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Case Presentation

Renal Tuberculosis: A Case History that makes or Breaks the Case, Nothing is more Deceptive

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Abstract

This manuscript presents a compelling case of renal tuberculosis in a 15-year-old male, elucidating the intricate diagnostic hurdles and strategic management approaches encountered. The patient initially presented with nonspecific symptoms, including intermittent low-grade fever, weight loss, fatigue, and diffuse skin rashes, which were initially managed as suspected enteric fever. However, as the patient's condition deteriorated, a comprehensive diagnostic exploration revealed renal tuberculosis. The report meticulously outlines the clinical presentation, diagnostic evaluation, and therapeutic trajectory, emphasizing the enigmatic nature of symptoms and advocating for a multidimensional diagnostic paradigm integrating clinical, radiological, microbiological, and histopathological assessments.

Furthermore, this case report provides a comprehensive review of urogenital tuberculosis, discussing its epidemiological underpinnings, clinical manifestations, diagnostic methodologies, and therapeutic tenets. It underscores the paramount significance of early recognition and prompt initiation of treatment in forestalling complications and optimizing patient outcomes.

This case report enriches the medical discourse by shedding light on the diagnostic intricacies and therapeutic imperatives pertinent to renal tuberculosis, especially in the younger demographic. We believe that the findings will contribute significantly to the understanding and management of this disease.

More Information

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Introduction

India is the leading country in tuberculosis, a disease caused by Mycobacterium tuberculosis. Its incidence is increasing, particularly in the developing world, with 9 million new cases annually, of which 55% are from Asia. Genitourinary TB is considered rare, and there is limited literature regarding renal TB with atypical presentations. To raise awareness of GUTB, a case of PCR-positive genitourinary TB is presented.

Step into the world of solving medical mysteries with us as we share the journey of diagnosing and treating renal tuberculosis in a young patient. We'll unravel the puzzling symptoms, map out the intricate path of diagnosis, and chart the course of treatment strategies. Experience the resilience of young care as we navigate through various approaches, ultimately achieving successful outcomes. Through our dynamic methods and insightful actions, this case report illuminates the path to overcoming complex medical challenges and ensuring lasting health for children.

Case presentation

A 15 years old Caucasian male, studying in 9th class, resident of Agra, Uttar Pradesh with no significant prior medical and family history presented with complaints of intermittent low-grade fever for the past 15 days, documented between 99 ^{0}C to 100 ^{0}C F and his fever used to subside after taking oral acetaminophen. After 30 days patient redeveloped fever, this time associated with chills and rigors, and was taken to a local physician where he was treated for enteric fever, though the general condition of the patient did not improve and the patient switched to an alternative medication for 2 months where he continued to have a low-grade fever. During this period patient denied any respiratory symptoms i.e., cough, sore throat, or runny nose, and did not experience any gastrointestinal symptoms such as vomiting or diarrhea. The patient also did not have any urinary symptoms such as blood in urine, frequent voiding, urgency, difficulty, or pain during urination. The patient has been diagnosed since birth to have scoliosis for which he took multiple rehabilitation

measures. Now for the past 5 months patient developed decreased appetite, an unintentional weight loss of 10 kgs, and increased fatiguability. Moreover, the patient developed skin rashes all over the body within the last 2 months. The patient denied a history of joint pain, flank pain, and hemoptysis. During the physical examination patient had no abdominal discomfort or tenderness during abdominal examination. His temperature was 98.4 F, BP- 96/50 mmHg, pulse rate was regular and 90 beats per minute and respiratory rate was 18 cycles per minute. Prominent lab findings had a raised ESR (30) and C reactive protein (5.28). Urea (55) and creatinine (2.2) were elevated. There was a slight decrease in creatinine with proper hydration but the creatinine did not normalise over the period. Autoimmune workups (RF, C3, C4, ANA, ANCA) were negative. Serology workups were also negative that including HIV, HBsAg, and HCV. Urine analysis showed trace protein, 0-1 RBC and 2-3 WBC. Blood and urine cultures showed no growth of any pyogenic agents. Renal ultrasonography and CT abdomen were done to rule out any calculus and showed inflammatory changes in the kidney. The patient was admitted to the nephrology department for further workup. A purified protein derivative skin test was obtained and it was negative. Renal biopsy was done which was suggestive of non-necrotizing granulomatous interstitial nephritis with diffuse chronic inflammation and marked tubulointerstitial chronicity. Mycobacterium TB was positive in acid-fast bacillus polymerase chain reaction (AFB-PCR).

A renal biopsy under light microscopy demonstrated 26 glomeruli none globally sclerosed. Glomeruli show non-proliferative morphology. Peripheral viable glomerular capillaries do not appear thickened. No evidence of endocapillary cellularity/ proliferation, tuft necrosis, congophilic deposits, or intracapillary thrombi in the visualized glomeruli. Tubular atrophy and interstitial fibrosis involve about 60% - 70% of the sampled cortex. Viable tubules show prominent cytoplasmic vacuolar change and moderate tubular injury. Several hyaline casts are seen in tubular lumina. Diffuse dense chronic interstitial inflammation, many areas of micro calcinosis, and many foci of interstitial non-necrotizing epithelioid cell granulomata accompanied by prominent multinucleated giant cell reaction are observed. Arteries and arterioles included appear unremarkable. Immunofluorescence staining for IgA, IgG, C1q, Kappa light chain, Lambda light chain - Negative, IgM- 1+ granular mesangial staining, C3- minimal granular mesangial staining.

Electron microscopic findings demonstrated suggestive of focal (minimal) effacement of visceral epithelial cell foot processes.

Treatment of TB with rifampicin, isoniazid, pyrazinamide, and ethambutol was started after establishing a diagnosis and is to be continued for six months. Upon the patient's clinical improvement, he was discharged from the hospital and advised to follow-up visits, and the patient and his family were educated regarding adherence to the drugs and about the disease (Table 1) (Figures 1-4).

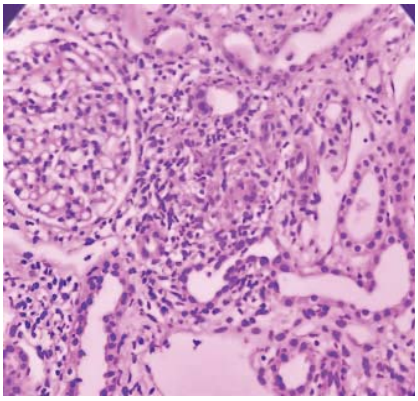


Figure 1: LM findings in renal biopsy.

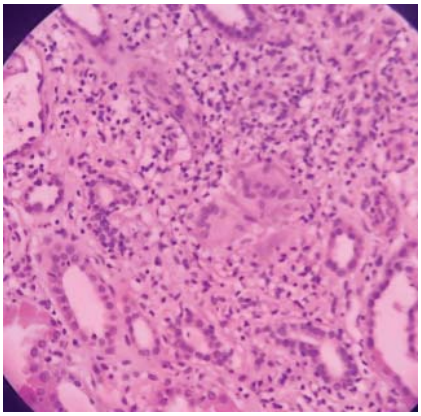


Figure 2: LM findings in renal biopsy.

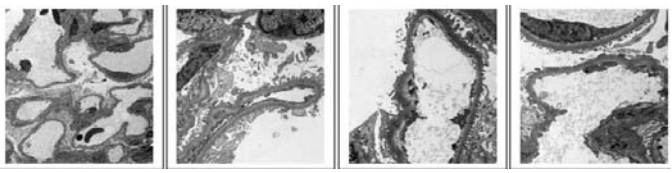


Figure 3: EM finding in renal biopsy.

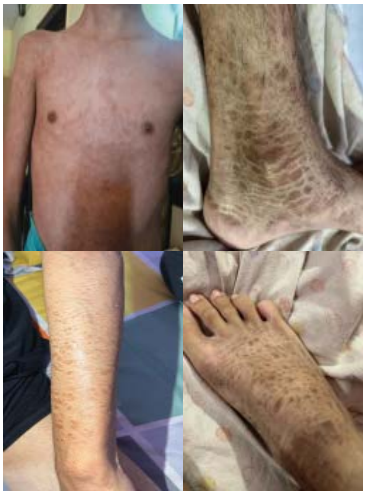


Figure 4: Skin manifestation of the patient at the time of presentation.

Table 1: Longitudinal Assessment of Clinical and Laboratory Parameters.

VARIABLES	13.05.22	01.05.23	04.05.23	15.05.23	20.06.23	28.07.23	07.08.23	24.08.23
HB (g/dl)	12.10	8.30		6.90	7.89	8.31	8.50	8.35
TLC (thou/mm3)	7.9	8.8		6.40	5.16	3.08	2.80	3.61
PC (thou/mm3)	3.25	2.90		2.44	2.34	2.22	2.36	2.64
ESR (mm/1st hr)	22	30						
MCV (Fl)	86	88		90.50	89.60	90.20	87.70	88.30
T.BILIRUBIN (mg/dl)	0.40	0.40					0.20	0.57
SGOT (U/L)	25	18					20	24.2
SGPT (U/L)	29	22					20	21.9
S.ALP (U/L)	180	90					188	246.80
S.ALBUMIN (g/dl)	4.10	3.90	3.30	3.06	3.05	2.55	2.35	2.64
UREA (mg/dl)		55	57.30	49.60	38.70	36.30	39	27.1
CREATININE (mg/dl)		2.20	2.14	1.94	1.90	1.90	1.47	1.30
SODIUM (meq/l)		140	136	135	135	138	139	135
POTASSIUM(meq/l)		3.60	4.01	4.15	4.10	3.60	3.14	3.50
CALCIUM (mg/dl)		10.70	9.60	9.40	8.54	5.48	10.40	8.14
PHOSPHOROUS (mg/dl)			4.60	5.32	4.37		3.34	3.90
URIC ACID (mg/dl)		3.30	3.50	3.30	3.70	5.80	4.30	6.70
TYPHIDOT IgM	WEAKLY POSITIVE							
MALARIA PARASITE	NEGATIVE							
FBS (mg/dl)		90						
URINE-R, M PROTEIN SPECIFIC			TRACES	NEGATIVE	NEGATIVE		NEGATIVE	NEGATIVE
GRAVITY PUS CELLS (WBC/HPF)			1.015	1.005	1.010		1.005	1.015
RBC (RBC/HPF)			2-3	NIL	0-1		NIL	0-1
CASTS			2-3 NONE SEEN	0-1 NONE	NIL NONE		NIL NONE	NIL NONE
CRP				5.28	6.38			
URINE (GENE EXPERT – MTB)							MTB TRACE DETECTED	
RENAL BIOPSY 01.08.23	LM (Figure 1) 26 GLOMERULI None globally sclerosed Glomeruli show non-proliferative morphology Peripheral viable glomerular capillaries do not appear thickened. No evidence of endocapillary cellularity/ proliferation, tuft necrosis, congophilic deposits, or intracapillary thrombi in the visualized glomeruli Tubular atrophy and interstitial fibrosis involve about 60-70% of the sampled cortex. Viable tubules show prominent cytoplasmic vacuolar change and moderate tubular injury. Several hyaline casts are seen in tubular lumina. Diffuse dense chronic interstitial inflammation, many areas of micro calcinosis, and many foci of interstitial non-necrotizing epithelioid cell granulomata accompanied by prominent multinucleated giant cell reaction are observed. Arteries and arterioles included appear unremarkable. IF (Figure 2) IgA- NEGATIVE IgG- NEGATIVE IgM- 1+ granular mesangial staining C3- minimal granular mesangial staining C1q- Negative Kappa light chain- Negative Lambda light chain- Negative							

Discussion

Tuberculosis (TB) is among the most common causes of death from infectious diseases worldwide. TB can affect any part of the body [1]. Of the 10 million annual incidences of TB, between 5% and 45% have features of extrapulmonary TB (EPTB) affecting all organs of the body. Common sites of EPTB are lymph nodes, pleura, bones, meninges, and the urogenital tract. TB affecting the kidneys, ureters, bladder, prostate, urethra, penis, scrotum, testicles, epididymis, vas deferens, ovaries, fallopian tubes, uterus, cervix and vulva were initially grouped as genitourinary TB. Currently, the term urogenital TB (UG-TB) is thought to be more appropriate as urinary tract TB occurs more often than genital TB. UG-TB is a neglected clinical entity and can easily be overlooked owing to non-specific symptoms, chronic clinical manifestations, and a lack of clinician awareness of the possibility of TB [2].

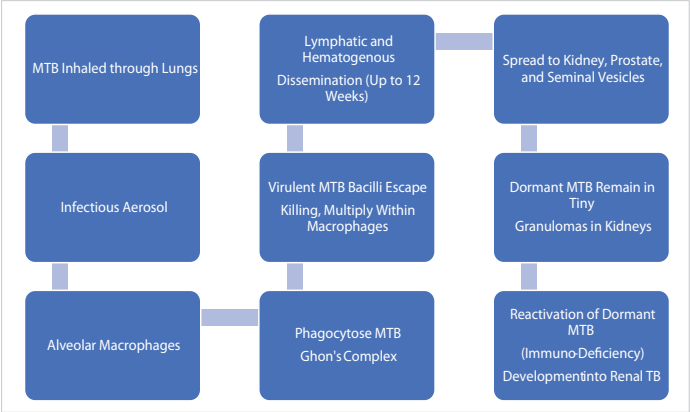
A delay in making a diagnosis results in disease progression, ureteral strictures, contracted bladder, obstructive nephropathy, renal parenchymal destruction, irreversible organ damage, and end-stage renal disease [3].

Risk factors for developing TB include malnutrition, HIV infection, diabetes, chronic renal and liver disease, alcohol and substance abuse, smoking, poor housing, pneumoconiosis,

genetics, vitamin deficiency, immunosuppressive drugs, renal transplantation, chronic renal disease, dialysis, and end-stage renal failure.

Mycobacteria of the MTBC can be transmitted to humans through various routes, including person-to-person transmission, inhalation of Mtb-infected droplet aerosols, ingestion of raw unpasteurized dairy products, transplacental transmission, parenteral instillation, and sexual contact with active genital TB lesions. After primary Mtb infection at any organ site, direct hematogenous or lymphatic spread from primary Mtb lesions leads to Mtb seeding into various parts of the urogenital tract. Mtb from the kidney can enter and lodge in the urothelium, ureter, bladder, urethra, seminal vesicles, and testes [4].

Infection, host immune response, and transmission



Renal TB and UG-TB Clinical Presentation

- Renal TB is the most common clinical presentation of UG-TB.
- Up to 10% of patients with renal TB have active pulmonary TB.
- 50% of patients with previous TB show abnormal chest X-rays.
- Kidneys are highly vascularized organs, often seeded with mycobacteria through hematogenous or lymphatic spread [5].
- Miliary microscopic tubercles enlarge and coalesce, becoming visible in the upper and lower poles of the renal cortex.
- Disease progression leads to chronic tubulointerstitial nephritis, papillary necrosis, ulcers, and fibrosis, with extensive caseous destruction of the renal parenchyma and formation of lobules dilated calyces, and cavities.
- Infection spread to the renal pelvis can cause tuberculous pyelonephritis, leading to pyonephrosis urinary flow obstruction, and dilated calyces.

According to the extent of tissue destruction, kidney TB (KTB) pathology can be classified into four stages [6]:

stage 1 (KTB-1; non-destructive form) refers to TB of the kidney parenchyma;

stage 2 (KTB-2; small destructive form) refers to TB papillitis;

stage 3 (KTB-3; destructive form), refers to cavernous kidney TB; and

stage 4 (KTB-4; widespread destructive form) is polycavernous kidney TB.

UG-TB symptoms and complications [7,8]

- Symptoms vary by disease site, with many asymptomatic in early stages.
- Common findings include dysuria, urinary hesitancy, and urinary frequency.
- Renal TB often leads to flank or renal angle pain.
- Urinalysis usually shows culture-negative, sterile pyuria and microscopic and macroscopic haematuria.
- Early diagnosis is crucial for successful treatment.
- No single diagnostic test exists for UG-TB

Furthermore, detection of Mtb is not possible in all cases of TB owing to the paucibacillary nature of the disease and, therefore, a combination of a good clinical history, imaging, and microbiological, molecular, and histopathological tests are often required to gather collective evidence of the probability of TB. GeneXpert outperforms AFB smear and culture for the detection of MTB in urine samples, which provides an alternative for the diagnosis of UTB [9].

UG-TB management overview

The acid-fast bacillus polymerase chain reaction (AFB PCR), is a laboratory technique used to detect the presence of Mycobacterium tuberculosis (the bacteria that cause tuberculosis) in clinical samples. This method amplifies specific DNA sequences of the bacteria, making them detectable even in low concentrations. In the context of renal tuberculosis diagnosis, AFB PCR can be performed on urine samples or tissue biopsies to identify Mycobacterium tuberculosis DNA. This molecular diagnostic tool offers higher sensitivity and specificity compared to traditional methods like acid-fast staining of sputum or culture techniques, making it particularly useful for diagnosing extrapulmonary tuberculosis, such as renal tuberculosis. A positive AFB PCR result supports the diagnosis of renal tuberculosis, especially when combined with clinical and imaging findings [10-13].

- Suspected UG-TB patients should have three

consecutive morning urines for AFB microscopy and culture.

- AFB smear microscopy requires 5×10^3 bacilli/ml of specimen for positive results.
- Management aims to eradicate Mtb infection with TB drug therapy, treat complications, and manage comorbidities and risk factors.
- Diagnosis requires a combination of clinical, pathological, and microbiological findings.
- Close follow-up monitoring is necessary for tracking adherence, response to therapy, TB drug toxic effects, drug resistance, TB drug levels in renal failure, and drug interactions with antiretroviral therapy in HIV-coinfected patients [14,15].

Conclusion

TB is a curable and preventable disease, but it remains the leading infectious disease cause of death worldwide. Between 15% and 40% of the global burden of the 10 million annual cases of TB present with EPTB. UG-TB is the third most common presentation of EPTB after lymph node TB and pleural TB; however, UG-TB remains a neglected clinical issue. Increased clinical awareness and early diagnosis of UG-TB is required. Treatment of UG-TB should follow WHO-recommended treatment guidelines and be supplemented by surgery whenever indicated.

Acknowledgement

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