Urinary Hematuria/Proteinuria

Learning Objectives

Discuss the pathophysiology of hematuria and proteinuria

Discuss the most common conditions/syndromes

Review evaluation after initial presentation

Complete an overview of treatment

Complete practice questions

Definitions

Hematuria

- Macroscopic
  - Visible color change to urine via naked eye
  - Urine appears pink/red, but may be tea colored (1ml of blood/L of urine)
  - Be aware that color change can occur from different foods or medications
- Microscopic
  - >5 RBCs on 2 or 3 different occasions
- Persistent hematuria defined as >4-6 weeks of >5 RBCs/HPF in absence of exercise, menses, or trauma

Proteinuria

- >100 mg/m^2/day or > 0.2 mg/mg Cr ([U p/c] >0.2) on single spot urine collection
- Nephrotic-range >1,000 mg/m^2/day or >50 mg/kg/day, or a Up/Uc >2 on single spot urine collection

Nephrotic syndrome

- Proteinuria, hypoalbuminemia, edema, hyperlipidemia

IgA nephropathy (Berger nephropathy)

Epi and Pathophysiology
- Most common chronic glomerular disease in children
- Familial clustering; M>F; East Asians and Caucasians
- Predominance of IgA mesangial glomerular deposits in the absence of systemic disease

Presentation
- Gross hematuria, usually within 1-2 days of URI or GI infection
- Often with nephrotic range proteinuria with microscopic hematuria, normal C3 levels
- Mild to moderate HTN, but no emergencies

Treatment
- BP control
- Management of significant proteinuria – ACE inhibitors, ARB; corticosteroids
- Renal transplant possible if needed

Prognosis
- No significant kidney damage in children

Alport Syndrome

Epi and Pathophysiology
- Hereditary nephritis; mutations in genes coding Type IV collagen
- Majority X-linked
- Glomeruli may develop mesangial proliferation, capillary wall thickening → progressive glomerular sclerosis

Presentation
- Asymptomatic microscopic hematuria
- Single or recurrent episodes of gross hematuria often occurring 1-2 days after URI
- Proteinuria is often seen in males; can progress to nephrotic range in 2nd decade
- Bilateral sensorineural hearing loss; may have ocular involvement (anterior lenticonus)

Treatment
- ACE inhibitors and ARB can slow progression and treat proteinuria

Prognosis
- Progressive renal dysfunction -> ESRD (typically before 30 yo)
- Risk factors for progression -> gross hematuria in childhood, nephrotic syndrome, & prominent GBM thickening

Membranoproliferative

Epi and Pathophysiology
- Older children/young adults; M=F; Caucasian
- Glomeruli w/ accentuated lobular pattern
- Type I (most common) immune complex mediated, Type II is not
- Secondary forms associated with subacute/chronic infections (HBV, HCV, syphilis, subacute bacterial endocarditis)

Presentation
- Equal proportions nephrotic syndrome, acute nephritic syndrome (hematuria, hypertension, and some level of renal dysfunction), or persistent asymptomatic microscopic hematuria and proteinuria
- Low C3 in most cases
- Dx made by renal biopsy

Treatment
- If secondary, treat underlying condition

Prognosis
- If crescents present, indicates poor prognosis
- Nephrotic syndrome and HTN at time of presentation results in more rapid progression

PIAGN (Post Infectious Acute GN)

Epi and Pathophysiology
- GAβHS infections are common in children; typically in throat or skin
- Glomeruli appear enlarged & relatively bloodless
- Molecular mimicry most likely mechanism via M protein

Presentation
- Most common in children 5-12yo; 1-2 wks after pharyngitis; 3-6 wks after pyoderma – elevated ASO antibody
- Ranges from microscopic hematuria w/ nl renal fxn to gross hematuria w/ ARF
- Pending degree of renal involvement, can develop gross hematuria, edema, HTN, & oliguria → sequelae related to each of these symptoms
- Low serum complements; renal biopsy may be required

Treatment
- Manage the acute effects of renal dysfunction and HTN

Prognosis
- Acute phase resolves in 6-8 wks; microscopic hematuria can persist for 1-2 yrs after initial presentation
- Recurrences are extremely rare

IgA vasculitis (aka Henoch-Schönlein purpura)

Epi and Pathophysiology

- Idiopathic systemic immune complex–mediated vasculitis associated with IgA deposition within small-vessel walls
- 90% of cases are in children w/ 50% preceded by URI
- Similar pathophysiology to IgA nephropathy

Presentation

- Purpuric rash and commonly accompanied by arthritis and abdominal pain
- Asymptomatic microscopic hematuria to severe, progressive glomerulonephritis
- Most who develop nephritis have urinary symptoms by 1 mo, & nearly all by 3-6 mo

Treatment

- Spontaneous resolution in majority of patients
- Consider immunosuppression although there is very little controlled data

Prognosis

- Acute nephritic or nephrotic syndrome at presentation has guarded renal prognosis, especially if they have concomitant necrosis or substantial crescentic changes on bx
- If progression to ESRD, transplant may be necessary

Lupus Nephritis

Epi and Pathophysiology

- SLE – most common cause of morbidity and mortality
- Deposition of circulating immune complexes as well as autoantibodies that result in complement stimulation
- Kidney Bx is the gold standard for dx

Presentation

- Normally present with extrarenal manifestations

Treatment

- Immunosuppression is the cornerstone
- ACE inhibitors and ARBs decrease proteinuria and progression to disease

Prognosis

- Proliferative lupus nephritis, poor renal function at presentation, or persistent nephrotic-range proteinuria exhibit the highest risk for progression to ESRD

UTI – General

Pathophysiology

- Bacteria invade and ascend the urinary tract
  - Typically colonic bacteria: *E Coli, Klebsiella, Proteus, Enterococcus, Pseudomonas*.
  - Immunodeficient children: *GBS, S. Aureus, Candida, Salmonella*
- Cystitis is when infection and inflammation is confined to bladder
- Pyelonephritis is when it ascends to the kidneys
- *E. Coli* attach to superficial cells of bladder lining → invade and multiply → cells shed in defense
  - Lower cells could be the source of recurrent UTIs
  - Toll like receptors activate the inflammatory response and attract WBC to the surface of the bladder

UTI – General Cont.

Evaluation

- Urinalysis and urine culture are the gold standard
- <2 yo can't hold their urine; there may not be enough time for GN bacteria to form nitrites
- Squamous cells are indicative of poor sample

Treatment

- Oral and IV antibiotics are equally effective, but IV is more appropriate in toxic appearing children who may have bacteremia +/- sepsis
- Empiric treatment based upon local susceptibility and patient history → tailor with patient susceptibilities

Next Steps

- No improvement with treatment in 12-24 hrs → renal US for anatomic abnormality or abscess
- VCUG in children <24 months w/ febrile UTI and abnormal US due to increased risk of VUR

UTI - Cont

< 24 mo

- Uncircumcised M <3 mo at increased risk
- Presents late in course due to nonspecific symptoms
  - Typically just with fever, emesis
- Catheterize for sample
- Can attempted a bagged sample, and if evidence of inflammation → cath

> 2 yo

- Consider bladder/ bowel withholding (constipation) or congenital anomalies
- Presents early in course as can localize symptoms
  - Dysuria, frequency, +/- suprapubic discomfort (cystitis)
  - CVA tenderness, abdominal pain, +/-fever can indicate it has ascended to pyelonephritis
- Children this age can submit clean catch urine samples

Trauma

Renal Trauma

- Cycling is the most common sporting activity involved in renal injures
- Children don't always manifest hematuria in low grade renal injuries
- Further imaging if hematuria, significant deceleration injury (fall or MVA), physical signs concerning for renal injury, i.e. flank ecchymosis, rib injury
- Evaluate with CT Abd/Pelvis → c/s Urology as surgical intervention may be necessary

Bladder Trauma

- Typically associated with multi-organ trauma, normally blunt trauma and associated pelvic fracture
- Absolute indication for imaging after blunt injury:
  - Gross hematuria w/ pelvic fx and inability to void
- Evaluate with cystogram via Urology consult

Orthostatic Proteinuria

Most common cause of persistent proteinuria in school age children

Normally asymptomatic and discovered on routine exam

- Hematuria, hypertension, hypoalbuminemia, edema, and renal dysfunction are absent

Assessed with 1st morning urine collection – absence of proteinuria on the 1st morning voiding for 3 consecutive days confirms diagnosis

Unknown etiology, but there is a correlation with increased BMI

Condition is completely benign

Practice #1

You are evaluating a 10 yo M of English ethnicity who is complaining of reddish urine for the past several days. He denies abdominal pain but reports having a fever intermittently for the past week. His mother thinks she remembers a similar episode, which resolved, when the boy was 5 years old. He appears well, and his BP is 100/64 mm Hg. His PE findings are normal. UA reveals numerous red blood cells without casts, and his serum complement value is normal. Of the following, which is the most likely diagnosis?

A. Henoch-Schonlein purpura.

B. Immunoglobulin A nephropathy.

C. Membranoproliferative glomerulonephritis.

D. Postinfectious acute glomerulonephritis.

E. Sickle cell trait.

Practice #2

A 5 yo F is brought to the ED because of suprapubic pain and fever for the past day. Her PE findings are normal except for obvious abdominal discomfort on palpation. A clean catch UA reveals large blood concentration, moderate LE, 5-10 WBC/HPF, and 50-100 RBC/HPF. Which of the following tests is most likely to reveal the diagnosis?

A. Abdominal radiograph.

B. Complete blood count.

C. Computed tomography scan of the abdomen.

D. Serum complement measurement.

E. Urine culture.

Practice #3

You have recently diagnosed a 3-year-old child as having nephrotic syndrome. The first-line treatment for this patient is:

A. Angiotensin-converting enzyme inhibitor.

B. Angiotensin II receptor blocker.

C. Antibiotic.

D. Renal dialysis.

E. Corticosteroids

Practice #4

A PH 6 mo F is brought to the ED with a 2-day history of fever. She has not had vomiting, diarrhea, cough, or nasal congestion. There has been no known contact with ill persons. She has continued to breastfeed and has not had a decrease in the number wet diapers. Her temperature is 102.4°F (39.1°C). She is mildly ill appearing but alert and interactive. Examination shows no focus of infection. A bag urine sample is collected and sent for UA. The UA shows a SG of 1.015, trace protein levels, 1+ LE result, +nitrite result, and 10-12 WBCs/HPF. Which of the following results from her UA has the highest specificity for having a UTI?

A. Leukocyte esterase.

B. Nitrite.

C. Protein level.

D. Specific gravity.

E. WBC microscopy

Practice #5

A 4 mo M presents with a 2-day history of fever. He is not vomiting and is alert and interactive. There is no focus of infection on examination. He is circumcised. A bladder cath performed. The UA shows a 2+ LE result, -nitrite, & 20-30 WBCs/HPC. He has no allergies and is started on oral Bactrim. The urine cx grows 50,000 CFUs of E. coli that is susceptible to Bactrim. After being sent home, his mother is called and states that he is acting well and has not had a fever in the past day. The mother is advised to have him complete the 10-day course of Bactrim. Which of the following is the most appropriate next step in management?

A. Dimercaptosuccinic acid renal scan.

B. No further testing or treatment indicated.

C. Renal and bladder ultrasonography.

D. Renal and bladder ultrasonography and voiding cystourethrogram.

E. Voiding cystourethrogram.

Practice #6

Which of the following is the most common cause of nephrotic syndrome in a school-aged child?

A. Finnish type.

B. Focal segmental glomerulosclerosis.

C. IgA nephropathy.

D. Membranous nephropathy.

E. Minimal change disease.

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Answer Key: 1. B, 2. E, 3. E, 4. B, 5. C, 6. E