Tubulointerstitial Disease

Mark D. Baldwin D.O. FACOI
ACOI Board Review Course 2016
Disclosures

• None, just working for The Man
Features of Tubulointerstitial Disease

1. Proteinuria - usually less than 1 Gm/da
2. Anemia - due to low level of Erythropoietin
3. Acidosis - RTA’s are common
4. Hypertension - common
5. Urinalysis - WBC’s and WBC casts seen
6. Electrolyte Abnormalities - Na and K

Many of the above features are seen at relatively mild elevations of Serum Creatinine
Features of Glomerular Disease

1. Proteinuria->3 Gm/da
2. Anemia-uncommon until late
3. Acidosis-uncommon until late
4. Hypertension-may occur at any time
5. Urinalysis-may see Oval Fat Bodies
6. Electrolytes-May see low Na

Unlike Tubulointerstitial Disease, many of these feature do not occur until late in the course of the underlying disease.
Types of Tubulointerstitial Disease

1. Acute Interstitial Nephritis
2. Chronic Interstitial Nephritis
3. Acute Tubular Necrosis
4. Renal Tubular Acidosis
5. Multiple Myeloma
Acute Interstitial Nephritis (AIN)

Seen as an allergic type reaction to a variety of medications, autoimmune process or infections.

An acute infiltration of the Renal Intersitium with Eosinophils, Plasma Cells, T-Lymphocytes, and Monocytes
Causes of AIN

1. Medication-Most common
   - Methicillin, Penicillins, Cephalosporins, Sulfas, NSIADs, COX-2 Inhibitors, Rifampin, can be seen with almost ANY medication

2. Infections-CMV, Legionella, Leptospirosis, Streptococcus

3. Autoimmune-Sarcoid
Clinical Features of AIN

- Rash
- Fever
- Azotemia
- Malaise
- Arthralgias
- Usually seen 7-10 days after starting a new medication
Laboratory Findings in AIN

- Eosinophilia
- Eosinophils in the urine - The Hallmark - remember Hansel’s Stain
- Elevated Sed rate
- Compliments may be low
- WBCs w/ Casts and RBCs may be seen
- Protienuria less than 1 Gm/da
- Azotemia
Treatment of AIN

• STOP THE DRUG!!!!!!!!
  - This usually brings about an improvement in renal function.
  - In severe cases, a trial of Steroids may be of benefit, but no large trials have confirmed this
Chronic Interstitial Nephritis (CIN)

- A chronic condition involving fibrosis of the interstitium and tubular destruction.
- The final common pathway of most chronic renal diseases
Causes of CIN

1. Chronic Obstructive Uropathy-Ureteral Reflux
2. Chronic Pyelonephritis
3. Chronic Renal Lithiasis
4. Medications-NSIADs, Lithium, aristolochic acid
5. Post Acute Tubular Necrosis
6. Autoimmune-Sjogren’s Syndrome
7. Radiation
Aristolochic acid

• Acute exposure: Chinese herb nephropathy-AKI, rapid decline in renal function
• Chronic exposure: Balkan endemic nephropathy-CIN/CKD slow decline over years from chronic exposure

Clinical Features of CIN

- Usually Asymptomatic
- STERILE PYURIA-The Hallmark of CIN
- Anemia
- Acidosis-Renal Tubular Acidosis
- Minimal Proteinuria
- Hypertension
Treatment of CIN

- Do NOT give antibiotics for pyuria unless there is bacteria present—this is a chronic inflammatory condition, NOT an infection
- BP control—The MOST important treatment
- ACE-I or ARBs—The drugs of choice
- Anemia control
- Acidosis control
- Phosphorus control
Acute Tubular Necrosis (ATN)

- Necrosis of the tubules due to microthrombi. This is frequently due to prolonged hypotension and augmentation of the immune system from sepsis.
Causes of ATN

1. Sepsis
2. Drugs—especially Aminoglycosides, NSAIDs,
3. Post-Operative-Post CABG, AAA Repair
4. Pancreatitis
5. Athroemboli
6. Glomerular Disease/Autoimmune Disease
7. Prolonged and Untreated Pre-renal Conditions
Clinical Features of ATN

• May be Oliguric or Non-Oliguric
• Azotemia
• Elevations in Serum Creatinine may NOT reflect the degree renal dysfunction
• Acidosis
• Hyperkalemia
Urinalysis in ATN

Sediment in ATN  Urine sediment showing multiple, muddy brown granular casts. These findings are highly suggestive of acute tubular necrosis in a patient with acute renal failure. Courtesy of Harvard Medical School.
Treatment of ATN

• Treat the underlying condition-Sepsis, Volume depletion, Hypotension
• Dopamine does NOT work
• Atrial Naturetic Peptide does NOT work
• High does of Loop Diuretics have limited utility in converting Oliguric to Non-Oliguric Renal Failure
• Dialysis with a Biocompatible membrane may increase survival
Renal Tubular Acidosis (RTA)

• The most common RTA is a Distal Type-IV RTA
• Distal Type-IV RTA is frequently seen with Diabetes and many types of Chronic Renal Failure
• Distal Type-I RTA is associated with Chronic Urinary Tract Obstruction
• Proximal Type-II RTA is associated with Fanconi’s Syndrome
## Differentiation of RTAs

<table>
<thead>
<tr>
<th>Characteristics of the Different Types of Renal Tubular Acidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type 1 RTA</strong></td>
</tr>
<tr>
<td><strong>Primary defect</strong></td>
</tr>
<tr>
<td><strong>Plasma bicarbonate</strong></td>
</tr>
<tr>
<td><strong>Urine pH</strong></td>
</tr>
<tr>
<td><strong>Plasma potassium</strong></td>
</tr>
</tbody>
</table>
Multiple Myeloma

• Infiltration of abnormal Plasma Cells and a common cause of renal failure of multiple etiologies.
• There are Monoclonal Proteins of the Globulin type in a variety of tissues.
Multiple Myeloma-Clinical Features

- Chronic Back Pain
- Males >50 y.o.
- African-Americans are more commonly affected
- Hepatosplenomegaly
- Cardiomyopathy due to Amyloid deposition
Acute Renal Failure due to Multiple Myeloma

- Plasma Cell infiltration of the kidney
- Secondary Amyloidosis
- Hypercalcemia
- Hyperuricemia
- Pyelonephritis—due to impaired immune response
- Light Chain Deposition
- Deposition of Bence-Jones Protein Casts in the Tubules
- Renal Tubular Acidosis—Fanconi’s Syndrome
- Acute Renal Failure from Contrast Infusion
Multiple Myeloma Laboratory Findings

- Elevated BUN and Creatinine
- Hypercalcemia
- Hyperuricemia
- Normocytic Normochromic Anemia
- Serum Protein Electrophoresis/ Urine Protein Electrophoresis positive for elevations in the Gamma fraction-Bence-Jones Protein
- Low Anion Gap
- Urinalysis may show NO Protein, unless Sulfa salicylic Acid test is done, which will be positive.
Congo red stain in amyloidosis  Congo red stain viewed under polarized light of a renal biopsy from a patient with renal amyloidosis. Green birefringence (white arrows) of interstitial amyloid deposits can be seen. Courtesy of Helmut Rennke, MD.
Glomerular amyloidosis  Light micrograph of glomerular amyloidosis shows nodular, amorphous material (arrows) extending from the mesangium into the capillary loops and narrowing or closing the capillary lumens. The nodules are more amorphous than those seen...
Renal amyloidosis  Electron micrograph showing expansion of the mesangium by amyloid fibrils measuring between 8 and 11 nanometers in diameter. The fibrillar
Malignancy Related Hypercalcemic Renal Failure

- Prostate
- Renal Cell
- Breast
- Lymphoma/Leukemia
- Lung
- Myeloma
- Thyroid
Mechanism of Hypercalcemia of Malignancy

- Direct bone invasion/destruction
- Secretion of PTH-like factors
- Lymphokines-Osteoclast Activating Factor, etc.
- Prostaglanins
- Vitamin-D like substances
Treatment of Hypercalcemia of Malignancy

- Hydration with Normal Saline (decreases Ca$^{++}$ Reabsorption)
- Calcitonin
- Zoledronic acid
- Biphosphonates
- Loop diuretics, only if there is a history of CHF-do not give thiazides as they promote calcium reabsorption
Tubulointerstitial Diseases - Conclusions

- Often overlooked as a cause of Chronic Renal Disease
- Look for Drug causes or Sepsis as a cause of Acute Renal Failure (i.e. AIN or ATN)
- Tubulointerstitial Diseases frequently have electrolyte abnormalities, acid-base disorders, and anemia as a common feature.