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# Genitourinary tuberculosis in a 54-year-old woman: diagnostic difficulty

**Case Report**

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**Abstract:** Genitourinary tuberculosis (GUTB) is an extrapulmonary manifestation of tuberculosis seen in 1.2% of all cases of tuberculosis. The clinical case of a 54-year-old woman diagnosed with GUTB is presented. Cloudy urine, abdominal pain, and microscopic hematuria led us to investigate for *Mycobacterium tuberculosis*. Although cultures were negative, positive Ehrlich-Ziehl-Neelsen (EZN) staining and a positive polymerase chain reaction (PCR) revealed the diagnosis of *M. tuberculosis* complex (MTC), which was confirmed by treatment success. It has been shown that PCR is a reliable and rapid method for establishing or supporting the diagnosis of tuberculosis and can be used in a routine diagnostic algorithm when conventional methods fail to identify MTC.

**Keywords:** *Genitourinary tuberculosis • Polymerase chain reaction • Mycobacterium tuberculosis complex*



## 1. Introduction

Tuberculosis (TB) is pandemic and a highly contagious disease. Two billion people, which are approximately one third of the global population, have been infected with *Mycobacterium tuberculosis*, and annually, 1% of that population is being introduced as carriers. Among carriers, TB develops in 7 to 8 million people, and 2 million patient deaths are due to the disease. Among the factors responsible for these figures are human immunodeficiency virus (HIV) infection, immigrants with health problems, and the deterioration of public health institutional infrastructure [1,2].

Extrapulmonary TB is observed in approximately 20% of all cases of TB. Moreover, an increased incidence has been observed in recent years [3]. Genitourinary TB (GUTB) is an important, but uncommon, presentation of TB found in approximately 1.2% of patients in a variety of geographic locations [4]. GUTB presents a challenge in diagnosis due to variations in clinical and radiological signs, insufficient patient history, and difficulty in isolating the bacilli [5].

## 2. Case Report

A 54-year-old woman with cloudy urine and right-sided abdominal pain for 8 months was admitted to our hospital. The patient had visited various health centers, including research hospitals, in which she was examined for renal calculi and bacterial infections. Radiologic studies, including ultrasonography and computed tomography, showed no renal calculus. She was given oral antibiotic therapy three times within 8 months for urinary tract infection at the other health centers. Urinalysis at our hospital showed 13 erythrocytes per high-power field, 2 leukocytes per high-power field, and ++ haemoglobin (Table 1). Abdominal ultrasonography showed mild stasis in the right kidney, with minimal dilatation and calcific foci in the right renal pelvis. Computed abdominopelvic tomography revealed calcific foci around the bladder and multiple areas of lymphadenopathy around the internal iliac artery and paraaortic region. The family history revealed that the patient's daughter had been treated for pulmonary TB 23 years previously.

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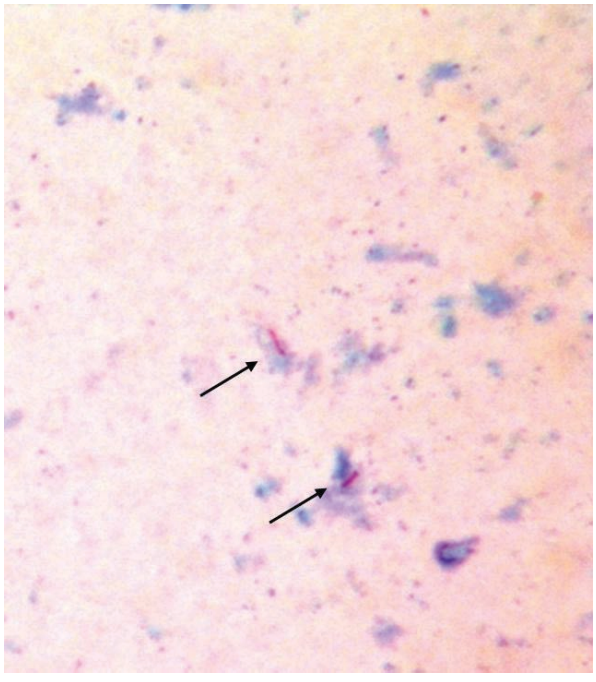
**Table 1.** The patient's urinalysis, complete blood count, and serological test results.

| Urinary analysis | Result | Reference | Unit | Complete blood count | Result | Reference | Unit |
|---|---|---|---|---|---|---|---|
| pH | 6 | 5-8 | - | WBC | 6.65 | 4-10.5 | x10.e3/microL |
| Density | 1.015 | 1003-1030 | - | RBC | 4.56 | 4.7-6 | x10.e6/microL |
| Glucose | Negative | Negative | - | HGB | 13.2 | 13.5-18 | g/dL |
| Protein | Negative | Negative | - | HCT | 37.5 | 39.5-50.3 | % |
| Bilirubin | Negative | Negative | - | MCV | 82.4 | 80.7-95.5 | fL |
| Urobilinogen | Normal | Normal | - | MCH | 29 | 27-31 | pg |
| Ketone | Negative | Negative | - | MCHC | 35.2 | 32-36 | g/dL |
| Leukocyte | 2 | 0-4 | In each field | PLT | 279 | 150-450 | x10.e3/microL |
| Erythrocyte | 13 | 0-4 | In each field | MPV | 7.3 | 6-9.5 | fL |
| Hemoglobin | ++ | - | - | %NEUT | 55.7 | 37-73 | % |
| | | | | %LYMPH | 31.2 | 20.5-51.1 | % |
| Serological tests | | | | %MONO | 6.92 | 5.1-10.9 | % |
| Erythrocyte sedimentation rate | 23 | 0-20 | mm/h | %EOS | 2.54 | 0.5-11 | % |
| C-reactive protein | 15 | 0-8 | mg/L | %BASO | 0.06 | 0-0.1 | % |

**Figure 1.** Acid-fast bacilli (black arrows) in an Ehrlich-Ziehl-Neelsen-stained smear from the patient's urine sample.



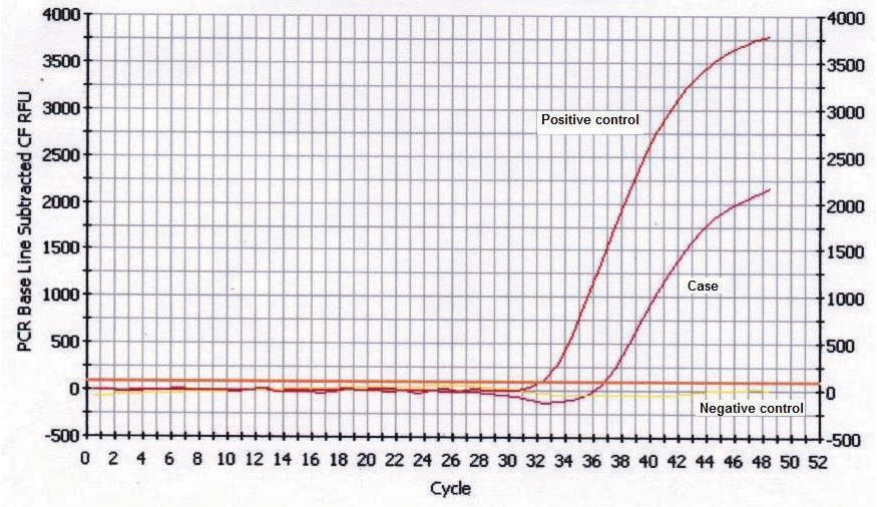
Ehrlich-Ziehl-Neelsen (EZN) staining of urine samples revealed acid-fast bacilli (AFB) (Figure 1). Urine samples were cultured by conventional (Löwenstein Jensen, Salubris Inc., Istanbul, Turkey) and radiometric (BACTEC 460 TB culture system, Becton Dickinson Diagnostic Instruments, Sparks, MD, USA) methods, but the cultures were negative. Urinary samples were analysed by real-time PCR and were extracted by QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany), according to the manufacturer's instructions. Real-time PCR was carried out with a qualitative commercial kit, Fluorion MTBC Real Time PCR Kit MTBC QLP 2.1 (Iontek, Istanbul, Turkey), in iCycler iQ Multicolor Real Time PCR Detection System (Bio-Rad, Hercules, USA); the results were positive for *Mycobacterium tuberculosis* complex (MTC) (Figure 2).

The tuberculin skin test was reactive with a 13-mm induration at 72 hours. The suspected clinical diagnosis was supported with EZN staining and a positive PCR result. Anti-TB treatment was started orally with four drugs: isoniazid (INH) (300 mg/day); rifampicin (RMP) (600 mg/day); ethambutol (1.5 g/day); and pyrazinamide (2 g/day) during the first two months, followed by INH and RMP for 4 months, according to the Word Health Organization (WHO) recommendations. High-dose pyridoxine (10 mg/day) was prescribed to prevent INH-related neuropathy during treatment [3,6]. The patient tolerated the anti-TB treatment well, and no complications occurred. Anti-TB treatment resulted in complete resolution of the signs and symptoms of the disease. Examinations of control specimens of urine with EZN staining, culture, and PCR were negative after anti-TB treatment. The erythrocyte sedimentation rate (Westergren) and C-reactive protein returned to normal ranges. Finally, the diagnosis of GUTB was confirmed definitively by the treatment success.

## 3. Discussion

GUTB is acquired through hematogenous spread of bacilli from a focus of infection in the lungs, bowel, or both. The kidney is usually the first organ of the urinary tract to be infected, with other parts infected by direct

**Figure 2.** Positive result of real-time polymerase chain reaction (Bio-Rad, Hercules, USA) for *Mycobacterium tuberculosis* complex (MTC). The positive control was amplified at 32 cycles. The amplification of the patient's MTC-DNA occurred at 37 cycles, when the negative control had no amplification.




extension [7]. Development of disease depends on the interaction between the pathogen and the host immune system, which may take up to 20 years from the primary infection [2,8,9]. Initial infection occurs at the renal cortex, where the bacillus lodges and forms granulomas. When the ureter is infected, the ureteral meatus becomes edematous and then forms granulomas that obstruct the ureteral orifice. In advanced stages, inflammation and fibrosis results in contraction, and the ureteral orifice acquires the classic "golf-hole" appearance [2,10].

The diagnosis of TB consists of signs and symptoms, x-ray findings, and detection of MTC. Currently, bacterial culture, smears, and PCR are employed to isolate MTC. The bacterial culture method is feasible if > 100 MTC organisms are present in 1 ml of the specimen. Although the specificity of the culture method is close to 100%, which allows the method to be used for final diagnosis, 3-8 weeks are required to cultivate the bacteria. The culture method is also not cost-efficient. Acid-fast smear is a relatively fast, simple, cost-efficient procedure. However, 5000-10,000 bacteria must be present in 1 ml of the sample, and this method does not discriminate MTC from other nontuberculous mycobacteria, leading to a low sensitivity (22-78%). PCR detects MTC directly in the specimen and does not require an incubation time of weeks, so it is fit for early diagnosis. Sensitivity of PCR in clinical samples reaches up to 94% in urinary samples. The disadvantage of the PCR method is that it detects both viable and nonviable MTC organisms [3,11-13].

Diagnosis of extrapulmonary TB is challenging for a number of reasons: lack of adequate sample amounts or volumes; the apportioning of the sample for various diagnostic tests (histology/cytology, biochemical analysis, microbiology and PCR) resulting in nonuniform distribution of microorganisms; the paucibacillary nature of the specimens; the presence of inhibitors that undermine the performance of nucleic acid amplification-based techniques; and the lack of an efficient sample processing technique universally applicable on all types of extrapulmonary samples. The specific gravity of the tubercle bacilli ranges from 1.07 to 0.79. Because of the low specific gravity of the AFB, a low centrifugal force has a buoyant rather than a sedimentary effect in high-density urine samples, and this results in a false-negative result on EZN stain. Hence, isolation of AFB from urine samples is more difficult than it is from other clinical samples [14]. The poor performance of conventional microbiological techniques in extrapulmonary specimens has stimulated the increased use of PCR tests in laboratory diagnosis of TB [3,15]. Hemal et al., compared diagnostic techniques in 42 patients with a clinical suspicion of GUTB; PCR, smear, culture, intravenous urography, and bladder biopsy for MTC had sensitivities of 94%, 29%, 37%, 88%, and 45% respectively, which proved PCR to be the superior method [12].

The diagnosis of GUTB is difficult because the symptoms are nonspecific. Knowledge of a TB infection early in the patient's life, either as primary pulmonary manifestation or as an extrapulmonary manifestation, gives an important clue in many cases [8]. Voiding problems; back, flank, and suprapubic pain; hematuria; urinary frequency; and nocturia are other symptoms. The most common laboratory and imaging findings are pyuria, albuminuria, hematuria and hydroureter, hydronephrosis, renal calcification, and an increase in wall density of the urinary tract [16,17]. A tuberculin skin test supports the diagnosis of TB [3]. Microbiological

diagnosis of TB is made by smear (EZN acid fast stain), culture, and PCR. Detection of AFB from urine samples by microscopy is unreliable because of the possible presence of *M. smegmatis*. A positive culture combined with PCR is still required in most patients for a definite diagnosis. In 25% to 30% of cases, the diagnosis of GUTB is established on the basis of histological pattern, by detection of MTC by PCR, or both [6,9].

To avoid diagnostic delays, physicians should keep GUTB in mind when a patient presents with vague, long-standing urinary symptoms without obvious cause. In our case, as in most cases in the literature, it has been shown that PCR is a reliable and rapid method for establishing or supporting the diagnosis of TB and that it can be used in a routine diagnostic algorithm when conventional methods fail to identify MTC.

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