IMAGING OF RENAL TUBERCULOSIS IN EASTERN TAIWAN: CORRELATION WITH CLINICAL COURSE AND DIFFERENT COMMUNITIES

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Hualien, located in eastern Taiwan, is a relatively isolated district. The population is composed of different ethnic communities. Our hospital is the only medical center in eastern Taiwan, so is the most important referral hospital for epidemic diseases. After reviewing our collected cases of renal tuberculosis (TB), we observed a great diversity in staging and outcomes. The aim of this study was to classify different imaging presentations and clinical outcomes in the ethnic communities represented by these cases (non-aboriginal and aboriginal). We retrospectively reviewed 22 cases from 1991 to 2001. We reviewed laboratory data, radiologic reports, and clinical outcomes. Before TB was proved by biopsy or culture, patients were not treated with an anti-TB regimen. Roentgenography showed that 68% of patients had renal calcification, 59% had dilated calyces, 55% had lung involvement, and 41% had auto-nephrectomy. The proportion of mild and severe forms was significantly different between aboriginal and non-aboriginal groups ($0.05 > p \geq 0.00409$). From this series, we recommend routine plain film roentgenography, including chest roentgenography and kidney, ureter, and bladder or abdominal roentgenography, followed by intravenous urography or computerized tomography as investigative tools for renal TB. Based on the significantly different outcomes of the disease between aboriginal and non-aboriginal groups, a stronger health education program for the isolated district in eastern Taiwan is necessary.

Key Words: aborigine, eastern Taiwan, renal TB, renal tuberculosis
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Our hospital is the largest medical center in eastern Taiwan, and the cases of renal tuberculosis (TB) that we see show great diversity in both radiologic features and clinical outcomes. Early diagnosis for renal TB is extremely difficult because of its hardly perceptible symptoms and signs. Acid-fast stain of urine is highly efficient but has very low specificity. TB culture of urine gives better specificity, but is less sensitive and time-consuming. In this study, we review the radiologic features of renal TB at different stages and discuss the pathologic mechanisms. We also analyze the differences between two ethnic groups: aborigines and non-aborigines.

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PATIENTS AND METHODS

From 1991 to 2001, many cases of renal disease were treated with anti-TB drugs in our hospital. Many were

treated before TB was proved by biopsy or urine culture. The modes of treatment were therefore controversial. In order to maintain an objective survey, all cases who did not receive anti-TB therapy [1] before TB was proved by pathologic or laboratory results [2] (usually by cystoscopic biopsy, nephrectomic specimen, or positive TB culture) were enrolled in this study. We reviewed 22 cases (all from eastern Taiwan, including Hualien and its neighboring county, Taitung) in a retrospective study of laboratory data, radiologic reports, and clinical results. The following items were recorded: laboratory data (acid-fast stain), radiologic features [3] including chest roentgenography, kidney, ureter, and bladder (KUB) or abdominal roentgenography, intravenous urography (IVU), and abdominal computerized tomography (CT) scan, and therapeutic methods such as medication (including rifampin, streptomycin, pyrazinamide, or ethambutol), surgical nephrectomy, and percutaneous nephrostomy (PCN).

Patients were classified as either non-aborigines (including provincial Taiwanese, Hakka, and mainland Chinese) or aborigines (including the Ami, Atayal, and Bunun tribes) according to the information recorded in our Hospital Information System regarding place of birth, residence, language, and customs.

Radiologic and clinical features of renal TB were recorded at first presentation. Cases were classified as either mild or severe. In mild disease, the patient had early-stage radiologic features, renal function was normal, imaging results were stable at least 6 months after presentation, and oral therapy controlled the disease. In severe disease, renal function was not controlled with the anti-TB regimen, surgical intervention such as nephrectomy or PCN were necessary, or imaging showed irreversible renal damage (auto-nephrectomy).

Any significant differences in radiologic and clinical features between the non-aboriginal and aboriginal groups were assessed using the Chi-squared test. A p value of less than 0.05 was considered statistically significant.

Results

Three cases had a negative acid-fast stain, but this did not correspond to positive culture or biopsy results. Thus, acid-fast stain had a 14% false negative rate. Radiologic features on admission and clinical outcomes are listed in Tables 1 and 2, respectively. Of the 64% of

Table 1. Imaging characteristics of the 22 cases of renal tuberculosis (TB) on admission

Radiologic feature	Number of cases* (%)
Renal calcification (parenchymal calcification or stone formation)	15 (68)
Dilated calyces	13 (59)
Chest roentgenography shows old or active pulmonary TB	12 (55)
Auto-nephrectomy	9 (41)
Hydronephrosis (poor renal function and non-visualized calyces on IVU)	5 (23)
Papillary necrosis	5 (23)
Cortical scarring	6 (27)
Renal abscess	3 (14)

*Patients may have more than one feature. IVU = intravenous urography.

Table 2. Clinical outcomes in the 22 cases of renal tuberculosis (TB)

Clinical outcome	Number of cases* (%)
Improvement with drug treatment	14 (64)
Poor control with persistent high Cr/BUN	8 (36)
Surgical nephrectomy at diagnosis/nephrectomy after TB regimen	6 (27)/1 (5)
Hemodialysis for uremia	3 (14)

*Patients may have more than one outcome. Cr = creatinine; BUN = blood urea nitrogen.

cases who maintained normal renal function, all were unilaterally infected. Three cases had been diagnosed as "end-stage kidney" without function and had undergone unilateral nephrectomy before TB involvement in their remaining kidneys [4]. Among cases associated with obstructive uropathy (radiologic evidence of hydronephrosis or hydroureter), one was remarkably improved by anti-TB therapy. One case was diagnosed with early-stage disease and rapidly deteriorating renal function and underwent nephrectomy. Two patients (9%) had already lost one kidney, because of previous nephrectomy due to traumatic rupture. One maintained normal renal function while the other underwent unilateral nephrectomy shortly after the diagnosis of renal TB and received regular hemodialysis. Six patients had two kidneys with abnormal function. Three of these had abnormal function at initial presentation, while in the other three, renal function deteriorated during medical treatment. We suspect that these six patients had bilateral renal TB.

Tables 3 and 4 show the comparison between aborigines and non-aborigines. There was a significant association between severe disease and aborigines, which is unlikely to be due to coincidence or random sampling. Thus, we concluded that the aborigine population has a higher relative risk of severe forms of renal TB.

The three cases who underwent PCN and drainage procedures had severe disease, and all presented with obstructive hydronephrosis secondary to strictures or renal stones. Rapid relief of hydronephrosis resulted. They were observed for at least 6 months and had stable renal function on imaging work-up. None had undergone nephrectomy by the end of our study [5,6].

Discussion

Imaging and pathology

TB pathogenesis in organs follows one of two processes. Caseous necrosis is a dangerous and destructive process, while sclerosis usually represents a healing process. Renal TB is unique in that both of these two processes deteriorate renal function [7]. TB bacilli's hematogenous dissemination to the renal cortex does not always cause active renal TB. TB can remain inactive for decades without any clinical symptoms. This

Table 3. Comparison of disease severity and clinical outcome in aboriginal and non-aboriginal groups

	Aborigines *n* (%)	Non-aborigines *n* (%)
Mild		
No evidence of hydronephrosis or auto-nephrectomy		
Good control with oral therapy		
Total	3 (23.0)	6 (66.6)
Severe		
Underwent nephrectomy	8 (61.5)	2 (22.2)
End-stage renal failure with hemodialysis	1 (7.7)	1 (11.1)
Died after diagnosis	1 (7.7)	0 (0)
Total	10 (76.9)	3 (33.3)

Table 4. Contingency tables to calculate *p* value

	Aborigines* Observed (Expected)	Non-aborigines* Observed (Expected)	Total
Severe presentation (not controlled by medication)	10 (7.68)	3 (5.32)	13
Mild presentation (controlled by medication)	3 (5.32)	6 (3.68)	9
Total	13	9	22

*Chi-squared = 4.18, $\sum(O-E)^2/E$, O = observed, E = expected; two-tailed $p = 0.0409$; p $(0.05 > p \geq 0.00409) < 0.05$.

situation is jeopardized only when the balance between the intrinsic mycobacterial virulence and the host immunologic response is upset. Proliferation of the mycobacteria will accelerate caseation. First, small cortical granulomata will be formed [8]. The granuloma may then enlarge and invade the renal medulla and cause papillary necrosis. It could also develop into a new tuberculoma or cause more destruction of medullary tissue and ulceration. Furthermore, it could involve the calyces and progress to the lower genitourinary system. At this stage, IVU shows irregular calyces caused by ulcerative papillary lesions (Figure 1). In more severe cases, the minor calyx may appear moth-eaten. IVU can also demonstrate communicating cavities formed by tuberculoma caseate.

An effective anti-TB drug cannot always guarantee a positive outcome. Even though the bacteria are killed by the drug, the following process of sclerosis or fibrosis may lead to cicatrization or stenosis in the calyceal infundibulum and renal pelvis (Figure 1) [9]. Any cicatrization in the urinary tract that causes urinary obstruction and hydronephrosis can be demonstrated by IVU and sonography (Figure 2) [10]. Focal stricture(s) in the renal calyx, ureter, and urinary bladder may also develop into beaded, corkscrew, or pipe-stem patterns. In cases without adequate anti-TB drug treatment, progressive destruction and caseating necrosis in the renal parenchyma inevitably lead to renal destruction. This appears as soap bubbles or shell-shaped lesions on IVU and as low-density irregular and lobulated cysts on CT. Angiography can show more detailed information such as avascular cystic structures (Figure 3). Other TB complications such as superimposing pyogenic infection (Figure 4)

Figure 2. *Intravenous urography shows severe hydronephrosis with different degrees of dilated calyces. Focal stenosis (arrow) is evident in the lower portion of the atonic right ureter.*

Figure 1. *Intravenous urography shows irregularity of the right pelvis and ureter (arrow) caused by early papillary necrosis. Poor visualization of the left calyceal system (arrowhead) is due to diminished renal function, as well as tuberculoma caseation in the creation of a communicating cavity.*

Figure 3. *Renal angiography shows that the parenchyma of the left lower kidney has been replaced by avascular cystic structures (arrow).*

with abscess or nephrolithiasis (Figure 5) may be seen. Various degrees of renal calcification due to accumulation of renal calculi (in the calyces) and parenchymal calcifications [11] have been reported in different stages of renal TB. Ring-like, punctated, and amorphous forms of calcification, or calcium milk in cavities, have also been reported. Plain roentgenography may not be able to differentiate parenchymal calcification from calyceal stone formation. More advanced disease or end-stage kidney, described as auto-nephrectomy, can easily be demonstrated on plain roentgenography or CT scan [12] (Figure 6).

Final analysis

Currently, there is no rapid and effective laboratory tool to screen for renal TB. Radiologic imaging may play an important role in diagnosis. In these studies, we found that parenchymal calcification (including stone formation) and dilated calyces are the two most important radiologic presentations. Plain abdominal or KUB roentgenography may demonstrate high-density or very subtle calcification – including speckled, curvilinear, or amorphous calcification – within renal shadow(s). More than half of the patients had previous or recent pulmonary TB, as shown by chest roentgenography. Thus, plain roentgenography (including chest and KUB) is necessary for radiologic evaluation. This led us to consider the correlation of renal disease with TB. Radiologists should always remind clinicians of the possibility of active renal TB with corresponding findings in chest and KUB

Figure 5. *Intravenous pyelography shows non-functioning of the right kidney with dilated calyces and stone impaction (arrow). The patient underwent percutaneous nephrostomy.*

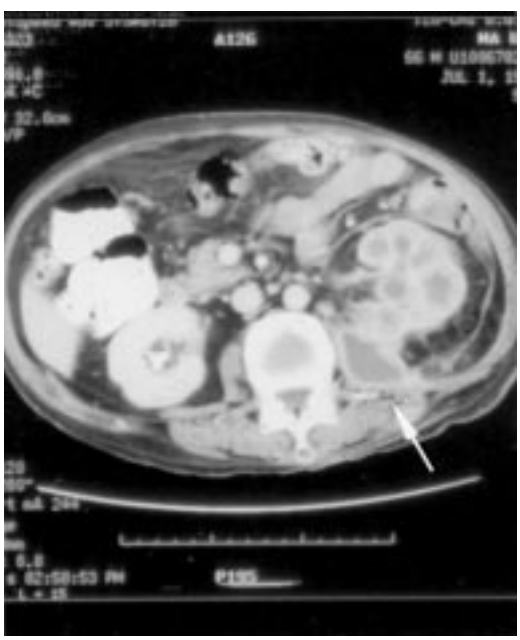

Figure 4. *Computerized tomography shows perinephric abscess formation (arrow) in a tuberculous kidney. Thickening of Gerota's fascia is due to perinephric inflammation. Bacterial infection was proved by culture.*

Figure 6. *Plain kidney, ureter, and bladder roentgenography shows a putty right kidney with atrophy (arrow).*

roentgenography. IVU study or CT scan are suggested for further evaluation of calyx, infundibulum, or cortex contours. The most characteristic renal TB manifestation is auto-nephrectomy, which represents final-stage disease. This was found in 40% of our cases. Before this irreversible disease stage, hydronephrosis, papillary necrosis, and cortical scarring are relatively non-specific findings. Others include downward trend of cicatrization from the kidney through the ureter to the urinary bladder.

Since 1992, TB has not been a fatal disease in Taiwan. However, it is still one of the major killers in Hualien district [13]. Our study shows that the radiologic and clinical presentation of renal TB in the aboriginal group was significantly advanced in stage and was worse in prognosis. This is an example of the long-term medical and social problems in eastern Taiwan. In 1997, an article published by Lee and Chiou [14] indicated that poor TB control in Hualien may result from low disease cognition and an inadequate health belief model. The aboriginal population responds inappropriately to severe health problems. The study concluded that the aboriginal population generally has a lower awareness of their physical illness and severity of disease [15], so they often miss the opportunity for optimal treatment. Based on this problem, programs promoting the value of health should be supported by both the government and aboriginal communities.

After decades of the application of anti-TB drugs, drug-resistant strains have developed worldwide [16]. They eventually compromise early success through medical control. Even successful mycobacteria-suppressing drugs for renal TB will unexpectedly cicatrize the renal calyx, ureter, and urinary bladder, which may cause obstructive uropathy and damage renal function. We consider that radiologic interventional treatment is a cost-effective and convenient method for fast relief of obstruction of the urinary tract. Based on our experience, combined treatment with anti-TB therapy and PCN yields the best results for obstructive TB uropathy. In addition, balloon dilation or stent placement can be delivered through the PCN tract to recanalize stenosis and obstruction of the urinary tract. The new radiologic technique provides better management than time-consuming surgical methods. It provides fast relief of obstruction before further damage leads to an end-stage kidney.

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