatitis; Tuberculous prostatitis; Prolonged fever

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Tuberculous prostatitis is rare, and usually occurs in immunocompromised patients. It can mimic benign prostatic hyperplasia and prostatic cancer. The most common cause of tuberculous prostatitis is secondary infections from hematogenous, lymphatic, and adjacent organ spreading. Primary tuberculous prostatitis is very rare; to date only 42 cases of this type have been documented⁽¹⁾. The present study was approved by the Human Research Ethics Committee of Khon Kaen University (HE631060).

Case Report

A 68-year-old man developed a low-grade fever, fatigue, and a 5-kg weight loss over 4 months. His medical history was notable for pulmonary tuberculosis (TB) and received a complete course of standard anti-TB therapy in the past 20 years. His underlying diseases were hypertension, dyslipidemia, and stable coronary artery disease.

Chest radiograph showed stable bilateral reticular infiltration at both lower lungs. Chest computed tomography

(CT) showed cystic bronchiectasis in both lower lobes with multiple sub-centimeter non-calcified mediastinal lymphadenopathies. The laboratory results revealed hemoglobin concentration 9.2 g/dL, white blood cell count was 14.6×10^3 per μL (90% neutrophils, 6% lymphocytes), globulin 4.7 g/dL with polyclonal gammopathy, albumin 2.3 g/dL, prostatic specific antigen (PSA) 15.1 ng/ml (0 to 4.0); Anti-HIV antibody and VDRL were negative. Anti-melioidosis antibody titer was 1: 80. Bronchoscopy with bronchial washing was performed; no endobronchial lesions were found.

Anti-TB therapy was started with Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide. After 1 week of administration, Pyrazinamide was changed to Levofloxacin due to severe vomiting. Ziehl-Nielsen staining, mycobacterial culture, bacterial culture, and polymerase chain reaction (PCR) for the Xpert MTB/RIF assay from bronchial washing fluid were negative.

After 1 month of treatment, he had newly developed bilateral inguinal lymphadenopathies without genitourinary symptoms. A rectal examination revealed a painless enlarged prostate with smooth surface and firm consistency. Urine after the 4-glass test of prostatic massage showed white blood cells 50 to 100 cells per high-power field, red blood cells 5 to 10 cells per high-power field, Ziehl-Nielsen staining, Mycobacterial culture, and PCR for the Xpert MTB/RIF assay were negative. A whole abdominal CT revealed an ill-defined less enhanced lesion at the left peripheral zone of the prostate base. A transrectal ultrasound (TRUS) guided prostatic biopsy was performed. Prostatic tissues revealed a few foci of chronic

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granulomatous inflammation; neither microorganisms nor malignancies were found (Figure 1). Prostatic tissues cultures, PCR for mycobacteria, and mycobacteria culture were negative. Bone marrow tissues cultures and PCR for mycobacteria were negative.

After two months of intensive anti-TB therapy, fever subsided, inguinal lymph nodes were impalpable, and PSA returned to normal. He received isoniazid and rifampicin for a further 7 months. No surgical intervention was required.

Discussion

At an early stage of tuberculous prostatitis, *Mycobacterium tuberculosis* infiltrates the prostate; the so-called 'infiltrative stage'. Later, *M. tuberculosis* forms cavities in the prostate; the so-called 'cavernous stage'⁽²⁾. Undiagnosed tuberculous prostatitis can lead to disseminated TB; the interval from tuberculous prostatitis to dissemination was 4 months in a case report⁽³⁾ and can be transmitted via sexual intercourse⁽⁴⁾.

Genitourinary symptoms are common in tuberculous prostatitis, and usually mimic other genitourinary conditions⁽²⁾. Perineal pain (96.8%) and dysuria (79.6%) were common symptoms, while the presence of fever was rare (5.3%)⁽²⁾. On palpation, most often the prostate was found to be non-tender, nodular, firm to hard, and rarely enlarged^(5,6). In the present study, the patient was presented with prolonged fever without genitourinary symptoms followed by bilateral inguinal lymphadenopathies and painless enlarged prostate.

A previous diagnosis of pulmonary TB or evidence of imaging was reported as 36.5%⁽⁷⁾ of genitourinary tuberculosis, and 10% were with concurrent active pulmonary TB⁽⁸⁾. In the present case, active pulmonary TB was excluded by the absence of microbiological evidence from bronchoscopy.

Urinary analysis in tuberculous prostatitis is usually normal, but prostatic secretion in tuberculous prostatitis

is frequently abnormal⁽¹⁾. Kulchavenya et al. found that prostatic secretion collected by prostatic massage showed leucospermia (73.1%) and hemospermia (51.6%). PSA was normal (less than 4.0 ng/ml) in 81.7%, however, the rise and fall pattern of PSA after treatment can support the diagnosis of tuberculous prostatitis in the present case⁽²⁾.

TRUS of the prostate often shows diffuse hyperechoic lesions within the peripheral zone, which can be found in adenocarcinoma, or other infections of prostate, prostatic biopsy should be performed⁽⁶⁾. A CT finding of tuberculous prostatitis is usually found hypodensity area within the prostate. Magnetic resonance imaging (MRI) can demonstrate the lesions better than CT. The diffuse, radiating, streaky areas of low signal intensity on T2WI, so-called 'watermelon skin sign', are typical MRI findings of tuberculous prostatitis⁽⁶⁾. In the present case, hypodensity area at the left peripheral zone of the prostatic base in whole abdominal CT was compatible with area of granulomatous inflammation.

A definite diagnosis of tuberculous prostatitis is made by positive cultures, Ziehl-Nielsen staining, and/or histopathological examination of prostatic tissues. A histopathological finding of tuberculous prostatitis diffuse caseating epithelioid cell granulomas can also be found in non-tuberculous mycobacteria, *Treponema pallidum*, herpes simplex virus, fungal infections, or non-infectious causes such as post-surgery and systemic granulomatous diseases⁽⁹⁾. This classical histopathological finding was found in only 24.7% in one study⁽²⁾. The data for prostatic tissue PCR for TB, culture, and Ziehl-Nielsen staining are limited. In the present study, no definite diagnosis of tuberculous prostatitis was confirmed but the patient was responding well to anti-TB therapy, tuberculous prostatitis was the most likely diagnosis. The authors hypothesized that receiving one-month of anti-TB therapy prior to prostatic biopsy resulted in negative mycobacterial culture.

Ziehl-Nielsen staining in a prostatic secretion has a low sensitivity (33 to 52.7%)^(6,10); mycobacterial culture in a prostatic secretion may take up to 6 weeks and is 80 to 90% sensitive⁽⁵⁾. Sensitivity and specificity of urine PCR for TB in tuberculous prostatitis are 95.59% and 98.2%⁽⁶⁾, however, PCR is unable to detect whether the TB infection is biologically active or latent.

A standard regimen of anti-TB therapy for 6 months is highly effective with the fastest culture-conversion and the lowest relapse-rates, however, most of anti-TB drugs, excluding rifampicin and fluoroquinolones, has suboptimal concentrations in prostatic tissues⁽¹¹⁾. Kulchavenya et al. found that adding ofloxacin to the intensive phase of the anti-TB regimen of isoniazid, rifampicin, pyrazinamide, and streptomycin for tuberculous prostatitis, resulted in better resolution of symptoms, pyospermia and the presence of

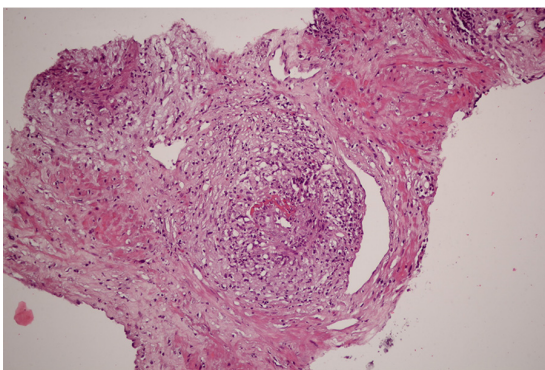


Figure 1. Prostatic tissue core biopsy revealed a few chronic granulomatous inflammations.

mycobacteria (77.8% vs. 44.0% in the standard group)⁽²⁾.

Surgical intervention is usually reserved for the minority of cases where anti-TB therapy has failed⁽⁶⁾. Buchholz et al. found that 52% of surgical specimens showed florid TB despite a previous 9-month course of anti-TB drugs⁽¹²⁾. Severity of Tuberculous Prostatitis, patient compliance, immune status, and infection of multi-drug resistant TB (MDR-TB) are key factors that affect the success of treatment. The PSA level often turns to normal after receiving the optimum treatment⁽¹²⁾.

In the present study, a fever persisted until the second month of Isoniazid, Rifampicin, Ethambutol, and Levofloxacin. It was then hypothesized that the causes of delayed treatment response were 1) tuberculous prostatitis in this case was in a cavernous stage which was considered as the late stage of tuberculous prostatitis and may have been related to a delayed treatment response, 2) the treatment regimen did not contain pyrazinamide which, in combination with rifampicin, is a very effective drug for tuberculous prostatitis, however, Levofloxacin also had good prostatic tissue distribution, an anti-bactericidal effect, and symptom reduction⁽²⁾.

Conclusion

Tuberculous prostatitis is an uncommon cause of prolonged fever and can be presented without genitourinary tract symptoms. Most tuberculous prostatitis patients have good response to standard anti-TB therapy and rarely require surgical intervention.

What is already known on this topic?

Tuberculous prostatitis is an uncommon manifestation of TB in immunocompetent patients. It is usually resulted from hematogenous, lymphatic, and adjacent organs spreading. Primary tuberculous prostatitis is exceedingly rare. Most patients are presented with dysuria and perineal pain, while fever is uncommon. Prostatic examinations and other laboratory investigations are usually non-specific. The presence of evidence of TB by positive culture, Ziehl-Nielsen staining, or histopathological examination of prostatic tissues can aid the diagnosis. Standard regimen of anti-TB therapy is the mainstay of treatment, while prostatic surgery is only reserved for patients who failed to respond to treatment.

What this study adds?

Despite absence of genitourinary symptoms, primary tuberculous prostatitis is still an unrecognized cause

of prolonged fever in immunocompetent patients. The presence of inguinal lymphadenopathy, elevated serum PSA, and hypodensity lesion in prostate are clinical clues of tuberculous prostatitis.

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Conflicts of interest

The authors declare no conflict of interest.

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