CLINICAL VIGNETTE

Renal Tuberculosis Presenting as Back Pain and Renal Failure

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Case

A 65-year-old female with hypertension and hypothyroidism presented with lower back pain for three days without inciting trauma. She denied history of renal disease, renal stones, urinary infections, or NSAID use and was free of recent fevers, chills, dysuria, hematuria, urinary frequency, nausea, vomiting, or diarrhea. There was no family history of renal disease and her home medications only included losartan and levothyroxine.

On presentation, she was afebrile. Exam revealed clear lungs, no costovertebral tenderness, and no lower extremity edema. Initial labs were notable for a sodium of 121 mmol/L, bicarbonate 13 mmol/L, BUN 158 mg/dL, creatinine 8.25 mg/dL, and a WBC 10.4 K/cu mm. Urine protein/creatinine ratio was 2.5 and the urinalysis showed large blood, large leukocyte esterase, negative nitrites, >182 RBC, and >182 WBC. Urine culture was obtained and CT abdomen and pelvis was remarkable for right sided hydronephrosis, left kidney atrophy with parenchymal thickening, and bilateral ureteral thickening. There were no renal stones and the bladder wall was thickened. She was admitted and Renal was consulted and felt the new diagnosis of renal failure was most likely chronic based on initial data. She was started on dialysis on hospital day #2 and additional CKD studies were obtained, including HIV, ANA, RPR, C3, C4, ANCA, SPEP. CT urogram showed persistent severe, left sided hydronephrosis, as well as bilateral ureteral thickening. Urology was consulted and placed a percutaneous, left nephrostomy tube.

On hospital day #4, the patient developed a fever to 38.2^{o}C. Urine culture on admission had only grown normal genital flora despite the initial pyuria. A repeat urinalysis showed persistent pyuria. Given the bilateral ureteral inflammation on CT imaging and persistent pyuria in the setting of a negative urine culture, urine acid fast bacilli (AFB) stains were ordered to evaluate for urinary TB. Of the three urine AFBs that were collected, one resulted positive with 2+ on acid fast stain.

Infectious Disease was consulted for the positive urine AFB smear. Given the positive quantiferon gold, obtained earlier in the admission for dialysis placement, CT findings of ureteral strictures and a positive urine AFB smear, raising likeliness of urogenital TB. Empiric TB therapy was initiated with rifampin 600mg daily, isoniazid 300mg daily, ethambutol 20mg/kg three times a week after dialysis (renally dosed), pyrazinamide 30mg/kg three times a week after dialysis (renally dosed), and pyridoxine. Pulmonary TB was evaluated with three negative sputum AFB smears given pulmonary nodules on CT chest. On hospital day #11, a Mag3 scan to evaluate renal function, showed left kidney at 11% function and right kidney at 82% function. Renal ultrasound showed resolution of left hydronephrosis but persistent right hydroureter. Urology placed a right ureteral stent and the patient was discharged on hospital day #19 with dialysis placement, urinary TB treatment with rifampin, isoniazid, ethambutol, and levofloxacin. Pyrazinamide was discontinued due to transaminase elevation. Follow up was scheduled with the county public health department for monitoring TB treatment. The single positive urine AFB smear eventually grew *Mycobacterium tuberculosis* in culture.

Discussion

Tuberculosis (TB) is a communicable disease caused by the bacterium *Mycobacterium tuberculosis (MTB)*. According to the World Health Organization (WHO) 2019 Global Tuberculosis Report, there were about seven million new reported cases of TB in 2018. Given the likely under-reporting of TB cases, it is estimated that that closer to 10 million people globally in 2018 were infected. While the most common manifestation of TB is pulmonary, around 15% of cases in 2018 were diagnosed with extra-pulmonary disease.[1] Urogenital TB is one extra-pulmonary manifestation. This usually develops from hematogenous spread of pulmonary TB and includes infections of the kidneys, ureters, bladder, prostate, and male and female reproductive organs.[2]

Renal TB is the most frequent manifestation of urogenital TB. After seeding the kidneys, the bacteria can lay dormant. The average elapsed time until reactivation is 22 years with reported range from one to 46 years.[2] The granulomas induced by the MTB populate the renal parenchyma, causing inflammation and eventually leading to a tubulointerstitial nephritis, papillary necrosis, fibrosis, and destruction of the parenchyma. Renal pyelonephritis can also occur, which can lead to fibrosis and scarring of the renal pelvis. Repeated inflammation and scaring of the renal tissue over time leads to necrosis and replacement of the renal parenchyma with a caseous material referred to as "putty kidney".[3] Unilateral renal involvement is more common, but bilateral renal disease can be seen. Bilateral involvement can be caused by an initial bilateral seeding with MTB or with unilateral renal TB that descended to the bladder and then ascended up the contralateral ureter to the other kidney.[2] TB

can also affect the ureters, causing inflammation and granulomatous ulcerations and fibrosis. This eventually leads to ureteral strictures and hydronephrosis. TB of the bladder usually occurs from a descending infection from renal TB.[3]

Clinical symptoms of renal/urologic TB include dysuria, hematuria, urgency, frequency, and nocturia. Systemic symptoms may include back pain, fevers, and weight loss. Because these symptoms mirror cystitis/pyelonephritis, patients are often misdiagnosed as having an acute bacterial infection before the TB is discovered.[2-5] Lab abnormalities usually include an abnormal urinalysis. Pyuria and urinary acidosis in the presence of a negative urine bacterial culture raises suspicion for renal TB. Microscopic hematuria may be present. Patients with interstitial nephritis can have WBC casts in the urine, while glomerulonephritis can show urinary dysmorphic RBC and RBC casts. Elevated Cr is often seen with bilateral renal involvement, interstitial nephritis, and glomerulonephritis. Imaging can show ureteral strictures in 60-85% of cases, hydronephrosis, and renal calcifications.[4]

The diagnosis of renal/urological TB is usually made through the urine. At least three early morning urine samples should be sent for acid fast bacilli (AFB) stain. A positive smear is not diagnostic because the AFB stain can also pick up non MTB. Five thousand organisms per milliliter are needed for the urine acid fast stain to yield a positive result and given that the MTB load in the urine is low, results in low sensitivity of 42-52%.[3,4] The gold standard remains recovering the MTB from the urine in a broth culture, but this can take up to six to eight weeks to result. In more recent years, testing has turned to urine PCR's, with faster turnaround times than culture and sensitivity of 87-100%.[3,4] Kidney biopsy can also be done if urinary studies are negative with high clinical suspicion.[4]

Once diagnosed, renal/urological TB should be treated with anti-tuberculosis medical therapy. Per the IDSA guidelines, the recommended regimens follow the same treatment as for pulmonary TB. This usually involves an initial intensive two-month phase, followed by a "continuation" four-month phase. The initial two months include a quadruple medication regimen commonly known as "RIPE" (rifampin, isoniazid, pyrazinamide, and ethambutol).[6] This is followed by a four-month continuation phase with isoniazid and rifampin, which helps eliminate any residual dormant bacilli.[3,6] The differences between the recommended IDSA regimens are in the dosing frequency, with the most preferred and effective regimens given seven days a week for both the two month and four month phases. With chronic kidney disease, ethambutol and pyrazinamide should be renally dosed and given three times a week if creatinine clearance <30ml/min or for those on dialysis.[6]

Surgical intervention may be needed as an adjunct to medical therapy in a few situations. Stenting may be needed if ureteral strictures develop, especially with hydronephrosis. Areas with strictures may fibrose and scar with medical anti-tuberculosis therapy and lead to worsening stenosis.[3,4] Stenting or percutaneous nephrostomy tubes will help relieve the obstruction and has improve recovery of renal function especially if there is limited renal involvement and a GFR>15ml/min.[5] Nephrectomy is indicated in those with a non-functioning kidney, extensive unilateral renal disease with concomitant hypertension or ureteropelvic junction obstruction, or if there is a co-existing renal cell carcinoma.[4] Renal TB can also lead to chronic disease and with continued inflammation and necrosis, eventually resulting in end stage renal disease and dialysis.[3]

Conclusion

Renal TB presents a clinical challenge to the physician, owing to its indolent nature and similarl presentation as acute bacterial urine infection. While most clinicians are adept at identifying symptoms associated with pulmonary TB, the low incidence of renal TB and its non-specific urinary symptoms leads to delays in diagnosis. Clinicians should consider renal TB if there is history of TB, the patient is from an endemic region, and persistent urinary symptoms and pyuria in the setting of a negative bacterial urine culture. As this case illustrates, a delay in diagnosis can lead to permanent renal damage.

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