Cysts and Stones

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OBJECTIVES

• Learn how to manage patients with single and multiple cystic conditions of the kidney (diet / lifestyle, blood pressure, imaging, follow-up, drug therapy)

• Learn what types of kidney stones can form and prevalence of each

• Learn how to prescribe effective preventive therapy for different stone types
CYST CLASSIFICATION – DISTRIBUTION / SIZE / NUMBER

- Simple cysts
- Complex cysts
- PCKD
  - Autosomal recessive
  - Autosomal dominant
- Acquired renal cystic disease
- Medullary Sponge Kidney
- Medullary Cystic disease (‘Autosomal Dominant Interstitial Kidney Disease’)
- Other
  - von Hippel Lindau
  - Tuberous sclerosis
SIMPLE CYSTS

- **Incidence:**
  - Varies by population, age (highest in older males)
  - < 1% below age 30; 30% above 70
    - Bilateral in 9% > 70 years

- **Histopathology:**
  - Single epithelial cell layer, clear or straw coloured fluid within resembling plasma

- **Significance:**
  - None
  - Some case series association with hyperfiltration, mild renal impairment, hypertension, albuminuria
  - Complications rare: Renin-induced hypertension, infection, bleeding (gross hematuria +/- flank pain), obstruction

- No follow-up imaging necessary
COMPLEX CYSTS

Bosniak Renal Cyst Classification System

I - **Simple cyst** with a hairline-thin wall.
- No septa, calcifications, or solid components.
- Water attenuation, no enhancement.

II - **Septa:** few hairline-thin in which not measurable enhancement may be appreciated.
- **Calcification:** fine or a short segment of slightly thickened may be present in the wall or septa.
- **High-attenuation:** uniform in lesions (< 3cm) that are sharply marginated and do not enhance.

IIIF - **Septa:** multiple hairline-thin in which not measurable enhancement of septum or wall is appreciated.
- **Minimal thickening of wall or septa,** which may contain calcification, that may be thick and nodular, but no measurable contrast enhancement.
- No enhancing soft-tissue components.
- **Intrarenal:** totally intrarenal nonenhancing high-attenuating renal lesions; these lesions are generally well marginated.

III - **Measurable enhancement**
Cystic mass with thickened irregular or smooth walls or septa in which measurable enhancement is present

IV - **Enhancing soft-tissue components**
Clearly malignant cystic masses that can have all of the criteria of category III but also contain distinct enhancing soft-tissue components independent of the wall or septa

Bosniak classification of renal cysts

1 - ~0% are malignant
2 - ~0% are malignant
2F - ~5% are malignant
3 - ~50% are malignant
4 - ~100% are malignant

MRI Observe
Most offered surgery
Resect
Cyst criteria for diagnosis if family history **known**:
- 15-39: 3+ cysts unilateral or bilateral
- 40-59: 2+ cysts per kidney
- 60+: 4+ cysts per kidney

If family history **unknown**: no definite number for unequivocal diagnosis, but 10+ per kidney ‘strongly suspect’
PCKD - FEATURES

- Incidence: 1/400
- Renal +/- liver (about 50%) +/- pancreatic cysts
- Cyst complications
  - Bleeding (gross hematuria +/- flank pain), infection, renin-induced hypertension, obstruction, stones
- Mass effects
  - Fullness/bloating, early satiety; transplant considerations
- Hypertension
  - Renin-induced
  - Renal parenchymal
- Extra-renal manifestations:
  - Intracranial aneurysm (incidence 5% < 30 yrs, 20% >60 yrs)
  - Inguinal hernia
  - Cardiac valvular: Mitral valve prolapse >> AR
  - AAA – possibly higher risk
  - Renal Cell Carcinoma- possibly higher risk
- Renal Failure

Chapman AB et al NEJM 1992;327(13):916
PCKD – RENAL FAILURE

• Incidence ESRD 6 PMP; ?majority with PCKD
• Comprise 5-10% of prevalent HD patients in Canada
• Once renal function drops, rate -5 mL/min/year

Higher risk of ESRD if:
  – Pt factors: Genetics (PCKD1 >> PCKD2), male, low birth weight
  – Clinical factors – HTN:
    • GFR > 60, age < 50 aim BP 95/60 – 110/70, choose ACE inhibitor (Schrier R et al, NEJM Nov 2014)
    • GFR 25-60, aim BP 110/70 – 130/80, choose ACE inhibitor (Torres V et al, NEJM Nov 2014)
  – Imaging factors: Nephromegaly
  – Laboratory factors: albuminuria, hyperuricemia, increased urine sodium excretion, increased plasma copeptin level (surrogate for vasopressin)

• Treatment
  – Diet / lifestyle: ? Protein restriction; low Na; fluids > 3L/day, avoid caffeine
  – BP control: ACE inhibitors 1st line; BP target
  – ? mTOR inhibitors, somatostatin, vasopressin receptor antagonists
  – Rarely nephrectomy required

Torres et al. KI 2009;76(2):149
MEDULLARY SPONGE KIDNEY
NEPHROLITHIASIS – A PAINFUL PROBLEM!

• Affects approx 10% of adults
  – Slight male predominance
• Incidence varies geographically
• Approx 50% have one or more recurrence at 10 years
  – Detailed evaluation generally performed for recurrent stone formers
• Can cause significant morbidity
• Rare cause of end-stage kidney failure
PATHOPHYSIOLOGY

- Supersaturation
- Stasis
- Structural abnormality
TYPES OF STONES

• Calcium
  – Calcium oxalate
  – Calcium phosphate

• Uric acid

• Struvite ‘staghorn’
  – Magnesium ammonium phosphate

• Drug-related
  – Creation of metabolic environment favouring stone formation
  – Crystallization of drug itself when supersaturated in urine

• Rare Stone Disorders:
  – APRT Deficiency, Dent Disease, Cystinuria, Primary hyperoxaluria
HOW CAN I TELL WHAT TYPE OF STONE MY PATIENT HAS?

• History
  – Age, comorbidities, medications, family history, occupation / environment, prior kidney or GI surgery

• Physical
  – Urinalysis
    • presence of crystals

• Lab testing
  – Serum: creatinine, bicarbonate, calcium, PTH, glucose/HgA1c, uric acid
  – Urine (24 hr): calcium, uric acid, oxalate, sodium, citrate
  – Urine pH: uric acid crystals form in acidic urine, calcium phosphate crystals form in alkaline urine, urine is alkaline with struvite stones

• Imaging:
  – Radiolucent (uric acid stones) vs opaque (most other stones)
  – ? Nephrocalcinosis

• Stone Analysis
SELECTED MEDICATIONS

• Change urine pH or composition:
  – Vitamin C
  – Vitamin D
  – Calcium (ie. CaCO3)
  – Diuretics: carbonic anhydrase inhibitors, loop diuretics, other (common OTC herbal remedies)

• Drug precipitates:
  – Antimicrobials: acyclovir, amoxicillin, ampicillin, ceftriaxone, ciprofloxacin, sulfamethoxazole
    • Protease inhibitors: indinavir
  – Guaifenesin
  – Triamterene
  – Methotrexate
CALCIUM OXALATE

• Most common (80-85%)
• Presumed diagnosis unless atypical features
• Higher incidence:
  – Post (partial) bowel resection
  – High dose Vitamin C
  – Family history
• Hypercalciuria not necessary
• Hyperoxaluria not necessary
URIC ACID STONES

• Reasonably common
• Risk factors:
  – Gout
  – Chronic diarrhea
  – Obesity
  – Metabolic syndrome / DM
  – Malignancy
• Not seen on plain X-ray
• Hyperuricosuria common
STRUVITE STONES

- Magnesium ammonium phosphate + calcium carbonate
- Formed in infected upper urinary tract:
  - Females, neurogenic bladder, urinary diversion
  - Can grow quickly so often present late
    - UTI symptoms, flank pain, gross hematuria
    - pH > 7
- Antibiotics and surgical removal required
CYSTINE STONES

• Cystinuria 1/7000 live births
  – Reduced renal absorption cystine
    (plus ornithine, lysine, arginine)
• +/- Family history
• Often presents in childhood
• Can form staghorn calculi
• Less radiopaque than calcium stones
WHAT PROVEN TREATMENTS ARE THERE?

• Increasing fluid intake
• Thiazide diuretic (reduces urine calcium)
• Allopurinol (reduces urine uric acid)
• Citrate (raises urine citrate / raises urine pH)
OTHER TREATMENTS

• Diet
• Oral calcium (oxalate binding)
• Disease-specific
  – ie. captopril or penicillamine for cystinuria
• Analgesia
• Alpha blockers (relax smooth muscle tone of ureters to help stone pass / relieve colic)
• Lithotripsy
• Surgical
  – Endoscopic
  – Percutaneous
  – Open

• MEDICAL THERAPY DOES NOT DISSOLVE STONES
## DIET - SUMMARY

<table>
<thead>
<tr>
<th>Diet Parameter</th>
<th>Goal (daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid</td>
<td>Enough for urine output &gt; 2.5 L</td>
</tr>
<tr>
<td>Sodium</td>
<td>&lt; 2000 mg, possibly lower</td>
</tr>
<tr>
<td>Calcium</td>
<td>800-1200 mg (NOT restricted!)</td>
</tr>
<tr>
<td>Oxalate</td>
<td>40-50 mg</td>
</tr>
<tr>
<td>Citrate</td>
<td>? Specific target</td>
</tr>
<tr>
<td>Protein</td>
<td>&lt; 6 oz</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>&lt; 1000 mg</td>
</tr>
</tbody>
</table>
Case 1 - Patient AS

• 34 F 4 year history of recurrent nephrolithiasis, onset with renal colic at age 26 when pregnant
  – Every 6 months, then monthly severe colic
  – Stone obstruction twice (9mm, 1.2cm); bilateral ureteric obstruction with urosepsis
  – Ureteric stents placed on multiple occasions

• No family history

• CT-KUB consistent with medullary sponge kidneys; multiple bilateral calculi up to 3 mm in size
• Normal serum biochemistry
• Stone analysis: calcium oxalate
• Urinalysis: pH 6.5, RBC 40-100/hpf
• 24 hr urine:
  – Volume 3.7 L
  – Calcium 5.2 (2.2-6.5 mmol/d)
  – Oxalate 344 (40-340 umol/d)
  – Citrate 4.44 (0.7-4.9 mmol/d)
  – Sodium 207 (40-220 mmol/d)
  – Uric acid 3.4 (1-3.8 mmol/d)
AS – follow-up 3 years later...

• Therapy:
  – HCTZ 12.5 mg po BID
  – Potassium citrate 50 mEq po TID
  – Prazosin 1 mg po OD
  – Cipro 500 mg po OD
  – Endoscopic stone extraction & laser lithotripsy x2

• Urine pH 8.5

• Urine volume still high, biochemistry still normal

• Right hydronephrosis with multiple impacted ureteric stones – currently awaiting surgery
Case 2 – Patient WM

- 32 F of Chinese descent, presented with creatinine 106 on routine lab testing
  - U/S: nephrocalcinosis, bilateral hydronephrosis, cortical thinning
  - CT: staghorn calculi bilaterally, multiple intrarenal stones
- Extensive surgery / subsequent surgeries
- Pregnancy with nephrolithiasis complicating
- Urine amino acid electrophoresis: urine cystine excretion 4x normal
- Increased fluids, diet control, and K citrate
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