

## Case Report

# Genitourinary Tuberculosis: About Two Cases in Infectious Diseases Department of Point G University Hospital, Bamako, Mali

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**Abstract**

Genitourinary tuberculosis (GUTB) is difficult to diagnose in its earlier stage due to the non-specificity of the symptoms. Usually, the absence of bacterial growth along with leukocyturia leads to the investigation for the acid-alcohol resistant bacilli. We report here two cases of GUTB in the department of infectious diseases at the University hospital of Point G. Two young men, both health care workers with negative HIV serology who presented non-specific lower urinary tract symptoms with no medical history or surgery. They have been unsuccessfully treated by antibiotics with large diffusion in urinary tract tissues. Their urines analyses were sterile for regular bacteria. The diagnosis of GUTB has been confirmed in the two cases by the presence of acid-fast bacilli (AFB) in their urines and the treatment response to anti tuberculous therapy. These highlight the importance to clinically suspect GUTB in patients with repeated non-specific lower urinary tract symptoms non responsive to conventional antibiotic therapy regardless their history of TB. Moreover, early diagnosis of GUTB warranty better management and limit complications. Clinicians should consider searching for TB in any etiologic checkup for urinary tract infection mainly in the presence of aseptic leukocyturia.

**ABBREVIATIONS**

GUTB: Genitourinary Tuberculosis; AFB: Acid-Fast Bacilli; TB: Tuberculosis

**INTRODUCTION**

Tuberculosis (TB) remains a major global health problem. It affects millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide [1]. In 2015, 10.4 million new cases of TB were estimated and 1.8 million died [2]. TB is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* [1,3]. Extrapulmonary TB accounts for 10% of all TB cases. Genito-urinary tract tuberculosis (GUTB) is the second common location of extrapulmonary TB with 30 to 40% after the lymph nodal form. An epidemiological study found GUTB in 2 to 20% of patients with pulmonary tuberculosis and 36.5% of patients with either known history of prior pulmonary TB or radiographic evidence of prior subclinical pulmonary

TB infection [4]. However, urinary tract localization as initial infection is not frequent [1]. Patients usually present a typical nonspecific urinary symptoms of bacterial cystitis [5,6]. GUTB is highly suspected in the presence of sterile leukocyturia [3,6]. Chemotherapy for late-diagnosed and complicated forms of GUTB is not enough effective [5,6]. In Mali, the incidence of TB was 57 per 100,000 habitants in 2015 and the frequency of extrapulmonary TB was 17% in 2011 [2,7]. We describe two cases of GUTB managed in the department of infectious diseases at the University hospital of Point G, Bamako.

**CASES PRESENTATION****Patient N°1**

A 31-years old male, health care worker with no particular medical and surgical history. For the last 10 years, he has been complaining about burning during micturition with no pus in the urine, pelvic pains, and lasting fever. He has performed many

times urine and prostatic fluid analysis which turned out negative except the isolation of *Staphylococcus* with negative coagulase sometimes. He received oral antibiotics such as ciprofloxacin, erythromycin, doxycyclin, pristinamycin and cefixime. The disease was progressing with alternance between clinical improvement and relapse of fever and genitourinary symptoms. The physical exam was normal. The blood cells count (CBC) found a normal level of leucocytes of 3600/ $\mu$ l and the patient was tested negative for HIV with determine. His chest radiograph was normal. Kidney-bladder and prostate ultrasound was normal. Urine samples were collected and processed at the University Biosafety Level 3 (BSL-3) laboratory. The auramine-rhodamine (Remel, Lenexa, KS 66215, USA) coloration using fluorescent microscopy was positive (Few AFB seen). The grading of urine smear microscopy has been done following the International Union Against Tuberculosis and Lung Diseases (IUATLD) grading criteria as negative (No AFB seen), Few AFB seen (10-99 AFB seen in 100 fields), Moderate AFB seen (1-10 AFB seen per field), and Many AFB seen (> 10 AFB seen per field) [8].

Urine pellet were put in culture for Mycobacteria for 6 weeks in both solid (MiddelBrook 7H11, Remel) and liquid (MGIT™, BD, USA) media and the result was negative.

The patient started first-line anti-tuberculous short-course regimen in April 2015 combining rifampin (R), isoniazid (H), pyrazinamide (Z), and ethambutol (E) for two months followed by four months of isoniazid and rifampin (2RHZE/4RH) according to the National TB Guidelines. After the first two months of TB treatment, the patient improved clinically with the disappearance of genitourinary symptoms and the fever and biologically with no AFB seen at the fluorescent microscopy.

#### Patient N°2

A 37-years old male, health care worker with no particular medical and surgical history. For 3 years, he has been presenting dysuria, burning during micturition, suprapubic pain and clear urethral discharge without pus. Repeated urinalysis did not isolate any germ and the 24-hours proteinuria was negative. A retrograde ureterocystography showed a spastic neck of the bladder. Treatment with oral antibiotics such as levofloxacin, cefixime, doxycyclin, tinidazol and ciprofloxacin was unsuccessful. The physical exam was normal. The CBC found a leukocyte count 3000/ $\mu$ l. The HIV test was negative. The chest X-ray was normal. Kidney-bladder and prostate ultrasound was normal. Morning first ejection of urine was collected and tested with auramine-rhodamine (Remel, Lenexa, KS 66215, USA) using fluorescent microscopy. The result was positive (Few AFB seen). The 6 weeks culture was negative. Urine was also tested negative with Xpert-MTB/RIF (GeneXpert™, Cepheid Inc., USA).

The patient started the new regimen of twelve (12) months of treatment recommended by the national TB program during his treatment course. The regimen combines rifampin (R), isoniazid (H), pyrazinamide (Z), and ethambutol (E) for two months followed by ten months of isoniazid and rifampin (2RHZE/10RH) in October 2015.

The two months treatment evaluation concluded to an improvement both regression of symptoms and absence of AFB in the urine sample and the result of the culture was negative after 6 weeks of Mycobacteria culture.

## DISCUSSION

Genitourinary TB is a rare disease, and mainly difficult to diagnose in resource limited setting. Patients usually present lower urinary tract symptoms typical of “conventional” bacterial cystitis, and rarely TB is suspected. Although with the widespread of HIV infection, the current tendency is the recrudescence of extrapulmonary forms of TB and the diagnostic of GUTB remains difficult even in TB endemic areas [5,6]. Its exact prevalence is unknown [6]. GUTB concerns particularly young adults aged 20 - 50 years old in two third of the patients [5]. Although, GUTB does not spare any age group [5], our two patients were young adults. Some studies have also reported a male predominance of GUTB with a sex-ratio between 1.6 and 2.5 [4,5]. A larger sample size will allow to appreciate the sex-ratio accurately. Most of the patients who present GUTB have either a known history of prior pulmonary TB or a radiographic evidence of prior subclinical pulmonary infection [1,4]. None of our patients had a history of TB disease nor an abnormal chest X-ray.

The period between symptoms onset and the GUTB diagnosis was 10 years for case 1 and 3 years for case 2. This period varies from 3 months to over 10 years in Slimen et al., series in Tunisia [5].

The symptoms are non-specific, our patients presented with lower urinary symptoms typical of “conventional” relapsing bacterial cystitis similar to the typical GUTB description in the literature [1,4-6] and systemic signs were absent in both cases. The physical exam is sometimes normal or non-informative.

The clinical presentation is less specific in HIV negative patients like in our two patients. In fact, extrapulmonary TB is common in HIV carriers in general except GUTB.

These various arguments without any specificity can induce the physician in error and lead to difficulties and delay in the diagnostic process.

The diagnosis was based on AFB positive smear for urine in both cases. But the rate of positive smear in the urine differs largely in the literature between 5 and 72 % due to the limits of this test and its low sensitivity. Our team uses the centrifugation and fluorescent microscopy to increase the yield of seeing AFB. This suggests the interest of serologic techniques or nucleic acid amplification tests that could show bacilli DNA fragments. These should be genitourinary tuberculosis diagnostic method of choice due to their rapid and high sensitivity and specificity; greater than 80% [5].

Despite the good sensitivity and specificity of nucleic acid amplification test, it was negative in one of our patients. The non-specific biology (sedimentation rate, renal function, serum ionogram and creatinine) doesn't contribute directly into the diagnostic of GUTB but it gives an estimate of the degree of the inflammatory process. The finding of abnormal leukocyturia by urinalysis becomes suspicious when an adapted antibiotic therapy is being properly used [3,5]. This sterile leukocyturia was absent in our series.

The definitive diagnosis of TB involves demonstration of *M. tuberculosis* by microbiological or histopathological methods. Urine culture is the gold standard method for establishing the

diagnosis, it has 20% of false negative rate [1,9]. In our cases, *M. tuberculosis* has been found through acid-fast bacilli staining and the urine culture was negative for *M. tuberculosis*. The noninvasive testing in establishing the diagnosis has many limitations (a lack of sensibility and specificity) [1,5]. However, in TB endemic regions like Mali, it appears reasonable to introduce anti-TB treatment in patients with clinical features highly suspicious of GUTB, despite the lack of a confirmed bacterial diagnosis [10]. Continuous collection of urine sample within 24h, and mainly when patients have fever, could improve the diagnosis of GUTB in different situations.

Many protocols of GUTB treatment have been tried. A 12-month regimen 2RHZE/10RH (two months of isoniazid, rifampin, pyrazinamide, and ethambutol, followed by ten months of isoniazid and rifampin) is recommended unless the TB bacillus is resistant to first-line TB drugs [11].

In the present series, both patients were successfully treated with first-line anti-TB therapy.

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