Best practice in the diagnosis and management of urogenital tuberculosis

Ther Adv Urol
(2013) 5(3) 143–151
DOI: 10.1177/1756287213476128

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Abstract: Tuberculosis (TB) is a current public health problem, remaining the most common worldwide cause of mortality from infectious diseases. Urogenital tuberculosis (UGTB) is the second most common form of extrapulmonary TB in countries with severe epidemic situations and the third most common form in regions with a low incidence of TB. In this article we present the terminology, epidemiology and classification of UGTB, as well as describing the laboratory findings and clinical features and approaches to chemotherapy as well as surgery.

Keywords: chemotherapy, diagnosis, tuberculosis, urogenital

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Introduction

Tuberculosis (TB) is a current public health problem, remaining the most common worldwide cause of mortality from infectious disease. TB (both pulmonary [PTB] and extrapulmonary [EPTB]) leads to male and female infertility [Khanna and Agrawal, 2011; Kulshrestha *et al.* 2011; Wise and Marella, 2003; Tzvetkov and Tzvetkova, 2006; Lenk and Schroeder, 2001; Scherban *et al.* 2008; Wise and Shteynshlyuger, 2008]. It is a sexually transmitted disease [Scherban and Kulchavenya, 2008] which explains why it is not only a medical, but also a big social problem.

Urogenital tuberculosis (UGTB) is ancient but remains an unsolved problem. Clinical features are flexible and variable and UGTB mimics numerous other diseases, which results in delayed diagnosis. Despite about 7000 articles available in the literature with the keywords 'urogenital / genitourinary tuberculosis', there are no good multicenter studies with a high level of evidence on this problem. UGTB is an embodiment of contradictions: from terms and classification to therapy and management. Nevertheless we have to overcome this quagmire to best understand this eternally enigmatic and potentially fatal dangerous disease.

Terminology

The first note of UGTB was made by Porter in 1894 [Porter, 1894]. Later, in 1937, Wildbolz suggested the term genitourinary TB [Wildbolz, 1937]. We prefer the term UGTB, because kidney TB (KTB), which is usually primary, is diagnosed more often than genital TB. Only 53% of patients with KTB have genital lesions, but in 61.9% patients with epididymorchitis and in 79.3% patients with TB of the prostate, a renal lesion can be diagnosed [Kulchavenya, 2009; Gómez García *et al.* 2010], although some authors believe that TB often affects the lower genitourinary system rather than the kidney. TB of the lower genitourinary tract most commonly affects the epididymis and the testis, followed by bladder, ureter, prostate and penis [Wise and Shteynshlyuger, 2008].

Actually the term UGTB is incorrect too, because it includes KTB and male genital tuberculosis (MGTB), with different clinical features and approaches to management. However, as this term is usually used in the literature, we shall use it here too.

Epidemiology

More than 95% of patients diagnosed with PTB live in developing countries, where the incidence is as great as 600/100,000 annually. It has been well described that the urogenital system is a common site of EPTB in adults, but the true incidence of UGTB is less clear, and reports have varied from 4% to 73% [Zarrabi and Heyns, 2009]. About 2 billion people are infected with *Mycobacterium tuberculosis* (MBT); they are carriers of latent infection, forming a large reservoir for reactivation of TB [Barry *et al.* 2009]. Thus,

any contemporary person has a risk to be infected with MBT and, in unfavorable conditions, to get sick with UGTB.

In 1984 EPTB remained a major health problem in Australia, where 24.3% of all new TB notifications were of extrapulmonary origin. The most common sites of disease were the lymph nodes, urogenital tract, pleura and bone [Dwyer *et al.* 1987]. By the 1980s, the availability of anti-TB chemotherapy reduced the incidence and prevalence of TB. Changing patterns of population migration and the development of large pools of immune-compromised individuals reversed the downward trend of TB [Wise and Marella, 2003].

In 2009 almost one-fifth of United States TB cases were extrapulmonary; unexplained slower annual case count decreases have occurred in EPTB, compared with annual case count decreases in PTB cases. Among 253,299 cases, 73.6% were PTB and 18.7% were EPTB, including lymphatic (40.4%), pleural (19.8%), bone and/or joint (11.3%), genitourinary (6.5%), meningeal (5.4%), peritoneal (4.9%) and unclassified EPTB (11.8%) cases [Peto *et al.* 2009].

UGTB usually results from the reactivation of old, dormant tuberculous diseases by pathogens of the MTB complex [Lenk, 2011] and is the second most common form of EPTB in countries with severe epidemic situations and the third most common form in regions with a low incidence of TB [Colbert *et al.* 2012; Kulchavenya *et al.* 2012b; Lima *et al.* 2012].

Predisposition

Factors leading to the increased incidence of TB include the high incidence of TB among the AIDS population and the emergence of drug-resistant strains of TB [Gusmão *et al.* 1998; Fekak *et al.* 2003]. TB with AIDS tends to occur in a younger population and is often extrapulmonary or with atypical lung involvement. Drug resistance is similar in patients with and without AIDS [Cremades Romero *et al.* 1998].

In Japan, because of the progress in chemotherapy for MTB, it has become quite rare to diagnose patients with UGTB; however, the incidence of TB remains comparatively high, particularly in older patients, in advanced countries [Miyake and Fujisawa, 2011]. Furthermore, infectious adverse events associated with intravesical instillation therapy with bacille Calmette–Guérin (BCG), which is one of the most useful agents against non-muscle-invasive bladder cancer, are frequently developed [Wise and Marella, 2003; Drechsler and Kirch, 2010; Miyake and Fujisawa, 2011; Kulchavenya *et al.* 2012a]. Congenital anomalies of the urogenital tract, renal cysts, kidney transplantation and urolithiasis significantly increase the risk of developing UGTB. The incidence of TB has been estimated to be as much as 10-fold higher among renal failure patients than among the general population [Chan *et al.* 1996; Gusmão *et al.* 1998; Kulchavenya and Muzyko, 2007; Korzeniewska *et al.* 2009; Rabbani *et al.* 2011; Takeshita *et al.* 2012].

Classification

UGBT is an infectious disease of the kidneys, urinary tract and male genitals, caused by MTB. A clear definition and classification are necessary for correct therapy. The following classification of UGTB is recommended [Kulchavenya, 2009, 2010]:

I. KTB:
Level 1 – nondestructive form, TB of parenchyma;
Level 2 – small destructive form, TB papillitis;
Level 3 – destructive form with one or two caverns (cavernous kidney TB);
Level 4 – widespread destructive form with more than two caverns (polycavernous kidney TB).

Complications of KTB: TB of urinary tract (TB of ureter, bladder grades 1–4, urethra), strictures, fistula and renal failure.

II. MGTB:
– Orchiepididymitis (monolateral and bilateral);
– Prostate TB (infiltrative or cavernous forms);
– TB of seminal vesicles;
– TB of penis.

Complications of MGTB: strictures, fistula, infertility, sexual dysfunction.

KTB levels 1–2 should be treated with chemotherapy, KTB level 3 may require partial nephrectomy, KTB level 4 is indicated for nephrectomy, by open surgery or laparoscopically. Stricture of the ureter is indicated for reconstructive surgery only in KTB levels 1–3, KTB level 4 with stricture of the ureter is indicated for nephroureterectomy. Bladder TB grades 1–2 should be treated by

chemotherapy, bladder TB grade 3 requires additional prescription of trospium chloride, bladder TB grade 4 is indicated for cystectomy and reconstructive enteroplastic operation. MGTB should be treated with chemotherapy; scrotal fistula is indicated for surgery.

Clinical features

Diagnosis is often difficult because TB has a variety of clinical findings. It can mimic numerous other disease entities. A high level of clinical suspicion allows early diagnosis and timely initiation of proper management [Teo and Wee, 2011; Muttarak *et al.* 2005]. The nonspecific clinical features of UGTB make the early and accurate diagnosis of this disease difficult. Hematuria, lower urinary tract symptoms, flank pain and scrotal swelling are the most common presenting features. Chronic epididymitis associated with a draining scrotal sinus is often associated with UGTB [Zarrabi and Heyns, 2009]. The most common presenting symptoms are polyuria, dysuria and acidic urinary pH with pyuria. A total of 80% of patients have abnormal imaging studies of the urinary system, with hydronephrosis being the most frequently found condition [Tanthanuch *et al.* 2010]. In a review of 8961 cases from the world literature there was shown a great difference between clinical features of UGTB in different regions depending on epidemic situation, economic state of the country, etc. [Figueiredo and Lucon, 2008].

Patients usually exhibit local symptoms. Fever, weight loss and anorexia are uncommon. A total of 89% of the patients have abnormal urinalysis (hematuria and/or pyuria) [Kao *et al.* 1996] Patients can present with unusual complaints not immediately suspicious for TB [Colbert *et al.* 2012] and this infection is easily overlooked unless clinicians maintain a strong awareness of its possibility [Patterson *et al.* 2012]. In Moscow, UGTB manifested with chronic cystitis in 13.1%, subacute orchiepididymitis in 13.1%, anatomofunctional alterations of the kidneys (hydronephrotic transformation, nonfunctioning kidney, ureteritis, etc.) in 28.5% of patients [Batyrov *et al.* 2004]. The diagnosis of renal tuberculosis (RTB) can be hypothesized in a nonspecific bacterial cystitis associated with a therapeutic failure or a urinalysis with a persistent leukocyturia in the absence of bacteriuria [Lima *et al.* 2012]. Nonoptimal empiric therapy for urogenital tract infections (UTIs) resulted in a high level of comorbidity UGTB and UTIs, and the old symptom of 'sterile pyuria' has now lost its significance [Kulchavenya, 2010].

Laboratory diagnosis

A delay in diagnosing UGTB is common and results in significant morbidity. Patients who are diagnosed at a late stage often have complications such as ureteral stricture with hydronephrosis, a shrunken bladder, autonephrectomy or destruction of the testis by a cold abscess. This is unfortunate, because effective medical therapy is readily available [Zarrabi and Heyns, 2009].

There remain four pillars to the diagnosis of UGTB: bacteriology, pathomorphology, radiology and provocative test with therapy *ex juvantibus*; however, some simple and cheap tests may also be useful.

Urinalysis in the diagnosis of UGTB

Urinalysis is the least invasive method of diagnosing UGTB. The classically described 'sterile pyuria' is not very sensitive or specific for UGTB, but persisting sterile pyuria in an individual at risk should increase the clinician's index of suspicion [Zarrabi and Heyns, 2009].

The introduction of the four-glass test in 1968 by Meares and Stamey (M&S) was a great step forward to diagnose chronic prostatitis not only by symptoms, but also by investigation of segmented urine and prostatic secretion specimens to localize the inflammation/infection to the urethra, bladder or prostate (or any of these combinations) [Meares and Stamey, 1968]. Thus, for many generations the Meares and Stamey four-glass test was considered as the 'gold standard' and recommended not only for research but also for the general practicing urologist as a routine test for diagnosing chronic prostatitis [Nickel, 2003]. Unfortunately, one had to realize that these recommendations were not followed for several reasons, because the test is (i) time consuming, (ii) difficult to perform, (iii) costly and (iv) bothersome for the patient [McNauhgton-Collins *et al.* 2000]

These were the main reasons why the premassage and postmassage two-glass test (PPMT) was developed [Nickel, 2000; Nickel *et al.* 2006]. However, by the PPMT only the laboratory burden (cost) is reduced by reducing the number of specimens, but the discomfort for the patient

remains the same, because the patient has to produce a midstream urine sample, interrupt micturition not to empty the bladder completely, because after the following prostatic massage by digital rectal examination (DRE) he is supposed to produce another urine specimen again during the same visit. First, not every patient can interrupt micturition before the bladder becomes empty. Second, voluntary stop of micturition converts laminar flow of urine in a turbulent one and thus provokes reflux of urine into the prostatic ducts, which is fraught with the risk of develop chemical burns, inflammation and prostatolithiasis. Another aspect of using the M&S four-glass test is probably even more serious. Patients assigned to the M&S four-glass test are usually not informed that between VB1 and VB2 (see below) and thereafter continuous urination without interruption is necessary to produce a true midstream urine specimen which is necessary to (i) diagnose concomitant cystitis and (ii) serve also as a basic comparative parameter by which localization of inflammation/infection to the urethra or prostate can be made possible. Interruption of urine flow between VB1 and VB2 and at the end of VB2 will lead to contraction of the prostate and thus contamination of urine with prostatic secretion.

In our previous work [Kul'chavenia *et al.* 2011], we developed a three-glass test for screening of patients with clinical signs and symptoms of chronic prostatitis with the option of further tests for final diagnosis only in those patients where additional investigations are needed. This KE three-glass test comprises three urine samples taken from only one continuous urine stream: VB1 comprises the first 10 ml, VB2 the midstream portion of a noninterrupted stream and VB3 the final portion at the very end of the stream. As the prostate is part of the external sphincter of the bladder, it contracts at the end of a micturition. Therefore, the urine sample at the end of the micturition (VB3) corresponds practically to the urine sample after prostatic massage. However, the discomfort of prostatic massage by DRE can be avoided. Leukocyturia in the first portion (VB1) indicates inflammation in the urethra, in the second portion (VB2) indicates general inflammation in the urinary bladder and/or upper urinary tract and in the third portion (VB3) indicates inflammation in the prostate. Leukocyturia in all three portions may mirror inflammation of the total urinary system.

Therefore the three-glass test (i) allows DRE for diagnosis of chronic prostatitis to be avoided and (ii) facilitates the use of total leukocyturia as a measure as highly suspicious of UGTB. Nonspecific bacterial prostatitis as well as nonspecific epididymitis very rarely are accompanied by pyelonephritis. In contrast, MGTB combines with KTB in up to 80% of cases. So for patients with epididymitis and/or prostatitis, having pyuria in all three portions of urine is highly suspicious of UGTB, as long as it is real pyuria, not contamination of urine by prostatic secretion, as is inevitable in the four-glass test. In our study UGTB was revealed in patients with chronic prostatitis using the three-glass test in 1.8% of patients [Kul'chavenia *et al.* 2011].

Bacteriology

At least six, but preferably nine or more, specimens of urine, expressed prostatic secretion and ejaculate should be cultured, each onto at least three slants (Lowenstein–Jensen, Finn–II, Middlebrook 7H9-12) [Lenk, 2011]. Nevertheless, the standard technique is positive in 36–57% of UGTB patients only [Kulchavenya, 2009; Batyrov *et al.* 2004; Lee *et al.* 2011; Tanthanuch *et al.* 2010]. Positive cultures were 15% higher if sowing was performed three times in 1 day [Zhuravlev *et al.* 2012]. For MGTB, to investigate prostatic secretion, then postmassage urine, then ejaculate and postejaculate urine in 1 day, by microscopy, culture and real-time polymerase chain reaction (PCR), each probe is recommended. It is very important to keep the shortest time between the collection of urine, prostatic secretion and ejaculate and their sowing; the optimal time should be no more than 40 min [Kulchavenya, 2010]. In order to identify mycobacteria and to perform anti-TB susceptibility tests, direct preparations stained with Ziehl–Nielsen (ZN) method to evaluate a smear microscopically or PCR method are insufficient; cultivation of mycobacteria is necessary [Aslan *et al.* 2007]. PCR has been found to be useful in diagnosing early disease as well as confirming diagnosis in clinically suspected cases. False-negative PCR is an important limitation of this technique [Thangappah *et al.* 2011].

TB is an anthropozoonotic disease; this is the reason for possible cross-contamination between humans and animals [Dumonceaux *et al.* 2011]. The presence of *Mycobacterium bovis* in urine accounted for 4.2–12.5% of all UGTB cases [Blagodarnyĭ *et al.* 1990; Berta *et al.* 2011; Singh *et al.* 2011a].

To overcome the limitations of current urine-based diagnostic assays of UGTB, isothermal microcalorimetry has been used to detect the metabolic activity of MTB and other commonly neglected pathogenic mycobacteria in urine and accurately determine their growth parameters [Kumar *et al.* 2012].

Pathomorphology

One more problem in the diagnosis of UGTB is the loss of pathomorphological signs of TB, especially in comorbidity with HIV infection. For identification of MBT biopsies and operation tissue should be investigated also using the ZN method. Histopathological examination (HPE) for the tissues obtained gives inconclusive diagnosis in the absence of caseous necrosis or stained acid-fast bacilli. A total of 78 tissue specimens (renal, prostate, epididymis, penile and soft tissue) from patients with clinically suspected UGTB were processed for both PCR and histopathology. In 87.1% samples, results for both PCR and HPE were in agreement. False positivity and false negativity was observed in 5.1% and 7.6% samples, respectively. With HPE as the gold standard, PCR has shown sensitivity of 87.5% and specificity of 86.7% and positive agreement between the two tests was observed as significant. PCR results were obtained within a mean period of 3.4 days while those of HPE were obtained in 7.2 days. The authors concluded that tissue PCR is a sensitive and specific method for obtaining early and timely diagnosis of UGTB. Application of tissue PCR results can augment the diagnostic accuracy to pathologically labeled granulomatous inflammations [Chawla *et al.* 2012]. In another study the possibility of the early rapid diagnosis of RTB by PCR on renal biopsy specimens was estimated. It was found that the sensitivity and specificity of real-time PCR were 93.3% and 56.7%, respectively. The sensitivity and specificity of the urine MTB culture were 23.3% and 100%, respectively [Sun *et al.* 2010].

There was no correlation between the histological findings and the mycobacteriological investigations. The investigation of tissue specimens on the presence of mycobacteria also from other organs of the urogenital tract is a suitable method to find bacteriological proof of TB, especially in the absence of positive bacteriological findings from the urine or accessory gland secretion for the estimation of species and resistance of these bacteria [Lenk *et al.* 1986].

It is necessary to keep in mind that biopsy for confirming UGTB by histology may have serious complications [Kulchavenya, 2010; Silva *et al.* 2011] until generalization of TB in untreated patient. Miliary TB has been diagnosed in a patient resulting from the hematogenous spread following transurethral ultrasound (TRUS)-guided prostate biopsy [Kim *et al.* 2011]. Biopsy may sometimes be useful in diagnostic UGTB [Shenoy *et al.* 2012], and histologic follow-up was estimated as a good method for monitoring the efficacy of treatment. Transrectal prostate biopsy may be an important tool for the diagnosis and follow-up of prostatic TB [Lee *et al.* 2001].

Radiology

Radiology is good method for diagnosis of UGTB, both prostate and kidney. Unfortunately this method is useful only for late cavernous forms, but our aim is early diagnosis. Pyelograms disclosed abnormalities in 94% and most revealed late changes [Kao *et al.* 1996] Caverns of prostate and/or kidney are absolutely pathognomonic symptom, but caverns mean late-diagnosed complicated form, cavernous UGTB cannot be cured by chemotherapy [Kulchavenya, 2010].

Provocation test

In many cases provocation test with injection of 20, 50 or 100 units of tuberculin subcutaneously may be useful. All laboratory investigations including body temperature are repeated 24 and 48 hours after tuberculin injection. The test is positive if leukocytosis, lymphocytopenia, leukocyturia, leukocytospermia and body temperature have increased by more than 1°C. Also local reaction (hyperemia, induration in place of injection tuberculin) is to be taken into account. After provocative subcutaneous tuberculin test, identification of MBT by culture or PCR increased by 16%. On the whole, this test improved the diagnosis of UGTB, especially the obscure, latent forms, to 63% [Kulchavenya and Kim, 2010; Kulchavenya and Krasnov, 2010].

Therapy ex juvantibus

Therapy *ex juvantibus* may be of first type, when patients receive antibiotics which do not inhibit MBT, and of second type, when patients receive antibiotics which inhibit only MBT. For therapy *ex juvantibus* first type, phosphomycin, cephalosporins and nitrofurantoin are suitable. For therapy *ex juvantibus* second type we can use isoniazid,

PAS, protionamide, ethionamide, ethambutol and pyrazinamide. For good results of the therapy *ex juvantibus*, pathognomonic therapy is also indicated: phytotherapy with canefron, nonsteroidal anti-inflammatory drugs, etc. [Kulchavenya and Kim, 2010].

Therapy

Drugs that can cure most TB patients have been available since the 1950s, yet TB remains the world's first highest cause of death among adults by infectious diseases. Unfortunately, during the last half a century no new drugs were developed. At the same time, resistance of MBT has increased enormously. Mono-, poly- and multi-drug-resistant MBT to the basic anti-TB drugs was found in up to 52.2% of EPTB patients and up to 78.7% of PTB patients [Kao *et al.* 1996]. Anti-TB drug treatment is based on an initial 2-month intensive phase with three or four drugs daily followed by a 4-month continuation phase with only two drugs [Lenk, 2011].

Medical treatment of genital TB is somewhat different from that of other TB, because prostatotropic drugs have to be preferred. In countries with a low incidence of TB three anti-TB drugs with bactericidal activity may be sufficient for bacterial eradication and prevention of resistance. In epidemic regions patients with MGTB should be treated with four or five anti-TB drugs: isoniazid 10 mg/kg + rifampicin 10 mg/kg + pyrazinamide 20 mg/kg + streptomycin 15 mg/kg + PAS 150 mg/kg (or ofloxacin 800 mg or levofloxacin 500 mg daily) simultaneously for 2-4 months, followed by 6–8 months of chemotherapy with isoniazid and rifampicin only [Kulchavenya, 2010].

The World Health Organization (WHO) recommended a reduction in the treatment time to 9 or 6 months with four drugs (isoniazid, rifampicin, pyrazinamide and streptomycin or ethambutol); in complicated or combined cases the length of the therapy may be 12–14 months. In cases of retreatment, immunosuppression and HIV/AIDS, the treatment time increases to 9 or 12 months [World Health Organization, 2004, 2008].

Chemotherapy for late-diagnosed complicated forms of UGTB is not effective enough, so surgery is indicated [Viswaroop *et al.* 2006]. The organ-removing operations were conducted in 73% of patients [Batyrov *et al.* 2004]. Surgery, whether in the acute setting (orchiectomy, nephrostomy) or after medical treatment (nephrectomy, cystoplasty), still plays an important role in the treatment of patients with UGTB [Zarrabi and Heyns, 2009].

To improve the chemotherapy complicated form of UGTB with bladder involvement, a modified scheme was developed [Kulchavenya, 2010]. The 'modified' tetrad included isoniazid 10 mg/kg + rifampicin 10 mg/kg + pyrazinamide 20 mg/kg + ofloxacin 800 mg for 2 months. This was followed by a 6-10 months treatment with isoniazid and rifampicin only. In addition from the first day of the therapy all patients received trospium chloride 15 mg b.i.d. for 3 months as pathogenetic treatment. The efficiency of the modified tetrad was compared with results of the standard chemotherapy (isoniazid 10 mg/kg + rifampicin 10 mg/kg + pyrazinamide 20 mg/kg + streptomycin 15 mg/kg). The outcome analysis showed that standard therapy was insufficient in more than a half of the cases: only 42.1% could be cured, 57.9% developed complications such as posttuberculous cystalgia (36.8%) and microcystitis (21.1%). Patients treated with the modified tetrad responded in a favorable manner: urinary frequency reduced by about 75%, bladder capacity increased an average of 4.7-fold. Recovery was reached in 84.3%. Posttuberculous cystalgia developed in 15.7% only. None of the patients developed microcystitis after the combined treatment. Tolerance to the treatment was good: only one patient had a mild side effect (mouth dryness).

Surgery

Unfortunately, mostly due to late diagnosis, medical treatment may not result in the resolution of symptoms. Thus, surgical intervention and reconstruction of the urinary tract are frequently indicated [Viswaroop *et al.* 2006; Wise and Shteynshlyuger, 2008]. The organ-removing operations have been conducted in 73% of UGTB patients. Preoperative tuberculostatic therapy reduces the frequency of postoperative complications. In early diagnosis, the organ has been saved in only 9.4% of operations [Batyrov *et al.* 2004]. It was found that eradicative techniques such as nephrectomy and nephroureterectomy still prevail. Early drainage of the kidney for its decompression allows preservation of the kidney and following reconstructive surgery in 70.6% of cases. The number of early and later complications have decreased considerably [Zuban' *et al.* 2008].

Bladder TB grade 4 (microcystitis) is indicated for cystectomy followed by enteroplasty [Kulchavenya and Krasnov, 2012]. Urinary bladder rehabilitation either by augmentation cystoplasty or orthotopic neobladder reconstruction increases the bladder capacity and storage time and also preserves the upper tracts [Singh *et al.* 2011b]. Bladder and ureter reconstruction with ileum is a good option in difficult cases of lack of or irreversible damage to the urinary way. Vesicoureteral reconstruction letting urethral miction improves quality of life [Resina *et al.* 2009; Singh *et al.* 2011b]. Following the full course of the therapy and, if it was indicated, surgery, patients should be under surveillance for 3–5 years with an annual check-up and antirelapse therapy, if necessary.

Conclusion

UGTB is a frequently occurring but mostly overlooked disease. The main reasons for late diagnosis are a lack of alertness on UGTB among urologists and general practitioners relative to patients with UTIs, kidney anomalies, renal cysts, etc., the nonspecific variable clinical features and decreasing positive cultures of MBT due to nonoptimal empiric therapy for UTIs following the prescribing of fluoroquinolones and amikacin. Standard chemotherapy is effective only for early diagnosed form of UGTB; in a complicated form, a modified scheme with five anti-TB drugs in combination with pathogenetic therapy is indicated. Destructive forms of KTB and MGTB cannot be cured by chemotherapy, so surgery is necessary.

Acknowledgement

The author would like to thank her student Denis Kholtobin for assistance.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The author declares no conflicts of interest in preparing this article.

References

Aslan, G., Doruk, E., Emekdaş, G., Serin, M., Direkel, S., Bayram, G. *et al.* (2007) Isolation and identification of *Mycobacterium tuberculosis* from the urine samples by conventional and molecular methods. *Mikrobiyolojy Bulteni* 41: 185–192.

Barry, C., III, Boshoff, H., Dartois, V., Dick T., Ehrt S., Flynn J., *et al.* (2009) The spectrum of latent tuberculosis: rethinking the biology and intervention strategies. *Nat Rev Microbiol* 7: 845–855.

Batyrov, F., Nersesian, A. and Merkur'evaIa, A. (2004) Urogenital tuberculosis: problems of present-day diagnosis and treatment. *Urologiia* 5: 16–24.

Berta, M., Sturm, G., Juri, L., Cosiansi, M., Barzón, S., Barnes, A. *et al.* (2011) Bacteriological diagnosis of renal tuberculosis: an experience at the regional tuberculosis laboratory in Córdoba Province, Argentina. *Rev Argentina Microbiol* 43: 191–194.

Blagodarnyĭ, I., Alimbekova, O. and Blonskaia, L. (1990) Characteristics of Mycobacteria from patients with genital tuberculosis. *Problemy tuberkuleza I bolezneĭ legkikh* 1: 37–41.

Chan, T., Ng, K., Ho, A., Scheel, O., Lai, C. and Leung, R. (1996) Urinary tract infection caused by *Mycobacterium terrae* complex. *Int J TB Lung Dis* 77: 555–557.

Chawla, A., Chawla, K., Reddy, S., Arora, N., Bairy, I., Rao, S. *et al.* (2012) Can tissue PCR augment the diagnostic accuracy in genitourinary tract tuberculosis? *Urol Int* 88: 34–38.

Colbert, G., Richey, D. and Schwartz, J. (2012) Widespread tuberculosis including renal involvement. *Proc Baylor Univ Med Center* 25: 236–239.

Cremades Romero, M., Menéndez Villanueva, R., Santos Durántez, M., Martínez García, M., Ferrando García, D. and Perpiñá Tordera, M. (1998) Characteristics of tuberculosis in a tertiary hospital during the years 1993–1996. Influence of the coinfection with HIV. *Arch Bronconeumol* 34: 333–338.

Drechsler, A. and Kirch, W. (2010) Urinary bladder tuberculosis and bacillus Calmette-Guérin instillation: reduced efficacy of bisoprolol in hypertension. *Aktuelle Urol* 41: 372–374.

Dumonceaux, G., St Leger, J., Olsen, J., Burton, M., Ashkin, D. and Maslow, JN. (2011) Genitourinary and pulmonary multidrug resistant *Mycobacterium tuberculosis* infection in an Asian elephant (Elephasmaximus). *J Zoo Wildlife Med* 42: 709–712.

Dwyer, D., McLeod, C., Collignon, P. and Sorrell, T. (1987) Extrapulmonary tuberculosis - a continuing problem in Australia. *Aust NZ J Med* 17: 507–511.

Fekak, H., Rabii, R., Moufid, K., Joual, A., Debbag, A., Bennani, A. *et al.* (2003) A rare cause of obstructive acute renal failure: urogenital tuberculosis. *Ann Urol* 37: 71–74.

Figueiredo, A. and Lucon, A. (2008) Urogenital tuberculosis: update and review of 8961 cases from the world literature. *Nat Rev Urol* 10: 207–217.

Gómez García, I., Gómez Mampaso, E., Burgos Revilla, J., Molina, M., Sampietro Crespo, A., Buitrago, L. *et al.* (2010) Tuberculous orchiepididymitis during 1978–2003 period: review of 34 cases and role of 16S rRNA amplification. *Urology* 76: 776–781.

Gusmão, L., Galvão, J. and Alfarroba, E. (1998) Tuberculosis and the kidney. *Acta Médica Portuguesa* 11: 1107–1111.

Kao, S., Fang, J., Tsai, C., Chen, K. and Huang, C. (1996) Urinary tract tuberculosis: a 10-year experience. *Chang Gung Med J* 19: 1–9.

Kim, C., Sano, T. and Takimoto, K. (2011) Miliary tuberculosis following transrectal ultrasonography (TRUS)-guided prostate biopsy. *Korean J Urol* 52: 425–427.

Khanna, A. and Agrawal, A. (2011) Markers of genital tuberculosis in infertility. *Singapore Med J* 52: 864–867.

Korzeniewska, A., Dyła, T., Kosacka, M. and Jankowska, R. (2009) Tuberculosis after renal transplantation. *Pneumonologiaialergologiapolska* 77(1): 61–65.

Kul'chavenia, E., Azizov, A., Brizhatiuk, E., Breusov, A. and Kholtobin, D. (2011) [A comparative study of efficacy of 2-, 3- and 4-glass tests in patients with chronic prostatitis]. *Urologiia* 6: 42–45.

Kulchavenya, E. (2009) Tuberculosis of urogenital system. In Lopatkin, N. (ed.), *Urology: National Manual*. Moscow: Geotar-Media, pp. 584–601.

Kulchavenya, E. (2010) Some aspects of urogenital tuberculosis. *Int J Nephrol Urol* 2: 351–360.

Kulchavenya, E., Kholtobin, D. and Filimonov, P. (2012a) Natural and iatrogenic bladder tuberculosis: two cases. *Mycobacterial Dis* 2:110. DOI: 10.4172/2161-1068.1000110.

Kulchavenya, E. and Kim, C. (2010) Male genital tuberculosis. In: Naber, K., Schaeffer, A., Heyns, C., Matsumoto, T., Shoskes, D. and Bjerklund Johanses, T. (eds), *International Consultation on Urogenital Infections,* Stockholm, Sweden, March 2009. Arnhem, The Netherlands: European Association of Urology, pp. 877–891.

Kulchavenya, E., Kim, C., Bulanova, O. and Zhukova, I. (2012b) Male genital tuberculosis: epidemiology and diagnostic. *World J Urol* 30: 15–21.

Kulchavenya, E. and Krasnov, V. (2010) *Selected Issue of Phthysiourology* (monograph). Novosibirsk: Nauka.

Kulchavenya, E. and Krasnov, V. (eds) (2012) *Diseases of Urinary Bladder*. Novosibirsk: Nauka.

Kulchavenya, E. and Muzyko, L. (2007) Two cases of tuberculosis after transplantation of the kidney. *Urologiia* 6: 80–82.

Kulshrestha, V., Kriplani, A., Agarwal, N., Singh, U. and Rana, T. (2011) Genital tuberculosis among infertile women and fertility outcome after antitubercular therapy. *Int J Gynecol Obstet* 113: 229–234.

Kumar, V., Jha, V. and Sakhuja, V. (2012) Putty kidney. *Iranian J Kidney Dis* 6: 255.

Lee, J., Park, H., Park, S., Lee, S., Moon, H., Kim, Y. *et al.* (2011) Clinical characteristics of genitourinary tuberculosis during a recent 10-year period in one center. *Korean J Urol* 52: 200–205

Lee, Y., Huang, W., Huang, J., Wang, J., Yu, C., Jiaan, B. *et al.* (2001) Efficacy of chemotherapy for prostatic tuberculosis-a clinical and histologic follow-up study. *Urology* 57: 872–877.

Lenk, S. (2011) Genitourinary tuberculosis in Germany: diagnosis and treatment. *Der Urologe Ausg A* 50: 1619–1627.

Lenk, S., Kalich, R. and Rothkopf, M. (1986) Detection of mycobacteria in tissue in urogenital tuberculosis. *Z Urol Nephrol* 79: 709–16.39.

Lenk, S. and Schroeder, J. (2001) Genitourinary tuberculosis. *Curr Opin Urol* 11: 93–98.

Lima, N., Vasconcelos, C., Filgueira, P., Kretzmann, M., Sindeaux, T., FeitosaNeto, B. *et al.* (2012) Review of genitourinary tuberculosis with focus on end-stage renal disease. *Rev Inst Med Tropical São Paulo* 54: 57–60.

McNauhgton-Collins, M., Fowler, F., Elliott, D., Albertsen P.C. and Barry M.J. *et al.* (2000) Diagnosing and treating chronic prostatitis: do urologists use the four-glass test? *Urology* 55: 403–407.

Meares, E, Jr., and Stamey, T. (1968) Bacteriologic localization patterns in bacterial prostatitis and urethritis. *Invest Urol* 1968; 5:492

Miyake, H. and Fujisawa, M. (2011) Tuberculosis in urogenital organs. *Rinshō shimyurēshon kenkyū* 69: 1417–1421.

Muttarak, M., ChiangMai, W. and Lojanapiwat, B. (2005) Tuberculosis of the genitourinary tract: imaging features with pathological correlation. *Singapore Med J* 46: 568–574; quiz 575.

Nickel, J. (2000) Prostatitis: lessons from the 20th century. *Br J Urol Int* 85: 179–185.

Nickel, J. (2003) Recommendations for the evaluation of patients with prostatitis. *World J Urol* 21(2): 75–81.

Nickel, J., Shoskes, D., Wang, Y., Alexander, R., Fowler, J, Jr., Zeitlin, S. *et al.* (2006) How does the pre-massage and post-massage 2-glass test compare to the Meares–Stamey 4-glass test in men with chronic

prostatitis/chronic pelvic pain syndrome? *J Urol* 176: 119–124.

Patterson, I., Robertus, L., Gwynne, R. and Gardiner, R. (2012) Genitourinary tuberculosis in Australia and New Zealand. *BJU Int* 109(Suppl. 3): 27–30.

Peto, H., Pratt, R., Harrington, T., LoBue, P. and Armstrong, L. (2009) Epidemiology of extrapulmonary tuberculosis in the United States, 1993–2006. *Clin Infect Dis* 49: 1350–1357.

Porter, M., III. (1894) Uro-genital tuberculosis in the male. *Ann Surg* 20: 396–405.

Rabbani, M., Ahmed, B. and Khan, M. (2011) Mycobacterium tuberculosis infection of a native polycystic kidney following renal transplantation. *Transplant Infect Dis* 13(1): 44–46.

Resina, R., Ruiz, B., López, R. and Romero, F. (2009) Complete vesico-ureteral reconstruction with ileum in a case of genitourinary tuberculosis. *Acta Surologica Sespañolas* 33: 706–711.

Scherban, M. and Kulchavenya, E. (2008) Prostate tuberculosis – new sexually transmitted disease. *Eur J Sexol Sexual Health* 17(Suppl. 1): S163.

Scherban, M., Kul'chavenia, E., Brizhatiuk, E., Kaveshnikova, E. and Sveshnikova, N. (2008) [Male and female genital tuberculosis. Reproductive function in a patient with tuberculosis]. *Problemy tuberkuleza I bolezneĭ legkikh* 9: 3–6 (in Russian).

Shenoy, V., Viswanath, S., D'Souza, A., Bairy, I. and Thomas, J. (2012) Isolated tuberculousepididymo-orchitis: an unusual presentation of tuberculosis. *J Infect Developing Countries* 6(1): 92–94.

Silva, G., Costa, R. and Dantas, M. (2011) Secondary amyloidosis associated with tuberculosis in renal biopsy. *Rev Soc Brasil Med Tropical* 44: 797.

Singh, D., Vogel, M., Müller-Stöver, I., El Scheich, T., Winzer, M., Göbels, S. *et al.* (2011a) TB or not TB? Difficulties in the diagnosis of tuberculosis in HIV-negative immigrants to Germany. *Eur J Med* Res 16: 381–384.

Singh, V., Sinha, R., Sankhwar, S. and Sinha, S. (2011b) Reconstructive surgery for tuberculosis contracted bladder: experience of a center in northern India. *Int Urol Nephrol* 43: 423–430.

Sun, L., Yuan, Q., Feng, J., Yang, C., Yao, L., Fan, Q. *et al.* (2010) Rapid diagnosis in early stage renal tuberculosis by real-time polymerase chain reaction on renal biopsy specimens. *Int J TB Lung Dis* 14: 341–346.

Takeshita, H., Amemiya, M., Chiba, K., Urushibara, M., Satoh, J. and Noro, A. (2012) Disseminated kidney tuberculosis complicating autosomal dominant polycystic kidney disease: a case report. *Clin Nephrol* 77: 242–245.

Tanthanuch, M., Karnjanawanichkul, W. and Pripatnanont, C. (2010) Tuberculosis of the urinary tract in southern Thailand. *J Med Assoc Thailand* 93: 916–919.

Teo, E. and Wee, T. (2011) Images in clinical medicine: Renal tuberculosis. *N Engl J Med* 365(12): e26.

Thangappah, R., Paramasivan, C. and Narayanan, S. (2011) *Indian J Med Res* 134: 40–46.

Tzvetkov, D. and Tzvetkova, P. (2006) Tuberculosis of male genital system - myth or reality in 21st century. *Arch Androl* 52: 375–381.

Viswaroop, B., Gopalakrishnan, G., Nath, V. and Kekre, NS. (2006) Role of imaging in predicting salvageability of kidneys in urinary tract tuberculosis. *J Pakistan Med Assoc* 56: 587–590.

Wildbolz, H. (1937) Ueberurogenicaltuberkulose.*Sch weizerischemedizinischeWochenschrift* 67: 1125.

Wise, G. and Marella, V. (2003) Genitourinary manifestations of tuberculosis. *Urol Clin N Amer* 30: 111–121.

Wise, G. and Shteynshlyuger, A. (2008) An update on lower urinary tract tuberculosis. *Curr Urol Rep* 9: 305–313.

World Health Organization (2004) *Treatment of Tuberculosis: Guidelines for National Programmes*. Revision approved by STAG, June 2004, 3rd edition. Geneva: World Health Organization.

World Health Organization (2008) Guidelines for the programmatic management of drug resistant tuberculosis— emergency update 2008. Available at: http://www.who.int/tb/publications/2008/programmatic_guidelines_for_mdrtb/en/index.html (accessed 22 October 2008).

Zarrabi, A. and Heyns, C. (2009) Clinical features of confirmed versus suspected urogenital tuberculosis in region with extremely high prevalence of pulmonary tuberculosis. *Urology* 74(1): 41–45.

Zhuravlev, V., Golubev, D., Novikov, B., Skorniakov, S., Medvinskiĭ, I., Arkanov, L. *et al.* (2012) Particular features of detection of patients with urogenital tuberculosis and their management. *Urologiia* 1: 11–15.

Zuban', O., Murav'ev, A. and Volkov, A. (2008) Surgical treatment of nephrotuberculosis in the present-day epidemiological situation. *Vestnik khirurgii imeni I. I. Grekova* 167(1): 92–95