When Your Patient Has Blood and/or Protein in Their Urine

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Disclosures
- none

Learning Objectives
- Safely and effectively care for children with hematuria and/or proteinuria
- Characterize the important differences between patients with nephritis and nephrosis
- Tailor the evaluation and management of patients with hematuria and/or proteinuria
- Understand if and when a patient with hematuria and/or proteinuria should be referred
1. Care for Children With Hematuria and/or Proteinuria

- The scenarios that we will tackle in the next 50 minutes
  √ A child comes to me with overt edema and urine that has a lot of protein
  √ A child comes to me with overt edema and blood as well as protein in the urine
  √ A child comes to me with red urine
  √ A child comes to me with brown urine

- I will probably call my nephrology consultant, but what do I do now

1. Care for Children With Hematuria and/or Proteinuria

- Normal urinary protein excretion
  ➔ < 4 mg/m²/hr (150-200 mg/24 hr)

- Nephrosis=nephrotic syndrome
  √ Nephrotic range proteinuria
    ➔ >40 mg/m²/hr (some use >50 mg/kg, some use >1.5-2.5g/24hr)
  √ Hypoalbuminemia
    ➔ Serum albumin < 3 g/dl
  √ Edema
  √ Hyperlipidemia

- Nephrotic range proteinuria ≠ nephrotic syndrome

1. Care for Children With Hematuria and/or Proteinuria

What does a urinary dipstick reading mean when it is:

- 300 mg/dl
- 300 mg/dl with a specific gravity of >1.030
- 300 mg/dl with a pH 8.0
- 300 mg/dl with a specific gravity of >1.030
- 300 mg/dl with a pH of 7 and a specific gravity of 1.010
1. Care for Children With Hematuria and/or Proteinuria

- Urinalysis in nephrotic syndrome
  - Aside from proteinuria is generally bland
- Children with primary (childhood) nephrotic syndrome generally present between the ages of 2-7 years

- Dipsticks measure albumin
- Microalbuminuria measures albumin
- Methodologies to quantitate urinary protein excretion
  - 24 hour urine collection for total protein
  - Random urinary protein: creatinine ratio
    - Random urinary protein in mg/dl divided by
    - Random urinary creatinine in mg/dl
    - Normal is < 0.20
1. Care for Children With Hematuria and/or Proteinuria

- Proteinuria most commonly occurs with a loss of the normal, anionic charge of the endothelial cells and the glomerular basement membrane (GBM)-minimal change disease
- There are other important causes of proteinuria
  - Circulating factors, e.g., in FSGS
  - Circulating immune factors, e.g., in lupus nephritis
  - Mutations in either podocyte or slit diaphragm proteins- e.g., congenital nephrotic syndrome, steroid resistant nephrotic syndrome
  - Overflow proteinuria, e.g., immunoglobulin light chains in multiple myeloma, (hemoglobin in intravascular hemolysis, myoglobin in rhabdomyolysis)

1. Care for Children With Hematuria and/or Proteinuria

- Glomerulonephritis ≠ microscopic hematuria and gross hematuria
- Glomerulonephritis = glomerular disease resulting from glomerular injury and inflammation
1. Care for Children With Hematuria and/or Proteinuria

- Causes of microscopic hematuria that are NOT examples of glomerulonephritis
  - Glomerulopathies
    - Alport syndrome
      - A defect in the structure of Type IV collagen
  - Tubulopathies
    - Renal hypercalciuria

- Causes of gross hematuria (red or brown urine) that are NOT examples of glomerulonephritis
  - Free hemoglobinuria
  - Myoglobinuria
  - Beeturia
    - Spin the urine, take a history
  - Upper or lower urinary tract bleeding
    - Wilm's tumor
    - Rhabdomyosarcoma of the bladder
    - Hemorrhagic cystitis secondary to cyclophosphamide use
      - Take a history + imaging

- What IS glomerulonephritis
  - Hematuria
  - Proteinuria
  - Edema
  - Hypertension
  - Active urinary sediment
    - RBCs
    - WBCs
    - Casts
      - Granular, red cell, white cell
1. Care for Children With Hematuria and/or Proteinuria
2. Differences Between Patients With Nephritis and Nephrosis

• It is not that simple

• Patients with biopsy proven nephrotic syndrome may have accompanying hematuria
  √ Up to 20%
  √ Typically low grade
  √ Microscopic, absent renal vein thrombosis

• Patients with glomerulonephritis have proteinuria and it is often nephrotic range with edema

Differences Between Patients With Nephritis and Nephrosis

• It is not that simple

• Hypertension in nephrotic syndrome
  √ Minimal change disease-10%
  √ Focal and segmental glomerulosclerosis-20%

• Hypertension in glomerulonephritis
  √ A defining characteristic-present in the vast majority of patients

Differences Between Patients With Nephritis and Nephrosis

• The active urinary sediment in glomerulonephritis often prompts an evaluation for urinary tract infection
  √ This is appropriate
    › In both conditions there can be visible or microscopic hematuria
    › In both conditions there can be evidence of inflammation
  √ Key differentiating factors include
    › Lack of fever
    › Lack of abdominal pain
    › Lack of urgency, dysuria, frequency, incontinence
    › Presence of hypertension
Differences Between Patients With Nephritis and Nephrosis

- Clinical manifestations of systemic disease
- Pediatric patients with primary nephrotic syndrome generally have few manifestations of systemic disease
  √ Edema
- Pediatric patients with glomerulonephritis may have
  √ Prodromal illness—PIGN, PSGN
  √ Skin manifestations—SLE, HSP, Kawasaki, endocarditis
  √ Joint manifestations—SLE
  √ Pulmonary manifestations—MPA, anti-GBM nephritis
  √ Ocular manifestations—SLE, TINU
  √ Hypertension-all

Differences Between Patients With Nephritis and Nephrosis

- Progressive renal disease
  √ Uncommon in nephrotic syndrome
    › When it occurs it generally is due to profound intravascular volume depletion or thrombosis
  √ Common with glomerulonephritis
- Infectious risk as a direct consequence of renal disease
  √ High in nephrotic patients
    › Urinary losses of C3b, opsonins (porperdin factor B), Ig
  √ Low in glomerulonephritis
    › Unless secondary to immunosuppressant
    › Increases in the face of nephrotic-range proteinuria

3. Patients With Hematuria and/or Proteinuria: E & M

- Age
- Clinical manifestations
  √ Abnormal vital signs
    › Hypertension, tachycardia, fever, weight gain or loss
  √ Edema
  √ Color of urine—information that is usually provided spontaneously
  √ Prodromal illness
  √ Rash
  √ Joint pain, swelling
  √ Cough, hemoptysis, sinusitis, bloody nose
  √ Shortness of breath
  √ Abdominal pain
  √ Headache
  √ Dysuria
  √ Visual change
3. Patients With Hematuria and/or Proteinuria: E & M

- Immunization status
- Family history

3. Patients With Hematuria and/or Proteinuria: E & M

- Laboratory Evaluation
  - Urine
    - UA-Macroscopic (dipstick)
    - UA-Microscopic
    - Random urinary protein: creatinine ratio
    - Urine culture
  - Blood
    - Serum creatinine (BMP)
    - \( \text{eGFR} = k \times \text{height in centimeters}/\text{S}_{\text{creat}} \text{ (mg/dl)} \)
    - Serum albumin

3. Patients With Hematuria and/or Proteinuria: E & M

- The “bland workup” suggestive of primary nephrotic syndrome:
  - Right age range
  - Bland UA, save proteinuria
  - A bland family history
  - A bland ROS
  - A bland exam, save edema
  - Normal renal function and labs, save hypoalbuminemia

- Administer
  - Prevnar 13 if behind schedule
  - Pneumococcal 23
  - TB skin test or Quantiferon Gold
  - Steroid treatment if comfortable
3. Patients With Hematuria and/or Proteinuria: E & M

- If the workup is not “bland”
- If the patient has evident renal dysfunction
- If the patient has hypertension
- If you need help
- If the family is anxious
- If

4. Referring a Patient With Hematuria and/or Proteinuria

- It is highly appropriate to pick up the phone and call your friendly, go-to pediatric nephrology consultant

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