

An Integrated Approach Using Liquid Culture System Can it Make an Impact for Clinical Diagnosis of Genitourinary Tuberculosis?

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Abstract

Tuberculosis (TB) is one of the major health problems in India. Genitourinary TB (GUTB) comprises 20% of all extrapulmonary TB, and is the most common extrapulmonary site to be affected by this disease. The spectrum of varied pathological changes occur in GUTB, hence a thorough knowledge is required to prevent complications related to GUTB. Diagnostic dilemma is a common problem faced as culture and polymerase chain reaction results vary in their sensitivity and specificity. A thorough knowledge of epidemiology, immunopathogenesis, and spectrum of the disease and importance of including liquid culture system for the diagnosis of this disease are presented in three cases.

Keywords: Genitourinary tuberculosis, Liquid culture, MTB complex

Introduction

The incidence of extrapulmonary tuberculosis (EPTB) and genitourinary TB (GUTB) in particular, in the general population has changed in the last century, and the incidence rates differ between developing and developed countries. GUTB is the second most common form of EPTB, after lymph node TB.^[1,2] Isolation of mycobacteria by acid fast bacilli (AFB) culture represents the corner stone on which definitive diagnosis of TB and other nontuberculous mycobacteria disease relies. Most of the laboratories in the developing world rely on conventional Lowenstein and Jensen media for culture followed by use of different biochemical tests for identification of mycobacteria, limitations of which are well-known. Use of automated liquid culture systems like BACTEC MGIT 960 (BD diagnostics), MB/BacT (Biomereix), Versa T rek (Trek diagnostics) are slowly increasing in disease endemic countries as India. These automated liquid culture systems, when combined with commercial molecular techniques like probe hybridization for species identification, are capable of producing positive results in 2 weeks or less for the vast majority of sputum smear

positive specimens, and within 3 weeks for smear-negative specimens.^[3] We hereby present three cases of GUTB which got diagnosed by MB/BacT liquid culture system. (Biomereix).

Case Reports

Case 1

History

The first case is about a 48-year-old male patient with no premorbid illness was admitted to Department of Urology with the complaints of left testicular swelling and pus discharge from scrotum. He was previously treated for epididymo-orchitis and left ureteric stone.

Examination findings

Left testis was enlarged, 6 × 4 cm, hard, firm, tender, and indurated all around. Thick pus point was present on the scrotal skin. Penis examination was normal. Provisional diagnosis was made as left scrotal abscess or testicular torsion.

Investigations done

Hemoglobin, hematocrit, total white blood cell count, platelet count, blood urea, serum creatinine, random blood sugar, and serum electrolytes were well within the normal limits. He underwent left orchietomy and scrotal tissue was sent for aerobic culture and mycobacterial liquid culture. Aerobic culture remained sterile, while Ziehl–Neelsen stain performed on the tissue revealed AFB (+). Later on *Mycobacterium tuberculosis* complex ([MTB] complex) was isolated in culture.

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Treatment given

Patient received antibiotics before culture and was started on antitubercular treatment (ATT) once culture yielded MTB complex.

Final diagnosis

Testicular TB.

Case 2

History

A 20-year-old, unmarried male, with no premorbid illness, was admitted to Urology department with a history of right loin pain since 6 months, which was intermittent in nature. He also complained of associated dysuria and hematuria.

Examination findings

His local as well as systemic examination was within normal limit.

Provisional diagnosis

Suspected of lower urinary tract stenosis or GUTB.

Investigations done

Ultrasonographic examination of the pelvis and abdomen revealed mild right sided hydrouretero-nephrosis. Intravenous urography findings showed fuzzy margins of right upper pole calyces with ill-defined amorphous calcifications along the lower parenchyma of the right kidney and associated mild atrophy of the lower parenchyma of the right kidney and reduced capacity of the bladder. He underwent cystoscopy, which revealed multiple erythematous patches on trigone with multiple papules. Biopsy was taken and sent for MB BacT culture, which yielded MTB complex.

Treatment given

Antitubercular treatment.

Final diagnosis

Genitourinary TB.

Case 3

History

Female patient a 22-year-old, unmarried, with no premorbid illness was admitted to Gynecology Department with history of irregular bleeding per vaginum since 1 month.

Examination findings

Her per abdomen examination revealed distension with a vague mass of size 3 × 3 cm in the right iliac fossa which was firm, smooth surfaced with restricted mobility.

Provisional diagnosis

Ovarian cyst was suspected and the patient was evaluated further.

Investigations done

Ultrasonographic examination of the abdomen revealed enlarged hypo echoic ovaries with large cystic lesions, multiple retroperitoneal lymph nodes, and minimal ascites. Contrast magnetic resonance imaging study revealed oblong cystic lesions suggestive of bilateral hydro/pyosalpinx with pelvic lymphadenopathy. Patient underwent laparoscopy and various tissue specimens were collected from the lesions. Specimens were sent for histopathological examination, MB BacT culture and polymerase chain reaction (PCR) for MTB complex. Histopathologic examination showed ulcerated fallopian tube, overlying multiple epithelioid cell granulomas with caseous necrosis and surrounded by epithelioid cells and Langhans giant cells suggestive of TB. PCR for MTB complex turned out to be positive and liquid culture yielded MTB complex.

Treatment given

Before culture report, patient was started on oral contraceptive pills. And after microbiology reports, patient was started on ATT.

Final diagnosis

Pelvic TB.

Discussion

Genitourinary TB has the propensity to affect both men and women of child-bearing age (that is, 20-40 years old), is responsible for extensive morbidity and can render patients infertile. The nonspecific presentation of GUTB can result in delayed diagnosis and management of the disease, which could worsen morbidity. Sequelae include structural damage, particularly renal failure, and infertility, especially in women. The sequelae result in prolonged morbidity and socioeconomic consequences.

In males, the sites most commonly involved are epididymis, followed by the prostate. Testicular involvement is less common and usually is the result of direct extension from the epididymis. Tubercular prostatitis usually results from antegrade infection within the urinary tract. Many theories have been postulated to define the precise route of infection to the epididymis. These include: (a) Infected urine theory (b) spread through the lymphatic system and (c) metastatic spread through the blood stream. Female to male transmission is very rare. Testicular involvement is usually as a result of local invasion from the epididymis, retrograde seeding from the epididymis and rarely by hematogenous spread. Involvement of scrotal wall suggests local extratesticular extension of the disease process. Male genital TB usually is associated with renal TB in 60-65% cases or with pulmonary TB in around 34% cases.^[4]

In females, MTB reaches the genital tract by three principal routes. The hematogenous route (90%), descending direct spread or by lymphatic spread. Primary infection of genitalia rarely may occur from direct inoculation during sexual intercourse with

patients with GUTB.^[5] Trans-serosal exudation may give rise to pelvic inflammatory disease and subsequently in extensive pelvic diseases.^[6] Very rarely sexual transport has been reported, as 3.9% men with GUTB harbor bacilli in semen.^[7]

In the kidney, hematogenous spread primarily involves the renal cortex and remains dormant. Abnormal host defense mechanism leads to reactivation of these foci with enlargement. Later, the abscess may rupture into the proximal tubule and loop of Henle with eventual development of enlarging, caseating granulomas with papillary necrosis. Spread to the renal pelvis produces pyonephrosis-like lesion, also known as a “cement” or “putty” kidney, which frequently spreads down to the ureters, bladder, or urethra, resulting into ureteric strictures and segmental dilation and obstruction.^[8] TB of the ureter usually starts in the ureterovesical junction.^[7]

In our study of the above three cases, we have observed that all the possible laboratory investigations were not asked except for the female patient where histopathology, culture and PCR were requested for clinical investigations of GUTB. Isolation and identification of the organism using MB BacT liquid culture and Accu Probe identification system (Gen Probe San Diego, Calif) gives appropriate and rapid evidence on the etiology of the disease compared with the use of conventional culture and other investigations.

Histopathology is easy and cheap method for the diagnosis as it provides the characteristic features of MTB infection, but due to the secondary nature of genitourinary infection the organisms may be scanty and the sample collected may not contain the characteristic features of tuberculous etiology and the diagnosis can be missed.^[9]

In GUTB cases diagnosis using PCR has major limitations as false-negative results are quite high. The possible explanation for these false-negative results of PCR could be due to paucibacillary nature of the specimen, and the portion of the specimen taken for PCR would not have had any MTB. The analyzed specimen may also contain inhibitors of PCR.^[10]

Clinically, suspected cases of GUTB showing PCR negative indicates the further need of evaluating other tests for diagnosis. Accurate detection of MTB is by the culture, which still remains the gold standard in the diagnosis of TB. In all the above GUTB cases, we could isolate the organisms in liquid culture system within a period of 2 weeks, compared with

several studies, which has reported low incidence of isolating the organism. The isolated organisms were identified as MTB complex using Accu probe identification kit.

For confirmation or excluding the diagnosis of GUTB, it is important that the samples collected should be subjected to the culture, which remains the gold standard for the diagnosis of TB along with histopathology and Molecular methods of diagnosis, as any of the following tests will indicate the presence of the disease. Moreover rapid Culture methods and sensitivity should be included as a part of laboratory investigations for GUTB cases as now a days multidrug-resistant TB rates are on the rise, especially in HIV patients.

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