

Unilateral Tuberculous Renal Insufficiency: A Case Report And Review Of Literature

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Citation

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Abstract

Genitourinary tuberculosis (GUTB) is a rare form of extrapulmonary tuberculosis (TB). The kidneys are the most common sites, secondary to the hematogenous spread of the disease. Although it causes various genitourinary conditions, including obstructive uropathy, interstitial nephritis, glomerulopathy, chronic kidney disease and even end stage renal disease (ESRD), atypical clinical symptoms and radiologic findings may lead to a lack of awareness regarding compromised renal function among patients. Diagnostic awareness may prevent unnecessary morbidity. Thus, GUTB should be considered in patients presenting with atypical clinical symptoms and radiologic findings, particularly in those with a history of tuberculosis. A 43-year-old woman underwent laparoscopic left nephrectomy based on the clinical diagnosis of chronic obstructive uropathy with a non-functional kidney. Cystically dilated, a small sized-atrophic kidney showed microscopically severe renal parenchymal injuries such as diffuse and global glomerulosclerosis, tubular atrophy, extensive interstitial inflammation, and cystically dilated renal pelvis, all consistent with the clinical diagnosis of a non-functional kidney. Along with these findings, multifocal granulomas with caseous necrosis were frequently found and these areas are positive for AFP and Tbc-PCR. Herein, we report a patient with renal TB showing histological findings of ESRD, radiologic urinary obstruction and no prominent clinical symptoms. Long-term untreated GUTB may progress to ESRD leading to a non-functional kidney that should be surgically resected. Diagnostic awareness may prevent unnecessary morbidity. Hence, this diagnosis should be considered in patients presenting with atypical clinical and radiological findings, and particularly in those with a history of TB.

BACKGROUND

Mycobacterium tuberculosis (*M. Tuberculosis*) causes tuberculosis (TB), which is a leading cause of death in adults worldwide, ranking above HIV/AIDS. However, the global incidence of TB peaked around 2003 and appears to be declining gradually. According to the WHO global TB report in 2019, 10 million people were ill with TB while 1.5 million succumbed to it. It is estimated that more than a quarter of the world's population is infected with *M. tuberculosis* [1]. The epidemiology of TB varies substantially worldwide, with eight countries accounting for two thirds of the global burden. The highest prevalence was seen in India (27%), followed by China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh, and South Africa.1 In the developed nations, TB is relatively uncommon and constantly declining in prevalence. However, an increasing trend has been observed in its risk factors, including HIV infection, multidrug-resistant bacilli, and immunosuppressive status secondary to dialysis, chronic

kidney disease (CKD), transplants, etcetera [2].

M. Tuberculosis typically affects the lungs but can spread to other organs/sites. According to the 2018 annual report by the Korea Center for Disease Control on TB, its estimated incidence was 51.5 per 100,000 individuals, while extrapulmonary TB (EPTB) accounted for 20.9% of the cases. The most common extrapulmonary sites were pleura, followed by lymph nodes, the intestine/peritoneum, bones/joints, the nervous system, and the genitourinary tract. There were 143 GUTB cases, accounting for 2.57% (6th most common) of all EPTB cases [3]. Although, the overall number of TB cases has reduced due to improvements in social conditions and medical treatment, the same has not been true for EPTB, resulting in a proportionate increase in EPTB cases compared with those of pulmonary TB [4,5].

GUTB frequently occurs by the hematologic dissemination of pulmonary TB, and renal involvement may present as obstructive uropathy, interstitial nephritis, and

glomerulopathy. Despite prevention and available treatment, it can progress to CKD and end stage renal disease (ESRD) [6]. In contrast to the high incidence of TB in developing countries, cases of ESRD are mainly observed in the developed world. This may be due to the wider availability of diagnostic methods for renal conditions in the latter [2].

Herein, we report on a patient with renal TB showing histological findings of unilateral ESRD and radiologic urinary obstruction, with no prominent clinical symptoms.

CASE PRESENTATION

Clinical summary. A 43-year-old woman was admitted to the Department of Urology, Chosun University Hospital (Gwangju, Korea), with a long history of obstructive uropathy. She revealed that symptoms of obstructive uropathy had begun eight years earlier, when she had received treatment for pulmonary TB. However, at the time, no evaluation or treatment was performed for the uropathy. Thorax computerized tomography (CT) showed findings of segmental atelectasis and multiple nodules suggesting post-inflammatory reaction to pulmonary TB. On enhanced pelvic CT (Fig 1A), atrophic left kidney with hydronephrosis was identified, however, the left urinary tract was not enhanced when compared with its right counterpart. There was no visible mass or stone at the left ureteropelvic junction (UPJ). The findings were suggestive of UPJ stenosis. Urine analysis revealed the presence of proteinuria (2+) and hematuria (2+). Based on the clinical diagnosis of chronic obstructive uropathy with a non-functional kidney, laparoscopic left nephrectomy was performed.

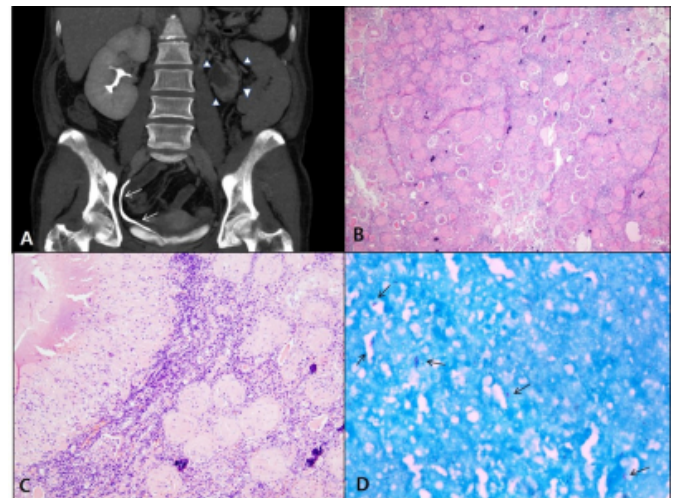
Pathological findings. Although, cystically dilated, a small sized atrophic kidney was submitted to the Department of Pathology for evaluation. Microscopically, severe renal parenchymal injuries were identified, such as diffuse and global glomerulosclerosis, tubular atrophy, extensive interstitial inflammation, and cystically dilated renal pelvis, all consistent with the clinical diagnosis of a non-functional kidney (Fig 1C). Along with these findings, multifocal granulomas with caseous necrosis were frequently found (Fig 1B). Ziehl-Neelsen stain revealed small amounts of acid-fast bacilli (Fig 1D). Further, renal tissue samples tested positive for TB based on the polymerase chain reaction (PCR) for *M. tuberculosis*.

Thorax CT was obtained postoperatively for the evaluation of the ongoing TB infection; however, only calcified nodules suggestive of old TB were found in both lungs. The patient was in good health, and without any sign and symptoms of

TB and altered renal function.

Figure 1

Fig.1. A) At enhanced pelvic CT, atrophic left kidney accompanied by hydronephrosis (arrow head) are identified, but there is no enhanced urinary tract in contrast to the right counterpart (arrows). B) Microscopically, a large granuloma with caseous necrosis is found (upper left) in the background of diffuse global sclerosis (lower right). C) most glomeruli show global glomerulosclerosis with tubular atrophy, extensive interstitial inflammation and scattered calcification. D) Ziehl-Neelsen stain reveals small amounts of acid-fast bacilli (arrows).



DISCUSSION

TB is a communicable disease that is one of the top 10 causes of death worldwide and a leading cause of death from a single infectious agent (HIV/AIDS). It is caused by a bacillus *M. tuberculosis*, and spreads by droplet transmission, i.e. through coughing, sneezing, or spitting. It typically affects the lungs but can also affect other sites [1]. In Korea, EPTB accounted for 20.9% of all new cases (n=5,550); while GUTB (n=143) accounted for 2.57% (6th most common) of all EPTB cases in 2018 [3]. However, data of North America is somewhat different from that of Korea. Genitourinary system was the third most common site of EPTB after pleura and lymph node in several countries; including Canada and United States [6]. Kim et al. [7] suggested that this difference may be due to the lower incidence of HIV infection (< 1%) and relatively higher incidence of pulmonary TB in Korea than in other countries.

Kidneys are the most common sites of GUTB [2]. Similar to its counterparts, renal TB is caused by members of the *M. tuberculosis* complex. Although, the most common causative organism is *M. tuberculosis*, *M. bovis* may be responsible occasionally. Intravesicular instillation of Bacille Calmette-

Gue'rin (BCG) vaccine, used for the treatment of bladder cancer, has also been known to cause renal lesions [2]. Renal TB is rare in developed countries; however, it remains a problem in the developing ones [8]. It presents with several forms of urinary tract injuries, including obstructive uropathy with hydronephrosis, interstitial nephritis, glomerulopathy, CKD, and even ESRD [6]. It is unusual that while most of the world's TB is localized in the developing countries; patients with ESRD, secondary to renal TB, are mainly reported in the developed world. This may be attributed to the wider availability of diagnostic methods for renal conditions in the latter [2]. Approximately 5% of patients with TB show renal involvement. The interval between the primary infection and manifestation of renal disease is typically 15–25 years. In reactivated infection this interval is reduced, typically to 4–8 years [8]. However, TB of the urinary system can be easily overlooked [2], since its clinical manifestations are nonspecific. Thus, the diagnosis is often delayed, during which GUTB progression may lead to CKD due to parenchymal destruction and obstructive uropathy [7]. Many patients with TB present with urinary symptoms typical of conventional bacterial cystitis. Hence, physicians may suspect TB only when there is no response to the treatment or when urine examination reveals pyuria in the absence of a positive culture.

Other symptoms mimicking conventional bacterial urinary tract infection may also occur sometimes, including back/flank/suprapubic pain, hematuria, frequent urination, nocturia, etc [2]. However, generally about 25% of patients are asymptomatic [8]. In an autopsy study by Figueiredo et al. [9] only 50% of GUTB patients were symptomatic and only 18% were clinically diagnosed with TB. Kim et al. [7] conducted a study in 56 GUTB patients; wherein, risk factors for CKD in GUTB were investigated. CKD and ESRD developed in 11 (19.6%) and 4 (7.1%) patients, respectively. Decreased renal function was correlated with older age, microscopic hematuria, proteinuria, acute renal failure (ARF), and a positive urinary PCR result in the univariate analysis. In the multivariate analysis, ARF and old age were independent risk factors for CKD in GUTB patients. Ultimately, in some patients, a tuberculous kidney may become calcified, if the gross anatomic distortion is advanced, with reduced renal parenchyma, and even bilateral involvement. Further, the GFR may fall; advancing the course of end-stage renal failure [2].

The diagnosis of GUTB may be established by demonstration of tubercle bacilli in the urine. As to improve

diagnostic yield, three to six early-morning urine samples should be sent for acid-fast stain, mycobacterial culture, and PCR for *M. tuberculosis* if feasible [10]. Repeated culture of early morning urine specimens may be necessary for identification of organisms because bacilluria tends to be intermittent [9]. The use of PCR (sensitivity and specificity: 87–100% and 93–98%, respectively) for detection of *M. tuberculosis* in urine or renal tissue has improved the diagnostic accuracy [11]. In later stages of the disease, intravenous pyelography identifies cavitory and destructive lesions [8].

Organisms reach the kidney by hematogenous spread from the primary source of infection. Mycobacteria incite immune reactions that are prototypically delayed-type hypersensitivity reactions. The establishment of infection leads to granuloma formation, and these are often localized to the glomeruli. Organisms may remain dormant in these foci for years [8]. In the kidneys; the preferred place for bacterial colonization is the medulla, in which granulomas with caseous necrosis can be formed, leading to local tissue destruction. The renal lesion begins at the cortex; and subsequently, the bacilli migrate to the cortico-medullary junction, and build cortical granulomas. The lesions remain stable for many years; however, during reactivation and with disease progression, the organisms cause papillitis, extensive papillary necrosis, and destruction of renal parenchyma; eventually forming cavities. The dissemination of infection to renal pelvis can cause a tuberculous pyelonephritis that can evolve to pyonephrosis. Dissemination from the ureter to the bladder causes granulomatous lesions gradually over several years. These are associated with fibrosis and ureter dilatation intercalated with strictures. Ultimately, renal dissemination of *M. tuberculosis* results in renal insufficiency, obstructive uropathy and ESRD [6,12].

Since kidneys are paired organs, in patients with unilateral renal disease, adaptive phenomenon occurs in the contralateral kidney that leads to reactive hypertrophy and improvement of the overall renal function [13]. Consequently, a person usually may not even know if one of their kidneys becomes non-functional. Nephrectomy may be the treatment of choice for most of the non-functional kidneys. Bangash et al. [14] studied the etiological factors of surgically resected non-functional kidneys, and found that the majority were complications caused by renal calculi, followed by chronic pyelonephritis, pelvic-ureteric junction obstruction (PUJO), and GUTB. The presentation was varied, including flank pain, palpable mass, high grade fever,

or hematuria, depending on the etiological factors. Because of these irregular symptoms, approximately 60% of patients did not know about their primary disease. The authors presumed that lack of awareness about primary diseases, improper urological treatment due to the fear of surgery, or low socioeconomic conditions, often led to patients presenting themselves at a later time, when irreversible loss of renal function had already occurred.

Previously, a tuberculous non-functioning kidney was recognized as technically challenging for laparoscopic surgery because of densely fibrotic adhesiveness, spillage of caseous material, and the high open conversion rate [15]. However, Lee et al. [16] proposed that the accumulation of experience with laparoscopic nephrectomy allowed for a safe and effective procedure, and suggested that it should be considered as an initial procedure for a tuberculous non-functioning kidney.

CONCLUSIONS

To summarize, we reported on a 43-year-old woman with renal TB who presented with a unilateral non-functional kidney. Although, TB is relatively uncommon in the developed nations, the risk of acquiring the disease is increasing with a surge in patients with altered immune function, such as immunosuppressed individuals, including patients on dialysis and transplantation. GUTB is a rare form of the EPTB, and the 6th most common type of EPTB in Korea. Kidneys are its most common sites; secondary to the hematogenous spread of the disease. Although, it causes various renal problems, including CKD and ESRD, the signs and symptoms of renal TB mimic those of the other renal infections. This often obscures the underlying damage and patients remain unaware regarding the compromised function of their kidneys. Long-term untreated GUTB may progress to ESRD leading to a non-functional kidney that should be surgically resected. Diagnostic awareness may prevent unnecessary morbidity. Hence, this diagnosis should be considered in patients presenting with atypical clinical and radiological findings, and particularly in those with a history of TB.

Abbreviations

M. tuberculosis: *Mycobacterium tuberculosis*; TB: tuberculosis; CKD: chronic kidney disease; EPTB: extrapulmonary TB; GUTB: genitourinary TB; ESRD: end stage renal disease; CT: computerized tomography; UPJ: ureteropelvic junction; PCR: polymerase chain reaction; BCG: Bacille Calmette-Guerin; ARF: acute renal failure;

PUJO: pelvic-ureteric junction obstruction

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Ethics approval and consent to participate

The study was approved by the ethics committee of Chosun University Hospital (Institutional review Board of Chosun university hospital, Gwangju, Korea), who waived the requirement for written informed consent due to the nature of the study.

Competing interests

The authors declares that they have no competing interests.

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