Management of Genito-Urinary Tuberculosis
A Rai, H Pahwa, V Jain, S Misra

Citation

Abstract
Nearly one third of the world’s population is estimated to be infected with Mycobacterium tuberculosis. Moreover, tuberculosis is the most common opportunistic infection in AIDS patients. Genitourinary tuberculosis is not very common but it is considered as a severe form of extra-pulmonary tuberculosis. The diagnosis of genitourinary tuberculosis is made based on culture studies by isolation of the causative organism; however, biopsy material on conventional solid media may occasionally be required. Drug treatment is the first line therapy in genitourinary tuberculosis. Treatment regimens of 6 months are effective in most of the patients. Although chemotherapy is the mainstay of treatment, surgery in the form of ablation or reconstruction may be unavoidable. Both radical and reconstructive surgery should be carried out in the first 2 months of intensive chemotherapy.

INTRODUCTION
Tuberculosis remains a major public health hazard. This is attributable to the increasing pool of immuno-compromised patients. The primary target of the Mycobacterium tuberculosis bacteria is the pulmonary system. Dissemination to the genitourinary system may occur in approximately 20% of the patients. Adrenal insufficiency, renal colic, hydronephrosis, chronic cystitis, scrotal masses and infertility can be manifestations of disseminated tuberculosis. Awareness and prompt recognition will enable the urologist to implement therapy and avoid disease progression with its significant morbidity and potential mortality.

EPIDEMIOLOGY
INCIDENCE
The World Health Organization (WHO) estimates that one third of the world’s population is infected with Mycobacterium tuberculosis and there are 8 to 10 million new active cases of TB each year (WHO, 1997). Globally, TB is the most common opportunistic infection in AIDS patients. Genitourinary TB has been inconsistently reported to account for 20% to 70% of all cases of EPTB in general population but rare in children. It is the second most common form of extrapulmonary TB after peripheral lymphadenopathy. It is estimated that genitourinary TB comprises 30% of non pulmonary TB.

ETIOPATHOGENESIS
Almost all M. tuberculosis infections are acquired by the inhalation of aerosolized droplet nuclei, which reach the pulmonary alveoli. Rarely, TB has been acquired by aerosolization from a patient’s skin ulcer or during an autopsy (Frampton, 1992; Templeton et al, 1995). Genitourinary TB is caused by metastatic spread of the organism through the bloodstream during the initial infection of M. Tuberculosis. The kidney is usually the primary organ infected in urinary tract, and other parts of the urinary tract become involved by direct extension. The primary site of infection of the genital tract is often the epididymis in men and the fallopian tubes in women, being spread by hematogenous spread. Similar to urinary disease, the infection then spreads to adjacent organs by direct extension. The transmission of genital TB from male to female is very rare despite the fact that men with genital TB can have M. tuberculosis in the semen.

Kidney: The organisms in the kidney settle in the blood vessels, usually close to the glomeruli. Casseating granulomas develop and consist of Langhans giant cells surrounded by lymphocytes and fibroblasts.

The healing process results in fibrous tissue and calcium salts being deposited, producing the classic calcified lesion. One may also develop papillary necrosis and strictures in the calyceal system or at the pelviureteral junction.

Patients with genitourinary TB have essential hypertension, which is unrelated to tuberculosis.

Ureter: Tuberculotic ureteritis is always an extension of the
disease from the kidney and leads to fibrosis and stricture formation. The site most commonly affected is the ureterovesical junction (UVJ). The disease rarely involves the ureteropelvic junction (UPJ) and is even less common in the middle third of the ureter. Very occasionally, the whole of the ureter is involved. Strictures are typically less than 5cm in length. Stricture is confined to the intermural part of the ureter or an area just proximal to it.

Bladder: Bladder lesions are without exception secondary to renal TB. The earliest forms of infection start around one or another ureteral orifice, Tuberculous ulcers are rare, occasionally, the whole of the bladder is covered by inflamed, velvety granulations with ulceration. If the disease continues to progress, ureteral orifice may assume the classic golf-hole appearance.

**CLINICAL PRESENTATION**

**A. URINARY TUBERCULOSIS**

Urologists should always consider the diagnosis of genitourinary TB in a patient presenting with vague, longstanding urinary symptoms for which there is no obvious cause. Most patients affected are aged 20 to 40 year of age, and the male to female ratio is 2:1. Genitourinary TB is very uncommon in children because the symptoms of renal TB do not appear for 3 to 10 or more years after the primary infection. The patient usually complains of frequent painless micturition. The urine has characteristic sterile pyuria; however, up to 20% of patients do not have any leukocytes in the urine. Commonly, the symptoms are intermittent. Microscopic hematuria is present in up to 50% patients. Ureteral colic is uncommon and occurs only if a small flake of calcification or a clot passes down the ureter. Recurrent cystitis is also a warning sign of urinary TB. If the cause is not confirmed and the symptoms persist or recur, investigation should be conducted repeatedly, because M. tuberculosis may be difficult to isolate from the urine.

**B. GENITOURINARY TUBERCULOSIS**

Hematospermia is a rare presenting symptoms of genital TB. All these patients have other clinical evidence of genitourinary TB. TB should be considered in patients who are seen with repeated attacks of hematospermia as the only presenting symptom, even if there is no other evidence of genitourinary TB. Tuberculous epididymitis may be the first and only presenting symptom of genitourinary TB. The usual presentation is a painful, inflamed scrotal swelling that is difficult to differentiate from acute epididymo-orchitis. Tuberculosis of the epididymis usually presents as a painless or only mildly painful swelling. An abscess may drain spontaneously through the scrotal wall. A chronic draining sinus should be regarded as tuberculous unless proved otherwise. TB of the testis is almost always secondary to infection of the epididymis via direct extension. Tuberculous epididymitis can also present as infertility due to scarring of the epididymis or multiple vassal obstructions.

TB of the prostate is uncommon, and in many cases the pathologist diagnoses it incidentally after a TURP. TB of the penis and of the urethra are also very unusual manifestations. Primary TB of the penis appears as a superficial ulcer of the glans. Clinically, it is indistinguishable from malignant disease. TB of the urethra is caused by spread from another focus in the genital tract. In acute phase, there is a urethral discharge and later urethral strictures can develop. The manifestations of Genitourinary tuberculosis are summarized below:

**INVESTIGATIONS**

**TUBERCULIN TEST**

A positive reaction is considered an indication that the person has been infected, but it cannot be regarded as an indication of active tuberculous disease or that patient’s symptoms are caused by TB.

Urine Examination: Urine is sent for routine and microscopic examination for RBC and leukocytes, pH & AFB. Overnight urine sample for 3 OR 5 consecutive days is sent for AFB staining . Urine is sent for culture and sensitivity. “Sterile pyuria” is the classic urinary finding on routine urinalysis and culture. Urine culture is traditionally used for diagnosis because acid-fast bacilli (AFB) smears are often negative. Compared with culture sensitivity, AFB staining is 52%. Specificity is 96%. The sensitivity of urine culture is as 80-90% but it takes 10-14 days for report. Cultures from the female genital tract or male seminal fluid on the other hand are usually negative and are therefore unreliable. Culture confirmation tests using DNA probes are now widely available. Molecular methods, like NAH, PCR of either DNA or rRNA, have been developed to more
rapidly identify to TB. The high sensitivity (95%) and specificity (98%) of urinary PCR made it a potential tool for rapid detection of mycobacteria and in the clinical management of GUTB.

**PLAIN RADIOGRAPHS**

Plan radiographs of the urinary tract are important because they show calcification in the kidneys and in the lower genitourinary tract. Ureteral calcification is very uncommon. Calcification rarely occurs in the bladder wall and seminal vesicles except in advanced disease.

**INTRAVENTOUS UROGRAPHY (IVU)**

High dose IVU has traditionally been the gold standard tool to diagnose and evaluate genitourinary TB. It is still in practice but in many institutions has been replaced by spiral CT. IVU findings are distortion of calyx, ureteral dilation above a UVJ stricture or a rigid fibrotic ureter with multiple strictures. The cystographic phase of the IVU can give valuable information about the condition of the bladder, which may be small and contracted (thimble bladder) or with filling defects.

**COMPUTED TOMOGRAPHY**

Spiral CT has arguably replaced IVU as the imaging modality of choice for the diagnosis because of 3 dimensional reconstructed images. It is equal to IVU in identifying calyceal abnormalities, hydrourephrosis or hydroureter, autonephrectomy, amputated infundibulum, urinary tract calcifications, and renal parenchymal cavities.

**ULTRASONOGRAPHY**

It is of limited value, though used for initial screening and follow up.

**CYSTOSCOPY AND BIOPSY**

Cystoscopy is rarely indicated however in some place it is used in assessing the extent of disease or the response to chemotherapy.

Biopsy is usually necessary to rule out malignancy and is not advised before the initiation of medical therapy.

**RETROGRADE PYELOGRAPHY**

Indications: 1. stricture at the lower end of the ureter, 2. Ureteral catheterization to obtain urine samples for culture from each kidney.

**PERCUTANEOUS ANTEGRADE PYELOGRAPHY**

It is an alternative to retrograde pyelography to aspirate contents of the renal pelvis or from the tuberculous cavities to estimate the quantity of drugs that has penetrated the walls. It can also be used for percutaneous nephrostomy tube placement in an obstructive system.

Arteriography, Radioisotope Investigation, and Magnetic Resonance Imaging are rarely indicated as they do not provide any additional information above imaging modalities.

**DIAGNOSIS OF GENITOURINARY TUBERCULOSIS**

Tuberculosis of the genitourinary tract should be considered in the presence of any of the following situations:

1. Chronic cystitis that refuses to respond to adequate therapy,
2. The finding of pus without bacteria in a methylene blue stain or culture of the urinary sediment,
3. Gross or microscopic hematuria,
4. A nontender, enlarged epididymis with a beaded or thickened vas,
5. a chronic draining scrotal sinus,
6. Induration or nodulation of the prostate and thickening of one or both seminal vesicles (especially in a young man). A history of present or past tuberculosis elsewhere in the body should cause the physician to suspect tuberculosis in the genitourinary tract when signs or symptoms are present.

The diagnosis rests on the demonstration of tubercle bacilli in the urine by culture. The extent of the infection is determined by:

1. The palpable findings in the epididymides, vasa deferentia, prostate, and seminal vesicles,
2. The renal and ureteral lesions as revealed by excretory urograms;
3. Involvement of the bladder as seen through the cystoscope
4. The degree of renal damage as measured by loss of function,
5. The presence of tubercle bacilli in one or both kidneys.

TREATMENT OF GENITOURINARY TUBERCULOSIS

Tuberculosis must be treated as a generalized disease. Even when it can be demonstrated only in the urogenital tract one must assume activity elsewhere. This means that the basic treatment is medical. Surgical Excision of an infected organ, when indicated, is merely an adjunct to overall therapy.

The cornerstone of antituberculous therapy is multidrug treatment to decrease the duration of therapy and diminish the likelihood that drug resistant organisms will develop. According to WHO guidelines, ETPB are kept under category I & III. Recommended drug treatment regimens for drug sensitive GuT TB for 6 to 9 months, however 6 months regimes are effective for most forms of TB. All the drugs should be administered in one dose, and they may be taken together at night just before bedtime, with or without milk. This has been found to be the best way of achieving maximal patient tolerance. Sputum smear should be checked at the end of 2nd month 5th month and at the therapy. Response to treatment can be monitored only through clinical observation. Weight of the patient useful indicator. Patients should be seen 3,6, and 12 months after the course of chemotherapy has finished. At each visit, three consecutive early morning samples of urine should be cultured. Treatment regimens for MDR TB patients must be designed according to the organism’s sensitivity and continued for 18 to 24 months or 12 to 18 months after cultures become negative.

Figure 2

### Table: Treatment regimens for genitourinary tuberculosis

<table>
<thead>
<tr>
<th>TB Diagnostic criteria</th>
<th>TB Patients</th>
<th>TB treatment regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>New smear-positive patient; New smear-negative PBT with extensive parenchymal involvement. Severe concurrent HIV disease or severe forms of EPTB</td>
<td>PIRZE 4 HR or 6 H2 daily</td>
</tr>
<tr>
<td>III</td>
<td>New smear-negative (other than in category I), Loe severe forms of EPTB</td>
<td>PIRZE 4 HR or 6 H2 daily</td>
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Pyridoxine, 10 to 25mg should be given to prevent neuropathy in malnourished or pregnant patients and those with HIV infection, alcoholism or diabetes.

When oral drugs are given daily, streptomycin is generally given five times per week (15mg/kg, or a maximum of 1g per dose) for an initial 2-12 weeks period and then (if needed) 2 to 3 times per weeks (20 to 30mg/kg, or a maximum of 1.5g per dose).

ROLE OF SURGERY

It has become an adjuvant to medical therapy in the treatment of genitourinary TB. The current focus is on organ preservation and reconstruction as opposed to excision. Furthermore, When surgical intervention is mandated it should be delayed until medical therapy has been administered for at least 4 to 6 weeks.

NEPHRECTOMY

A nonfunctioning kidney with or without calcification. extensive disease involving the whole kidney together with hypertension and UPJ obstruction

Coexisting renal carcinoma.

Nephrectomy, is commonly performed through an open approach given the difficult dissection due to inflammation and scarring.

Partial Nephrectomy, rarely performed. Indications are:

The localized polar lesion containing calcification that has failed to respond after 6 weeks of intensive chemotherapy

An area of calcification that is slowly increasing in size and is threatening to gradually destroy the whole kidney.

Abscess Drainage: Open surgical drainage of an abscess unnecessary because contents of an abscess can be aspirated in a minimally invasive manner.

Ureteric stenting by DJ stent for passable strictures or in acute phase of illness.

**Figure 3**

<table>
<thead>
<tr>
<th>Drug/ Formulation</th>
<th>Adult Dosage (daily)</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (INH)</td>
<td>5mg/kg (max 300mg)</td>
<td>Hepatotoxicity, Peripheral neuropathy</td>
</tr>
<tr>
<td>Rifampicin (RIF)</td>
<td>10mg/kg (max 600mg)</td>
<td>Hepatotoxicity, skin rash, fever</td>
</tr>
<tr>
<td>Pyrazinamide (PZA)</td>
<td>30-25mg/kg</td>
<td>Hypersensitivity, Arthritis, Hepatotoxicity, Gastrointestinal</td>
</tr>
<tr>
<td>Ethambutol (EMB)</td>
<td>12-25mg/kg</td>
<td>Dose related increased vision</td>
</tr>
</tbody>
</table>

Dose related increased skin rash.
Urinary diversion by PCN in obstructed system in acute phase of illness where stenting failed.

Ureteric reimplantation for UVJ structure after intial failed ATT therapy

Augmentation Cystoplasty: When there is intolerable frequency of micturition, day and night, together with pain, urgency, and hematuria because of thimble bladder. Renal failure is not a contraindication to surgery. Creatinine clearance of more than 15mL/min should be accepted for augmentation cystoplasty.

Epididymectomy: The main indication is a caseating abscess that a not responding to chemotherapy. It should be done through a scrotal incision.

References

Author Information

Anurag Rai, MS(surgery)
Department of Surgery, C.S.M. Medical University

H.S. Pahwa, MS,MCh(Uro),FMAS
Consultant Urologist & Minimal Access surgeon Assistant Professor, Department of Surgery, C.S.M. Medical University

Vinod Jain, MS,,FMAS
Consultant Urologist & Minimal Access surgeon Assistant Professor, Department of Surgery, C.S.M. Medical University

Samir Misra, MS(surgery)
Assistant Professor, Department of Surgery, C.S.M. Medical University