Blood or Protein in the Urine: How much of a work up is needed?

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Disclosure

• In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturers of the products or providers of the services discussed in my presentation.

• This presentation will not include discussion of pharmaceuticals or devices that have not been approved by the FDA.
Screening Urinalysis

- Since 2007, the AAP no longer recommends to perform screening urine dipstick
- Testing based on risk factors might be a more effective strategy
- Many practices continue to order screening urine dipsticks
STATE OF LOUISIANA
COMPREHENSIVE PHYSICAL EXAMINATION REPORT

Labs (if indicated) □ Not indicated
Hct or Hgb: □ WNL  □ UTD  □ UTO
Values: ________
Urine Dipstk: □ WNL  □ UTD  □ UTO
Comments: __________________
Lead if indicated (see criteria) ___

KEY: WNL = Within Normal Limits
UTD = Up to Date
UTO = Unable to Obtain
IP= In Progress
Outline

- Hematuria
  - Definition
  - Causes
  - Evaluation
- Proteinuria
  - Definition
  - Causes
  - Evaluation
- Cases
You are about to leave when...

- 10 year old female seen for 3 day history of URI symptoms and fever. Urine dipstick showed 2+ for blood and no protein.
Questions?

- What is the etiology for the hematuria?
- What kind of evaluation should be pursued?
- Is this an indication of a serious renal condition?
- When to refer to a Pediatric Nephrologist?
Hematuria: Definition

- Dipstick ≥ 1+ (large variability)
  - RBC vs. free Hgb
  - RBC lysis common
- > 5 RBC/hpf in centrifuged urine
- Can be
  - Microscopic
  - Macroscopic
Hematuria: Epidemiology

- Microscopic hematuria occurs 4-6% with single urine evaluation
- 0.1-0.5% of school children with repeated testing
- Gross hematuria occurs in 1/1300
Localization of Hematuria

- Kidney
  - Brown or coke-colored urine
  - Cellular casts
- Lower tract
  - Terminal gross hematuria
  - (Blood clots)
Glomerular Causes of Hematuria

- Acute post-infectious GN
  - Gross hematuria 1-2 weeks after acute illness
- IgA nephropathy
  - Gross hematuria during an acute illness, microhematuria when well
Glomerular Causes of Hematuria

- **HSP nephritis**
  - Hematuria +/- proteinuria with purpuric rash, arthralgias, abdominal pain
- **Hereditary nephritis**
  - Alport syndrome, associated with hearing loss, CKD
  - Thin basement membrane nephropathy (benign)
- **Systemic (SLE)**
Causes of Hematuria

- Kidney: non glomerular
  - Hypercalciuria
  - Stones
  - Interstitial nephritis
  - Malformations, cysts
  - Sickle cell disease/trait
  - Trauma
  - Tumor (Wilms)
Causes of Hematuria

- **Lower urinary tract**
  - Bacterial/viral UTI
  - Structural (obstruction, polyp)

- **Rare causes**
  - Coagulopathy
  - Thromboses (newborn)
  - Nutcracker syndrome
Hematuria: Evaluation
History

• Patterns/ Characteristics of hematuria
• Associated Symptoms
• Prior infections
• Past medical history
• Family history
• Medications
Physical Examination

- Vitals including BP
- Volume status
- Abdominal masses
- CVA tenderness
- GU exam
- Edema, arthritis
- Rashes
Hematuria: Evaluation

- Confirm dipstick on 2 subsequent visits
- Formal UA with microscopy
- Urine culture
- Parental UAs
- Urine Ca/Cr ratio (normal < 0.21)
- Sickle cell disease testing
- Kidney ultrasound
Urine Color and Results of Dipstick

• Positive dipstick
  – Myoglobinuria
  – Hemoglobinuria

• Negative dipstick
  – Medications (rifampin)
  – Dyes (beets)
  – Metabolites (uric acid crystals)
Hematuria + Proteinuria = Glomerular Disease

- History and physical (HTN, edema)
- UA with microscopy
- Serum chemistries, CBC, C3, C4, ANA
- Renal ultrasound
- Referral to Nephrology
- Kidney biopsy (unless post-infectious GN suspected)
Hematuria: Evaluation

- Renal biopsy: not necessary in most cases; consider if:
  - Other signs of nephritis (proteinuria)
  - Positive ANA, persistently low C3
  - Gross hematuria > 2 weeks
  - Microhematuria > 1 year
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Hypercalciuria</td>
<td>15%</td>
</tr>
<tr>
<td>Benign familial hematuria</td>
<td>15%</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>10%</td>
</tr>
<tr>
<td>Acute glomerulonephritis</td>
<td>5%</td>
</tr>
<tr>
<td>UTI</td>
<td>2%</td>
</tr>
<tr>
<td>Other specific diagnosis</td>
<td>3%</td>
</tr>
<tr>
<td>Unknown</td>
<td>50%</td>
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</tbody>
</table>
Proteinuria
A relative need a physical

- 16 year old athlete had 3+ protein in a routine physical examination
Questions?

- What is the etiology for the proteinuria?
- What kind of evaluation should be pursued?
- Is this an indication of a serious renal condition?
- Would you refer to a Pediatric Nephrologist?
Asymptomatic Proteinuria

Epidemiology

- Peaks in adolescence
- Up to 10% of 8-15 year olds have proteinuria on single urine sample
- Repeated testing reduces incidence to <1%
Proteinuria: Quantification

- Dipstick method
  - Semiquantitative
  - Negative to trace normal
  - 1+ approx. 30-100 mg/dl
  - 2+ approx. >200 mg/dl
Proteinuria: Quantification

- Sulfosalicylic acid test (SSA)
  - Add equal volume of SSA to urine
  - This precipitates protein
  - False positives
    - Contrast
    - Antibiotics

<table>
<thead>
<tr>
<th>Negative</th>
<th>No turbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trace</td>
<td>Slight turbidity</td>
</tr>
<tr>
<td>1+</td>
<td>Turbidity through which print can’t be read</td>
</tr>
<tr>
<td>2+</td>
<td>White cloud without precipitate</td>
</tr>
<tr>
<td>3+</td>
<td>White cloud with fine precipitate</td>
</tr>
<tr>
<td>4+</td>
<td>Flocculent precipitate</td>
</tr>
</tbody>
</table>
Proteinuria: Quantification

- **Timed urine collection**
  - 4mg/m²/hr normal (<200mg/d)
  - >40mg/m²/hr nephrotic range

- **Spot urine protein/Cr ratio (mg/mg)**
  - <0.2 normal
  - >3 nephrotic range
Mechanism of Proteinuria

- **Glomerular** (increased filtration)
  - Mild to massive
  - Predominantly albumin
- **Tubular** (decreased reabsorption)
  - Mild
  - Predominantly small plasma proteins
Patterns of Proteinuria

- Transient
- Orthostatic (postural)
- Fixed
  - Non-nephrotic
  - Nephrotic (usually with edema)
Transient Proteinuria

- Self-limited proteinuria seen with an underlying illness/stress
  - Febrile illness
  - Dehydration
  - Exercise
  - Seizure
  - Urinary tract infection
Orthostatic Proteinuria

- Accounts for majority of proteinuria found during well child care visits
- Benign condition in adolescents
- Proteinuria < 1 gram/24 hours (prot/Cr < 1)
- Proteinuria only seen in urine produced in upright position; urine produced when supine is negative for protein
- Etiology unknown
Fixed Proteinuria

- Proteinuria present at all times of the day and night
- Indicates kidney disease
  - Focal segmental glomerulosclerosis (FSGS)
  - Membranous nephropathy
  - Reflux nephropathy
  - Renal dysplasia
  - Polycystic kidney disease
Initial Evaluation of Proteinuria

- Hx & PE
- U/A: rule out hematuria
- (BUN & Cr)
- Rule out proteinuria at rest
  - If first morning UA is:
    - Negative for protein---Orthostatic proteinuria
    - No further evaluation in most cases!
    - Positive for protein---Fixed proteinuria, refer to Nephrology
Further Evaluation of Proteinuria

- Laboratory
  - CBC, BUN, Cr, albumin
  - Complement, ANA
  - Hepatitis B & C titers
- Consider renal imaging
- Consider renal biopsy
Clinical Scenarios
Case 1

- 10 year old female seen for URI symptoms and fever. Urine dipstick showed 2+ for blood and no protein. Microscopy 5 RBC per high power field
  - Family history unremarkable
  - Physical examination
  - Repeat urines x2 negative for blood
Case 1

- Diagnosis
  - Transient hematuria otherwise healthy
- Follow up
  - Reassurance to the patient and family
Case 2

- 6 year boy with persistent microscopic hematuria. No proteinuria

**Family history:** Several males with deafness and renal failure

**Physical examination:** normal

**Laboratory evaluation:** Urinalysis 15-20 RBC
Negative for protein
Case 2

- Diagnosis: Alports syndrome
- Management: referral to Pediatric nephrology
- Long term follow up with risk to develop renal failure
Case 3

- 8 yrs old female with dysuria and frequency
- Urine 1+ blood, 5 RBC per high power field
- Urine culture negative
Case 3 Evaluation

• Physical examination: normal
• Family history: Mother has kidney stones
• Calcium creatinine ratio 0.4
Case 3

- Diagnosis
  - Hypercalciuria
Case 3

• Management
  – Refer to Pediatric Nephrologist
  – 24 hour urine collection
  – Increased fluid intake, Decreased sodium in diet
  – Consider thiazides if patient develops kidney stones
Case 4

• 10 year old with brown colored urine for 2 days
• UA showed 3+ blood, 2+ protein
Evaluation

- Oliguria, periorbital edema, weight gain
- BP 145/95
- Urine microscopy
- Cr 1.8, C3 15, ASO 500
Diagnosis

Post Streptococcal Glomerulonephritis
Management

• Immediate referral to a Pediatric Nephrology Service
  – Hypertension
  – Electrolytes abnormalities
  – Fluid overload
    • Diuretics
Case 5

- 16 year old athlete had 3 + protein in a routine physical examination
Evaluation

- Normal physical examination
- First morning urine
  - Trace protein
  - Urine prot/creat ratio 0.12
Diagnosis

Orthostatic proteinuria
Management

• Conservative follow up
• Obtain first morning urine for future urine evaluations
Case 6

- 15 year old female with 4+ protein detected during a routine physical examination
Evaluation

- Occasional headaches
- BP 136/90. No evidence of edema
- First morning urine
  - 4+ protein
  - Urine prot/creat ratio 3.0
  - Cr 1.9 mg/dL
Diagnosis

- Nephrotic range proteinuria
  - Rule out Focal Segmental Glomerulosclerosis
Management

- Referral to Pediatric Nephrologist
- Renal Biopsy
- Immunosuppressive therapy
- Additional therapy
  - ACE/ARB
  - Diuretics
Hematuria

- Positive dipstick, > 5 RBC/HPF
- Hematuria resolves in most cases
- Patients with hematuria and proteinuria or gross hematuria require further evaluation
**Proteinuria**

- ≥ 1+, Protein/Creatinine ratio > 0.2
- In most cases, proteinuria is transient or orthostatic
- Nephrotic range proteinuria warrant further evaluation to rule out glomerular disease
Two principles that might apply to your practice

• Repeat urine studies twice in pts with isolated microscopic hematuria prior to considering more extensive evaluation
• Consider to obtain a first morning urine for protein/creatinine ratio in children with isolated asymptomatic proteinuria
References

4. Lunn A, Forbes TA. Haematuria and Proteinuria in childhood. Paediatrics and child health (2012); 315-321
The Nutcracker Syndrome

Normal

Renal Vein Compression

SMA

Left renal vein

Ao

Ovarian / testicular vein

SMA

Left renal vein

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