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Case Report

Extrapulmonic presentation of tuberculosis: An atypical urogenital presentation of a common disease

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ABSTRACT

Mycobacterium tuberculosis is the leading cause of infectious disease-related death worldwide. However, it is less frequently encountered in developed countries, and 90% of cases are reported in adults, making it a less commonly encountered entity in pediatric radiology. The disease is treatable, but symptoms of renal disease are nonspecific and should be identified early. A high index of clinical suspicion and supportive imaging studies, particularly in immigrant or exposed children, is prudent to prevent irreversible organ damage. We report a rare case of a 16-year-old Mexican immigrant male who presented with chronic dysuria, urinary frequency, intermittent hematuria, hydronephrosis, ureteral stenosis, and evolving autonephrectomy secondary to renal *M. tuberculosis*.

Introduction

Tuberculosis is caused by bacilli of the *Mycobacterium tuberculosis*(MTB) complex, of which *MTB* and *Mycobacterium africanum* are most common [1]. MTB remains a global epidemic as one of the top 10 causes of death worldwide reported by the World Health Organization. However, it is rarely encountered among practicing pediatric radiologists and trainees in the United States in which its incidence is only 3% [1]. Symptomatic MTB usually causes pulmonary disease, but 5% to 45% of patients will present with extrapulmonary involvement, of which 2% to 10% of these will manifest in the urogenital tract [2]. Moreover, rarely is renal TB reported in young

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children, as disease progression is indolent and takes years to develop [3].

Renal tuberculosis results from hematogenous seeding of the glomeruli and peritubular capillaries with MTB from a primary site of infection in the lung or gut. Both kidneys are seeded with the bacilli, though active disease typically only affects 1 kidney [2]. Infection then spreads to the ureters and lower urogenital system with the ensuing consequences of insidious, chronic granulomatous inflammation of the entire urogenital tract [4]. Clinically, patients will present years later with dysuria, hematuria, and flank pain, generally without constitutional symptoms of fatigue, weight loss or fever [2]. Sterile pyuria or partial/poor response to antibacterials for cystitis may ultimately prompt the diagnosis. If urine culture confirms the diagnosis, imaging plays a critical role in localizing the site and extent of disease, determining the need for surgical intervention and monitoring response to treatment [5]. Early findings are nonspecific, but later changes may be more suggestive, including papillary necrosis, calcification, ureteral strictures, hydroureteronephrosis, and autonephrectomy [1].

Renal MTB is an elusive clinical diagnosis, with only indolent and nonspecific symptoms a clue to the insidious yet destructive infection. Delay in diagnosis leads to end stage obstructive uropathy and renal failure. Although a rare childhood disease within the United States, early diagnosis with a high index of suspicion, particularly in immigrants or exposed children, immunocompromised, and in patients with chronic debilitating diseases, is prudent. We report a rare case of renal tuberculosis in a 16-year-old male diagnosed in the United States.

Case report

A 16-year-old Mexican-born male presented to adult Urology clinic with a several month history of left-sided low back pain, dysuria, hematuria, and naproxen overuse, along with a several week history of malaise, anorexia, weight loss, and subjective fevers. The patient reported the passage of occasional jelly-like clots while urinating. Additional history obtained at presentation was negative for cough, chest pain, night sweats, shortness of breath, bone pain, gastrointestinal symptoms, skin lesions, or neurological symptoms.

The patient immigrated to the United States at the age of five and lived with his grandparents, two siblings, and his mother. His grandmother traveled to and from Mexico for 3 to 6 months every year, but the patient did not report any ongoing travel himself or amongst any other family members, and had not had any visitors. A family member which remained in Mexico had a remote history of pulmonary tuberculosis treated 15 years prior to the patient's presentation. All family members were asymptomatic for TB. He had never received a bacille Calmette-Guerin vaccine.

Physical exam was significant for obesity and hypertension. Urinalysis demonstrated pyuria and hematuria. Urine bacterial cultures were sent and he was started on a 10-day empiric course of trimethoprim/sulfamethoxazole (800 mg/160 mg), pending these results. The following week, a computed tomography (CT) of the abdomen and pelvis with and without contrast was obtained and demonstrated an enlarged left kidney, hydronephrosis, and urothelial thickening of the left ureter (Fig. 1A-1E). Postcontrast images showed urothelial enhancement with delayed excretion of contrast on the left. The urinary bladder demonstrated irregular wall thickening and enhancement anteriorly (Fig. 2). His bacterial urine culture was sterile.

He returned to urology clinic the following week. Repeat UA was unchanged, and repeat urine culture was sent. Clinical evaluation for suspected urogenital TB began with three subsequent early morning urine stains and cultures sent for acid fast bacilli (AFB). When 2 of the 3 AFB stains returned positive, he was referred to the local health department. Serum interferon gamma release assay and purified protein derivative was positive at 14 mm for MTB. Blood tests revealed a normal white blood cell count (8.4 k/μL, reference range 3.8-12.0), and normal creatinine 1.11 (ng/dL, reference range 0.76-1.27). Erythrocyte sedementation rate was elevated at 90 (range 0-20 mm/h). His chest radiograph was negative for pulmonary tuberculosis. His serum HIV antibody test was negative. He was then referred to Pediatric Urology, Pediatric Infectious Disease, and Pediatric Nephrology at Wake Forest Baptist Medical Center. Further imaging with cystoscopy and retrograde pyelogram with contrast demonstrated a "beaded" appearance of the left ureter and collecting system (Fig. 3A and 3B).

The patient was started on a 6-month directly observed multidrug therapy regimen that included daily rifampin, isoniazid (INH), pyrimethamine, and ethambutol (RIPE) for 2 weeks followed by bi-weekly RIPE [6]. His bacterial urine cultures were sterile, but 1 of 3 urine AFB cultures grew *MTB*. Drug susceptibilities were pending. He was also started on amlodipine for hypertension.

Clinical follow-up of the patient at 3 weeks revealed improvement in fevers and hypertension but worsening renal function from presumed obstructive nephropathy, prompting placement of a left double J ureteral stent. His urine AFB smear was still positive at this time, but AFB culture remained negative. Two consecutive monthly AFB urine cultures remained sterile, and initial drug susceptibility testing confirmed susceptibility to INH and rifampin, so at 8 weeks he was switched to this 2-drug regimen to complete his 6-month course of antimicrobial therapy.

Within a year of diagnosis and treatment, much of his symptoms improved except for increased urinary frequency. His hypertension and renal function normalized and he remained on tapering doses of amlodipine. Repeat ultrasound imaging of the abdomen revealed progressive cortical thinning, hydronephrosis and infundibular stricturing of the left kidney. A nuclear medicine renogram was then performed that failed to demonstrate left renal tracer excretion, consistent with complete loss of function (Fig. 4). Cystogram revealed an evolving small capacity bladder of 50 cc.

Discussion

We report a rare case of urogenital/renal TB in a 16-year-old male in the United States, in which diagnosis was considered after he presented in adolescence with prolonged nonspecific symptoms of dysuria, gross hematuria, low back pain, a

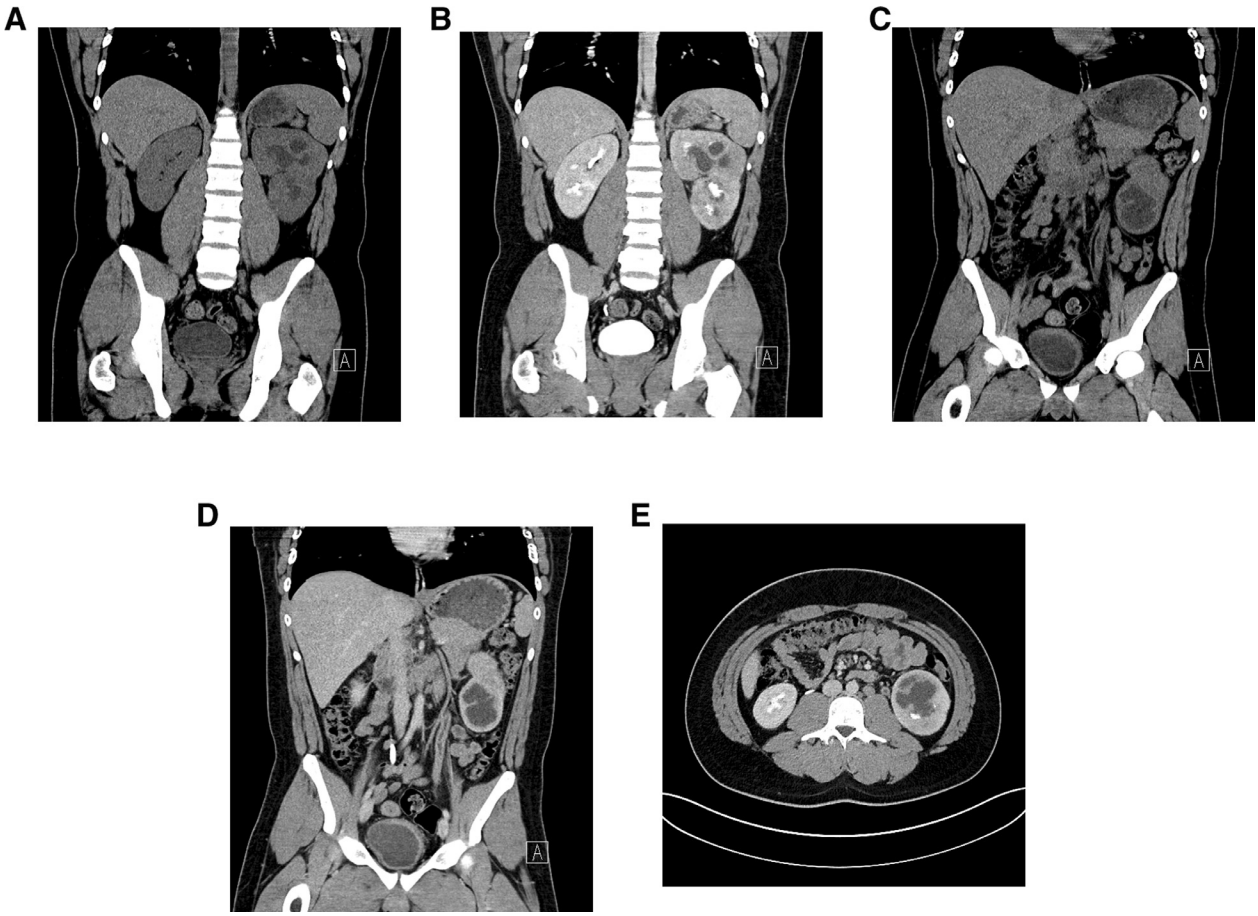

Fig. 1 – (A) Noncontrast coronal image through the renal hilum demonstrates an edematous and hydronephrotic left kidney. (B) Contrast-enhanced coronal image at a same level as Fig. 1A demonstrates a slight delayed nephrogram on the left with hydronephrosis. (C) Noncontrast coronal imaging through the lower pole of the left kidney to include portions of the left ureter, which appears thickened. (D) Contrast enhanced coronal image at the same level as Fig. 1C demonstrates the hydronephrotic left lower pole along with urothelial thickening and enhancement of the left ureter. (E) Contrast-enhanced axial image through the lower poles again demonstrates a slight delayed nephrogram on the left, a hydronephrotic appearance of the left kidney and thickened, enhancing left ureter.

history of remote exposure to MTB, and sterile pyuria. Systemic symptoms of fever, weight loss, and fatigue were additional clues to the diagnosis, but these are generally lacking at presentation unless patients have concurrent pulmonary or extrarenal disease, which he ultimately did not. Only 10% of patients have active pulmonary TB and only 50% have evidence of previous pulmonary infection on lung imaging [7]. Presumably, progression of his primary disease, beginning remotely in the lung or gastrointestinal tract, occurred as it does in 5% to 10% of patients, leading to local spread but likely widespread dissemination of mycobacteria via bloodstream and lymphatics to his kidneys, after which chronic granulomatous inflammation of the urogenital tract ensued [1].

Urinalysis supported an inflammatory process in the genitourinary tract, and despite the limited sensitivity (30%-40%) of AFB culture in a single urine specimen [6], revealed the MTB organism without evidence of multidrug resistance, confirming the diagnosis of urogenital TB. Imaging studies including contrast-enhanced CT of the abdomen and pelvis, cystoscopy with retrograde pyelogram, and ultrasound were then utilized to confirm the location and extent of disease in his kidneys, ureter and bladder, monitor his disease progression, and to support the necessity of his ureteral stent placement [1,4,8].

The sequela of hematogenous or lymphatic seeding of the urogenital tract with MTB includes disseminated caseous destruction, progressive fibrosis, and obstructive scarring of the renal parenchyma, ureters, and bladder due to chronic granulomatous inflammation. Papillary necrosis (initially a “moth eaten” appearance on imaging), lobules, dilated calyces, and cavities can be appreciated [1,9]. In the late stages and in 20% to 40% of instances of renal MTB, varying degrees of ill-defined, irregular renal parenchymal calcification occur [1]. Two types of renal nephrocalcinosis have been described in the setting of renal MTB: amorphous calcifications (appearing as granular opacification on imaging), associated with granulomatous masses and active infection, and punctate calcifications sec-

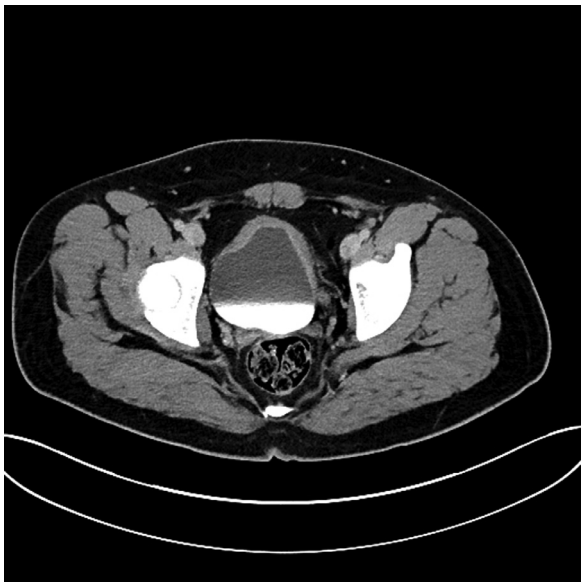

Fig. 2 – Contrast-enhanced axial image through the urinary bladder demonstrates irregular wall thickening with enhancement anteriorly.

ondary to healed granulomas [10]. The various patterns of renal parenchymal calcifications culminate in the classic "putty kidney" appearance of an atrophied and eventually nonfunctional kidney [1].

Ureteric involvement is seen in approximately 50% of renal TB cases [1]. Early manifestations include a dilated ureter, but quickly evolve to urothelial thickening and multiple strictures, leading to progressive hydroureteronephrosis [4]. In up to 21% of patients, chronic inflammation and cystitis of the bladder wall and detrusor muscle can lead to thickening with trabeculation and calcification and reduction in the bladder capacity (thimble bladder) [1]. Fibrosis and stricture formation at the ureterovesical junction leads to reflux and further contributes to hydroureteronephrosis.

Urogenital TB is best characterized with computed tomography, excretory urography, and antegrade or retrograde pyelography. Radiographs may show calcifications if present or confirm concurrent pulmonary disease [1]. Ultrasound is useful but may be initially normal. CT can show calcification with increased sensitivity, dilated calyces, parenchymal loss, and extrarenal spread. Pooling of contrast may indicate strictures, which can occur in the renal parenchyma and commonly at the ureteropelvic junction and distal ureter. The classic "beaded" appearance of alternating areas of strictures eventually leads to periureteral fibrosis and a "pipestem ureter" appearance as a later finding [1,2]. Imaging findings without history or lab confirmation of TB are nonspecific and the differential considerations are broad and include chronic pyelonephritis, medullary sponge kidney, papillary necrosis, xanthogranulomatous pyelonephritis, calyceal diverticulum, renal cell carcinoma, transitional cell carcinoma, and squamous cell carcinoma [4].

Despite effective treatment for MTB, it was delayed, and thus ongoing infundibular cicatrization and obstruction with autonephrectomy occurred in our patient as a consequence

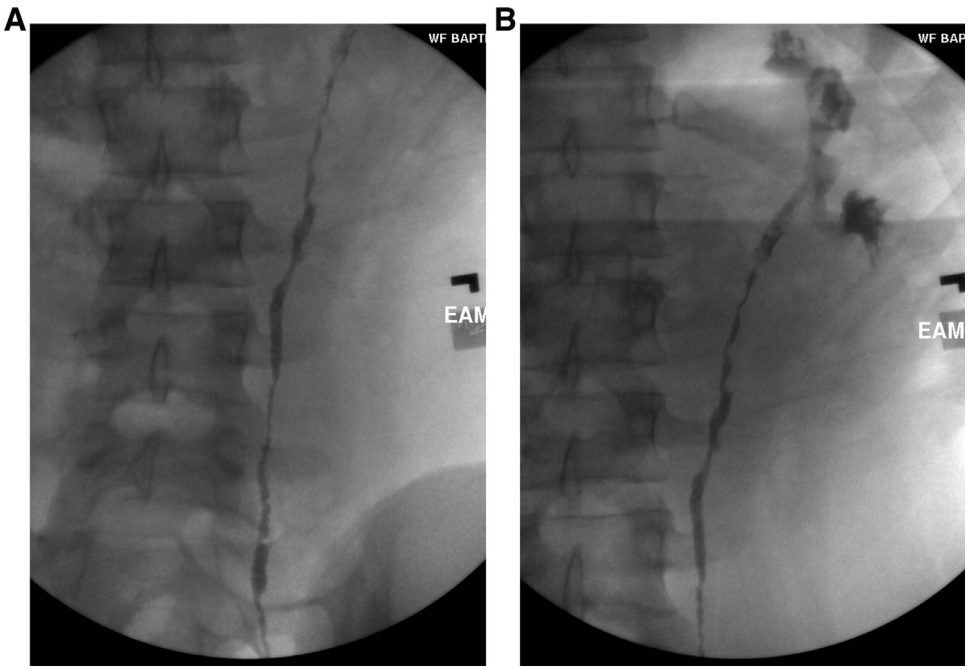

Fig. 3 – (A and B) Images from a retrograde ureterogram on the left with an irregular, beaded appearance of the left ureter on image A. Additional image at the time of retrograde ureterogram with irregular beaded appearance of the left ureter as well as irregular calyceal impression involving the left kidney.

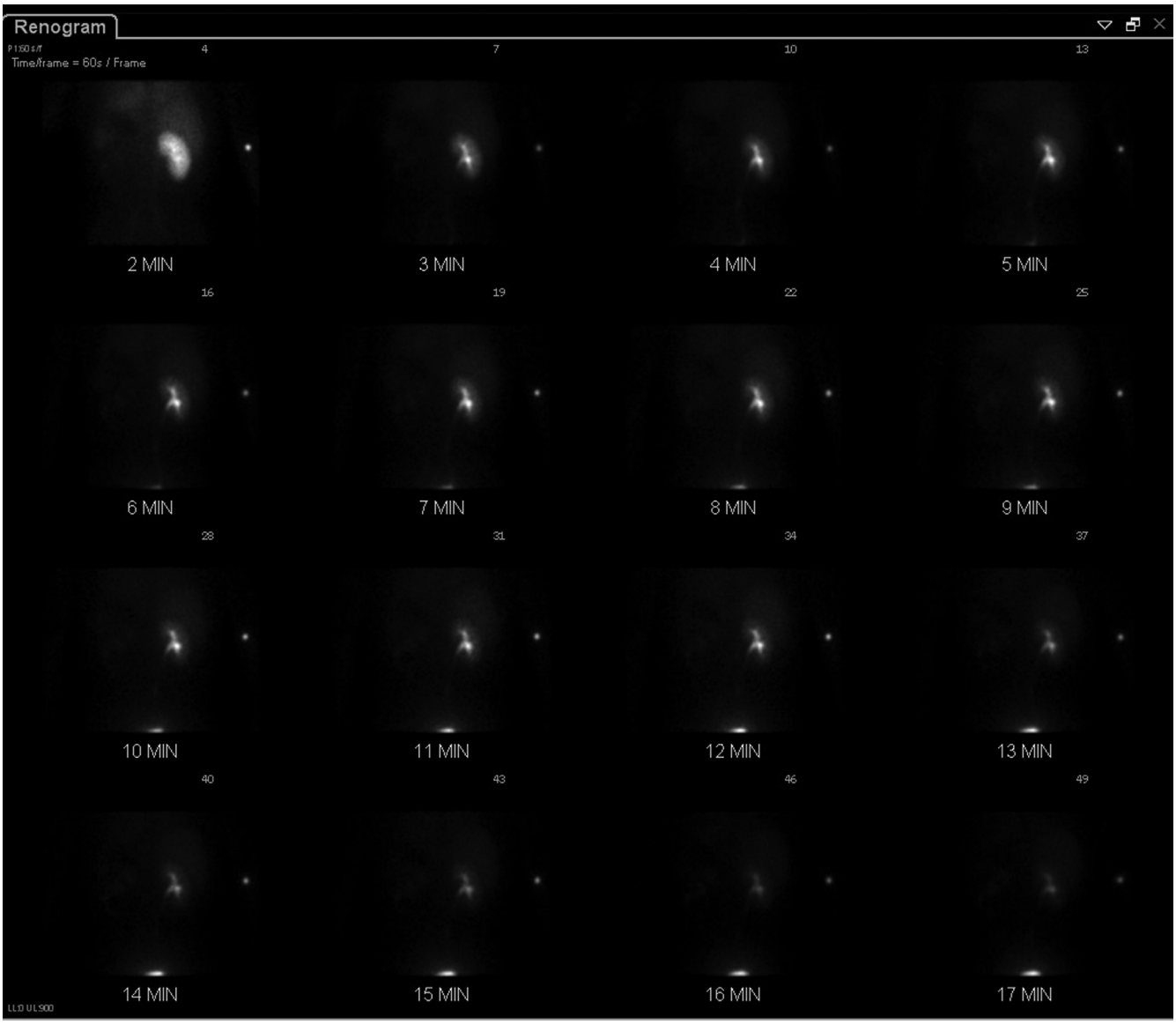

Fig. 4 – Renogram following multidrug therapy with 100% of the renal function on the right and a nonfunctioning left kidney.

of years of insidious granulomatous disease. Similar to 50% of patients during or following chemotherapy for MTB, he required adjunctive surgical intervention for ureteral obstruction [1]. Reconstructive bladder surgery to improve functional capacity was declined by the patient and he did not require nephrectomy.

Mycobacterial infections of the genitourinary tract are chronic and insidious following remote pulmonary TB exposure, and presenting symptoms are nonspecific. A delay in diagnosis can result in progressive end organ disease, obstructive uropathy, and renal failure. Earlier accurate detection of UG-TB and new more effective vaccines could be prioritized to improve outcomes. A rare disease seen by trainees and pediatricians in developed countries, a heightened and early index of suspicion, particularly in immigrant or exposed children in the United States, is prudent. Imaging can aid in earlier diagnosis, prognosis, surgical management, and response to treatment.

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