Case Report

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A Child Presenting with Persistent Asymptomatic Microscopic Hematuria: a Case Report

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Abstract

Tuberculosis (TB) is a serious and important infectious disease worldwide. Children commonly develop renal tuberculosis (TB) as a complication of primary pulmonary infection with Mycobacterium tuberculosis characterized by hilar lymphadenopathy often with lung opacity. Renal TB accounts for up to 27% of extra-pulmonary cases. The disease is more prevalent in children with immunodeficiency syndromes and the recipients of organ transplantations. The signs and symptoms of renal TB are non-specific and challenging. Most patients present with persistent non-glomerular microscopic hematuria without abdominal or flank pain. Some may have signs and symptoms of the lower urinary tract such as voiding dysfunction. A diagnosis of renal TB is suspected upon detecting pyuria in the absence of common bacterial infections and is confirmed by isolation of acid-fast lactobacillus in the urine or tissue biopsy. Anti-tuberculosis drugs most frequently used in the pediatric age group are a combination of isoniazid, rifampicin, pyrazinamide, and ethambutol.

Keywords: Non-glomerular hematuria; Renal tuberculosis; Diagnosis; Treatment; Child; Mycobacterium tuberculosis.

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Introduction

The first step in the evaluation of microscopic hematuria is to determine the source of bleeding. Patients with glomerular hematuria often present with edema, oliguria, abnormal renal function, hypertension, and proteinuria (1-3). Furthermore, the presence of granular and red blood cell casts in the urine can also help to find the source of bleeding (4, 5). Benign hematuria or thin-basement membrane disease (TBMD) and IgA nephritis are the two most common causes of glomerular hematuria (3, 6). Hematuria in patients with IgA nephropathy is usually associated with microalbuminuria (7).

By contrast, the red blood cells originating from the extra-glomerular sources are isomorphic with a normal shape and size and hemoglobin volume (8). The most common cause of non-glomerular hematuria is idiopathic hypercalciuria (9). Other causes may include urinary tract infection, interstitial nephritis, urolithiasis, congenital anomalies of kidney and urinary tract (CAKUT), nephroblastoma, sickle cell trait, and renal tuberculosis (Table 1) (10-13).

A hemoglobin electrophoresis may be necessary to rule out sickle cell disease if clinically indicated (13, 14).

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Case Report

A 10-year-old female was referred for evaluation of asymptomatic microscopic hematuria of 6-month duration that was not accompanied by proteinuria or hypertension. She had no significant medical history in the past and did not use any medications. On examination, her blood pressure was 120/72 mmHg, heart rate was 78 beats/min, respiration rate was 15/min, and temperature was 37.0°C. The abdomen was soft, non-tender, and without any masses or hepatosplenomegaly.

The results of urinalysis were as follows: specific gravity: 1020, pH: 8.0, protein: trace, blood: positive. Microscopic examination of the urine sediment revealed 75 leukocytes and many isomorphic red blood cells per high power field (HPF) without granular or red blood cell casts. The white blood cell count was 8,400/mL, the hemoglobin concentration was 12.9 g/dL, and the platelet count was 315,000/mL. Serum electrolytes, BUN, and creatinine were all normal. A chest radiogram was unrevealing. Coagulation screen including PT, PTT and INR all were normal and a urine culture showed no bacterial growth. The urinary microalbumin-creatinine and calcium-creatinine ratio was 15 µg/mg and 0.15 mg/mg, respectively. Renal ultrasound was normal without hydronephrosis and cystic or mass lesions. Hemoglobin electrophoresis showed 96% Hb A, 3% HB A2, and 1% Hb S.

Enhanced-contrast computed tomogram (CT) revealed papillary necrosis in a single calyx of the lower pole of the left kidney. Cystoscopy revealed a normal bladder and active bleeding was seen from the right ureter. A Doppler ultrasonography did not detect any vascular abnormalities. A tuberculin skin test (PPD) was negative. Sterile pyuria in association with non-glomerular hematuria suggested renal tuberculosis (TB). A positive urine culture for Mycobacterium tuberculosis confirmed the diagnosis.

Table 1. Causes and investigations of non-glomerular hematuria

Acronym	Causes TIGS	Investigations
T	Tumor (nephroblastom) Tuberculosis Trauma TBMD	CT of abdomen PPD IVP Urine MA/Cr Renal biopsy
I	Interstitial nephritis Infection (UTI) IgA nephritis	Renal biopsy Urine culture Urine MA/Cr Renal biopsy
C	CAKUT Cystic lesions	Renal ultrasound
S	Stone & Hypercalciuria) Sickle cell trait	Renal ultrasound Urine Ca/Cr Hemoglobin electrophoresis
Others	Nutcracker phenomenon Coagulopathy Vascular malformations	MR angiography PT, PTT, INR MR angiography

TBMD= thin basement membrane disease. (Familial benign hematuria);
UTI=urinary tract infection; CAKUT=Congenital anomaly of the kidney and urinary tract;
PPD= purified Protein derivative; IVP=intravenous pyelogram;
MA/Cr=microalbumin/creatinine ratio; Ca/Cr=calcium creatinine ratio;
MR=magnetic resonance

Discussion

The clinical symptoms of renal TB in children are very nonspecific and challenging (15-18). Renal TB should be suspected in children presenting with painless non-glomerular hematuria associated with sterile pyuria (15-18).

A tuberculin skin test should be included in the workup of painless non-glomerular hematuria. However, it may not be helpful for diagnosis of renal TB because of its low sensitivity and specificity (60%), particularly in patients with

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HIV or other immune deficiency syndromes (15-18). Interferon Gamma Release Assay (IGRA) is more sensitive and specific than the PPD for detecting latent TB (15-16).

Microscopic isolation of lactobacillus in the urine or biopsy specimens is the gold standard for the diagnosis of renal TB. *Mycobacterium tuberculosis* is excreted intermittently; therefore, at least 3 to 5 consecutive morning urine samples should be cultured. A urine culture usually takes as long as 6-8 weeks for a definite result (19). To avoid this prolonged turnaround time, polymerase chain reaction (PCR) may be requested for detection of Mycobacterium tuberculosis in the urine during early stages of diagnostic evaluation (20). PCR is not only is a highly sensitive test for detection of *Mycobacterium tuberculosis* (95%), particularly in immunocompetent patients, but it also has a fast turnaround time of 24 hours (20).

Renal TB responds better to a short course of treatment compared to pulmonary TB. The American Academy of Pediatrics (AAP) and WHO recommend a 4-drug regimen, including rifampin 10-20 mg/kg and isoniazid, pyrazinamide, and ethambutol for 2 months followed by isoniazid and rifampin for 4 months (Table 2) (21).

Table 2. Pediatric drug regimens and dosing for renal tuberculosis

Drugs \ Dose and duration	Daily dosage	Maximum daily dose	Duration
Isoniazid	10-15 mg/k/day	300 mg/day	6 months
Rifampin	10-20 mg/kg/day	600 mg/day	6 months
Pyrazinamide	30-40 mg/kg/day	2000 mg/day	The first 2 months
Ethambutol	15-20 mg/kg/day	1000 mg/day	The first 2 months
Pyridoxine	15-50 mg	50 mg/day	6 months

¶Dosing should be reduced in patients with impaired renal function according to glomerular filtration rate

Patients with impaired renal function should receive the usual doses of rifampicin, isoniazid, and pyrazinamide because these drugs are metabolized in the liver. However, ethambutol is cleared by the kidney and its dose needs to be adjusted when the drug is given to patients with renal insufficiency according to the glomerular filtration rate (GFR) (21-24). Pyridoxine should be administered along with isoniazid to children with nutritional deficiencies.

Conflict of Interest

Authors declared no conflict of interest.

Ethical Consideration

Ethical issues (including plagiarism, data fabrication, double publication) were completely observed by the authors.

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