JAMA Diagnostic Test Interpretation

Urinalysis in the Evaluation of Proliferative Glomerulonephritis

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A 62-year-old woman with a 10-year history of hypertension presented with elevated serum creatinine (2.26 mg/dL; reference range, 0.6-1.2 mg/dL). She had not visited a physician for several years but reported feeling well with no active symptoms. She had no risk factors for hepatitis B, hepatitis C, or HIV and reported no use of nonsteroidal anti-inflammatory drugs or herbal medications. One year ago, her urine was tea-colored during an upper respiratory tract infection. Examination results were normal except for elevated blood pressure (154/90 mm Hg). Although her hemoglobin concentration was low (10.5 g/dL; reference range, 11.6-15.2 g/dL), white blood cell count, platelet count, and electrolytes were normal. Her kidneys appeared structurally normal on ultrasound. Urine studies were performed (**Table**).

HOW DO YOU INTERPRET THESE TEST RESULTS?

A. Urinary tract infection is the most likely diagnosis.

B. Proliferative glomerulonephritis is the most likely diagnosis.

C. Nonproliferative glomerulonephritis is the most likely diagnosis.

D. Hypertensive nephrosclerosis is the most likely diagnosis.

Table. Patient's Urinalysis Test Results

Laboratory Test	Result	Reference Standard/Range
Urinalysis		
Color	Yellow	Yellow
Specific gravity	1.010	1.005-1.030
pH	7.0	5.0-8.0
Blood	3+	Negative
Protein	2+	Negative
Glucose	Negative	Negative
Leukocyte esterase	Negative	Negative
Nitrite	Negative	Negative
Urine microscopy		
RBCs	20/hpf	0-5/hpf
White blood cells	0/hpf	0-5/hpf
Casts	1 RBC cast/hpf	None
Dysmorphic RBCs	Negative	None
Urinary protein:creatinine ratio[a]	1500 mg/g	<150 mg/g

Abbreviations: hpf, high-powered field; RBC, red blood cell.

[a] Adults with average muscle mass excrete approximately 1 g per day of urinary creatinine. The urine protein to creatinine ratio (mg/g) approximates urinary protein excretion (mg/24 h).

Answer

B. Proliferative glomerulonephritis is the most likely diagnosis.

Test Characteristics

Hematuria (>2 red blood cells [RBCs] per high-powered field) is the classical feature of proliferative glomerulonephritis.[1] The differential diagnosis of hematuria includes urinary tract infections, nonproliferative glomerular diseases, tubulointerstitial kidney disease, structural abnormalities of the urinary tract (eg, stones, or tumors), or an instrumented urinary tract (eg, bladder catheterization) (**Box**).[2]

A urine dipstick (Medicare fee, $2.97)[3] detects heme peroxidase activity (specificity, 65%-99%),[4] which may reflect intact RBCs, filtered free hemoglobin, or filtered myoglobin. Accordingly, a positive dipstick result requires microscopic evaluation of the sediment (Medicare fee, $4.18).[3] A dipstick result that is negative for heme peroxidase (sensitivity, 91%-100%)[4] rules out the presence of active proliferative glomerular conditions. Menstrual blood contaminating the urine may lead to false-positive results.

When RBCs traverse an injured glomerular capillary into the urinary space, they may undergo a change in morphology from their usual biconcave shape and become dysmorphic. Phase contrast microscopy is thought to be the optimal method for detecting dysmorphic RBCs, but standard light microscopy (lowering of the condenser lens from the stage until optimal resolution of the RBC shape is seen) is of comparable quality.[5] Proliferative glomerulonephritis is suggested when more than 15% of urine RBCs are dysmorphic (specificity, 85%; sensitivity, 47%)[6] or if acanthocytes (a dysmorphic RBC with vesicle-shaped protrusions) constitute at least 10% of visualized RBCs (specificity, 85%; sensitivity, 42%).[7]

Injured glomeruli allow the entry of RBCs into renal tubules where they interact with Tamm-Horsfall proteins to form casts. RBC casts suggest proliferative glomerulonephritis (specificity 78%)[8] but may also be present anytime RBCs enter the renal tubule (eg, interstitial nephritis, glomerular hemorrhage due to excessive anticoagulats, and diseases associated with nephrotic syndrome).[8]

High-grade proteinuria in the setting of hematuria suggests a proliferative glomerular lesion (specificity 91% for proteinuria >2 g/d vs <200 mg/d).[9] However, the limited sensitivity of high-grade proteinuria (18% for proteinuria >2 g/d vs <200 mg/d) means

Box. Common Sources of Hematuria[a]

Glomerular
IgA nephropathy; thin basement membrane disease; hereditary nephritis (Alport syndrome); proliferative glomerulonephritis excluding IgA nephropathy (eg, immune complex glomerulonephritis, pauci immune glomerulonephritis, and anti–glomerular basement membrane glomerulonephritis); nonproliferative glomerulonephritis

Vascular
Renal vein thrombosis; arterial emboli or thrombosis; renal infarct; arteriovenous fistula

Tubulointerstitial
Acute pyelonephritis; renal cystic diseases (eg, polycystic kidney disease, medullary sponge kidney); tuberculosis; analgesic nephropathy; acute interstitial nephritis; renal allograft rejection

Uroepithelium
Nephrolithiasis (at any level of the urinary tract); urinary tract infection (at any level of the urinary tract [eg, cystitis, prostatitis, urethritis]); malignancy; renal trauma and urinary tract instrumentation; parasitic disease (eg, schistosomiasis); papillary necrosis

Other
Exercise induced; idiopathic; coagulation abnormalities; hypercalciuria; hyperuricosuria

[a] Conditions causing hematuria are presented in order of descending frequency of presentation, by origin.

that patients with hematuria and normal or minimally elevated protein excretion may still have a proliferative glomerular lesion.[9]

Application to This Patient

The patient may have proliferative glomerulonephritis given the positive hematuria, RBC casts, and proteinuria. The absence of dysmorphic RBCs does not rule out a proliferative glomerulonephritis since sensitivity is only 47%.[6] Measurement of serum complement, tests for antinuclear and antineutrophil cytoplasmic antibodies, and serology for hepatitis B, hepatitis C, and HIV were performed to screen for systemic conditions associated with proliferative glomerulonephritis.

The combination of the patient's urinalysis results, normal serological workup, and the history of previous episodes of possible hematuria during episodes of upper respiratory tract infection makes a diagnosis of IgA nephropathy (the most common form of proliferative glomerulonephritis) most likely.

What Are Alternative Diagnostic Testing Approaches?

The diagnosis of proliferative glomerulonephritis and the underlying etiology can be confirmed with a renal biopsy, an invasive procedure associated with the risk of major bleeding requiring transfusion or angiographic intervention in up to 0.9% of cases.[10] However, the need for a renal biopsy depends on whether the result will help establish the patient's prognosis, inform management, or both.

Patient Outcome

A kidney biopsy confirmed IgA nephropathy. The patient began taking an angiotensin converting enzyme inhibitor to reduce proteinuria and manage hypertension. Five months later, her kidney function remained stable, blood pressure was well controlled, and proteinuria was 0.5 g per day. She continues biannual follow-up with a nephrologist and her glomerular filtration rate remains stable.

Clinical Bottom Line

- The following urine findings suggest proliferative glomerulonephritis: dipstick-positive hematuria combined with proteinuria, dysmorphic RBCs—particularly acanthocytes, and RBC casts.
- Proliferative glomerulonephritis should be suspected in individuals with the aforementioned urinary findings in addition to hypertension, edema, and variable degrees of renal insufficiency.
- A kidney biopsy may be required to guide the management of the underlying condition.

ARTICLE INFORMATION

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