Hematuria and Proteinuria

When to Refer?

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Learning Objectives

- Hematuria
  - Evaluation, differential diagnosis
- Proteinuria
  - Evaluation, differential diagnosis
- When to refer

Hematuria

- Age and sex of patient
- History
- Macroscopic vs Microscopic
- Glomerular vs Non-glomerular bleeding

http://library.med.utah.edu/WebPath/TUTORIAL/URINE/URIN070.html
Patients Age/Sex

- Usually age <35 yo is transient and of no clinical significance
- Age > 35 yo may be transient, higher risk of malignancy
- However, nephritic disease can occur at all ages
- Be careful with menstruation

History

1. Concurrent pyuria and dysuria
2. Upper respiratory infection
3. Family history of renal disease
4. Unilateral flank pain, which may radiate to the groin
5. Recent vigorous exercise or trauma
6. Bleeding disorder or bleeding from multiple sites due to excessive anticoagulant therapy
7. Hematuria in women that is most prominent during and shortly after menstruation
8. Medications that might cause nephritis
9. Sickle cell trait or disease
10. Travel or residence in certain areas
11. Sterile pyuria with hematuria

Macroscopic

- Bleeding that is visually seen and gives the urine a red to brown color
- Most times there is associated blood clots then lower urinary tract is source
Microscopic

- Very long differential diagnosis and it is very important to distinguish between glomerular and non-glomerular bleeding
- False positive with myoglobinuria

Glomerular vs Non-Glomerular Bleeding

- Glomerular
  - RBC cast, dysmorphic RBC (Acanthocytes), may have protein in urine (Nephritic disease), Coca-Cola urine
- Non-Glomerular
  - May have clots, little to no proteinuria, Pink to red urine

RBC cast
Dysmorphic RBCs
Glomerular bleeding without Proteinuria

- Persistent
- IgA nephropathy
- Thin Basement membrane disease
- Mesangiproliferative GN without IgA deposit
- Hereditary nephritis (Alport)
- Transient
- PIGN
- Exercise induced

Causes

- Upper system
  - Benign and Malignant renal masses
  - Glomerular
  - Anatomic distortion
  - Infection
  - Renal vein thrombosis
  - Papillary necrosis

- Lower system
  - Bladder cancer
  - Cystitis
  - Prostate cancer
  - BPH
  - Unilateral
  - Traumatic Foley catheter placement

- Nephrolithiasis
- TB
- Ureteral malignancy
- Stricture
- Hydronephrosis
- Malignant HTN
- AV malformation

Role of imaging

- Bleeding that is not caused by glomerular disease there is strong indication for Imaging evaluation
- CT Urography is Gold standard
- Ultrasound
- Cystoscopy
Proteinuria

- Usually about 150 mg/day of protein is excreted in one day in healthy adults
- Sign of increased glomerular permeability and illness of filtration membrane
- Albumin usually not filtered due to size and negative charge

Proteinuria

- Important to quantify the protein to decide if nephrotic range proteinuria (>3.5g/day)
- >300 mg/day is considered macroalbuminuria

Types
- Isolated - Transient
- Overflow
- Post-renal
- Glomerular

Evaluation

- Dipstick - detects albumin
- SSA - used to detect non-albumin proteins
- 24 hour urine creatinine clearance vs Spot urine protein/creatinine ratio
- Serology workup
**Isolated - Transient**
- Younger age
- After illness or exercise
- Repeat testing is negative
- Usually protein is <1 g/day
- No other systemic signs or symptoms of renal disease
- No other activity noted on urine dipstick

**Overflow proteinuria**
- Increase production of low molecular weight proteins that get filtered and excreted. This can be related to nephrotic range disease
- Myeloma, Rhabdomyolysis, Intravascular hemolysis

**Post renal**
- Usually < 1g/day, associated with bleeding and possible clots
- Urinary tract infection
- Bladder tumor
- Nephrolithiasis
Glomerular

- Due to changes in the filtration membrane that causes increase in permeability to proteins not otherwise filtered and then excreted. There are a multitude of changes that can occur to the basement membrane and associated structure.
- Usually associated with active urine (hematuria)
- Can be associated of renal dysfunction or not

Nephritic vs Nephrotic

- Any range or protein, can have nephrotic range proteinuria in nephritic diseases
- Hematuria with associated RBC changes
- > 3.5 g/day protein
- Nephrotic syndrome
- Can have bland sediment
Nephritic Diseases with commonly normal renal function

- 15 to 40 years old
  - IgA nephropathy
  - Thin basement membrane disease
  - Lupus nephritis
  - Hereditary nephritis
  - Mesangial proliferative glomerulonephritis

- > 40 years old
  - IgA nephropathy

Nephritic Diseases with commonly decreased renal function

- 15 to 40 years old
  - PIGN
  - RPGN
  - Lupus nephritis
  - Fibrillary GN
  - Membranoproliferative glomerulonephritis

- > 40 years old
  - RPGN
  - Vasculitis
  - IgA nephropathy
  - Fibrillary GN
  - PIGN

Nephrotic disease

- 15 to 40 years old
  - FSGS
  - Minimal change disease
  - Membranous nephropathy
  - Diabetic nephropathy
  - Pre-eclampsia
  - Late stage of PIGN

- > 40 years old
  - FSGS
  - Membranous nephropathy
  - Diabetic nephropathy
  - Minimal change disease
  - IgA nephropathy
  - Primary amyloidosis
  - Benign nephrosclerosis
  - Late stage of PIGN
Effects of Race

• African American
  • FSGS, about 60%
  • Membranous nephropathy
  • Minimal change disease
• Caucasian
  • Membranous, about 40%
  • FSGS
  • Minimal change disease
  • IgA nephropathy

Serologic testing

• Nephritic disease and presentation
  • ANA, dsDNA
  • Complements
  • SPEP with immunofixation
  • Hepatitis panel, cryoglobulins
  • HIV
• Nephrotic range and presentation
  • ANA, dsDNA
  • Complements
  • ASO titers
  • Anti-GBM
  • ANCA
  • Hepatitis panel, cryoglobulins
  • HIV
  • Blood cultures

When to Refer?

• Any patient with Presentation of Nephrotic syndrome
• Patient with Isolated hematuria or proteinuria with abnormal renal function
• Questions of renal biopsy
• Hematuria and proteinuria with new onset hypertension
• Urologic evaluation for gross hematuria and even microscopic hematuria considered to be non-glomerular
• Family history of Renal disease
• High suspicion for glomerular disease without abnormal renal function
References

- RBC cast, http://library.med.utah.edu/WebPath/TUTORIAL/URINE/URIN070.html
- Granular cast, www.udel.edu