



Kidney Stones

Diagnosis and Management of Acute and Chronic Nephrolithiasis

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5/25/04

Swedish Family Medicine Didactics

Learning objectives

- Discuss the diagnosis and acute management of suspected nephrolithiasis
- Discuss how to approach established nephrolithiasis

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2

- 1. Discuss the diagnosis and acute management of suspected nephrolithiasis:** In doing so, we will review the epidemiology, etiology, risk factors, and clinical manifestations of kidney stones. I will also discuss diagnostic tools and weigh their sensitivity and specificity as well as costs in determining what test to order. In terms of management, we will be looking out both surgical and medical management.
- 2. Discuss how to approach established nephrolithiasis:** In particular, we will review when to order metabolic tests and how to do this effectively.

Epidemiology

- In the United States, rates of nephrolithiasis vary regionally.
- Reported annual incidence: 100 per 100,000 men and 36 per 100,000 women.
- 12% of men and 5% of women will develop a symptomatic stone by age 70.
- Rates of nephrolithiasis increases with age, is higher in men compared to women and in whites compared to blacks.

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3

These statistics stem from a population based study in Rochester, Minnesota.

In terms of regional variation, on study of over 4,00 men between the ages of 45 and 70, the risk of having a history of kidney stones was 13% lower in the mid Atlantic area and 31 percent lower in the northwestern states as compared to southwestern U.S. Why? Maybe d/t temperature, sunlight (i.e. Vit D activation as it relates to Ca regulation?) and regional beverage choices and habits.

Etiology

- 80% of patients with nephrolithiasis form calcium stones, most of which are composed primarily of **calcium oxalate** or, less often, calcium phosphate.
- The other main types include uric acid, struvite (magnesium ammonium phosphate), and cystine stones.

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4

Stone formation occurs when normally soluble material (e.g., calcium) supersaturates the urine and begins the process of crystal formation.

Risk factors

- The risk of nephrolithiasis is affected by certain diseases and patient habits.
- For calcium stones, these include hypercalciuria, hyperuricosuria, *hypocitraturia*, and dietary characteristics such as high protein and low water intake.

Risk factors (cont.)

- Prior history of calcium stones (greatest risk factor).
- Positive family history.
- HTN (twofold increased risk)
- Medications: triamterene, indinavir, and sulfadiazine.
- Marathon runners
- High ingestion of soft drinks, some juices
- Gout
- H/O UTIs due to urease producing organisms such as Proteus or Klebsiella

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6

Prior history of calcium stones (greatest risk factor): One report of patients with a first stone estimated that the likelihood of forming a second stone was approximated 15% at one year, 35-40 percent at 5 years and 50% at 10 years, with men being more likely to recur than women.

High ingestion of soft drinks, some juices: Ingestion of more than one liter per week of soft drinks acidified with phosphoric acid may modestly increase the risk of stone disease (d/t the small acid load which increases the urinary excretion of calcium and uric acid and reduces that of citrate (citrate inhibits stone formation by forming a poorly dissociable but soluble complex with calcium)).

Clinical Manifestations

- Symptoms usually produced when stones pass from the renal pelvis to the ureter.
- Pain-varies from mild to severe, typically waxes and wanes, and lasts 20 to 60 minutes.
- Pain is related to movement of the stone in the ureter and associated uretral spasm.
- Site of obstruction determines the location. (i.e Flank vs. abd vs pelvic etc)

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7

Site of obstruction determines the location. (i.e Flank vs. abd vs. pelvic etc): Upper uretral or renal pelvic obstruction leads to flank pain or tenderness, whereas lower uretral obstruction causes pain that may radiate to the ipsilateral testicle or labia. The location of the pain may change as the stone migrates.

Clinical manifestations (cont)

- Hematuria: gross or microscopic. Single most discriminate predictor of a kidney stone in patients presently with unilateral flank pain.
- Other symptoms: Nausea, vomiting, dysuria, and urgency.
- May lead to persistent renal obstruction and sepsis.

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8

Hematuria: gross or microscopic. Single most discriminate predictor of a kidney stone in patients presently with unilateral flank pain. On the other hand, the absence of hematuria in the setting of acute flank pain does not exclude the presence of nephrolithiasis. Hematuria is not detected in approximately 10 to 30 percent of patients with documented nephrolithiasis.

Differential Diagnosis

- Renal carcinoma (may give hematuria but likely not pain).
- Ectopic pregnancy
- Aortic aneurysm
- Acute intestinal obstruction
- Malingerers (with self induced hematuria, yikes!)

Diagnosis

- Gold standard: Non contrast enhanced helical CT.
- One study of 417 patients presenting with acute flank pain suggested that CT was 95, 98, and 97 percent sensitive, specific and accurate.
- CT can also detect secondary signs of urinary tract obstruction.

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10

Standard CT cuts are generally 8 mm but 3 to 5 mm cuts are optimal for the detection of stones.

Diagnosis

- Other options:
 - ◆ KUB
 - ◆ IVP
 - ◆ Ultrasound: Procedure of choice in patients who should avoid radiation (I.e pregnant).

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11

1. **KUB: will identify radiopaque stones such as calcium containing, struvite and cystine stones but will miss radiolucent stones and will not detect obstruction.**
2. **IVP has high sensitivity and specificity. However, it takes longer than CT, it can produce reactions and costs \$400 vs \$600 dollars for a CT, (not an overwhelming savings...)**
3. **U.S can detect radiolucent stones but may miss small stones and uretral stones.**
4. **The combination of U/S and KUB provides somewhat comparable results to that observed with non contrast helical CT.**

Acute therapy

- Many patients with acute renal colic can be managed conservatively with pain medication and hydration until the stone passes.
- Likelihood that uretral stones will pass depends on size and location.
- Smaller (***less than 5mm***) and more distal stones are likely to pass.
- Average time to pass stone is anywhere from 8-22 days depending on size of stone

Acute therapy

- NSAIDs and narcotics. Prospective studies suggest NSAIDs are at least as effective as opiates.
- Caution with NSAIDs in pts with obstruction or preexisting renal disease.
- Hospitalization is required for those who cannot tolerate oral intake or have very severe pain.
- Urine should be strained for further stone analysis.

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13

NSAIDs and narcotics. Prospective studies suggest NSAIDs are at least as effective as opiates. This was illustrated by a double blind study in which 51 patients with renal colic were randomly assigned to receive indomethacin by rectal suppository or IV morphine. No significant difference except opiates had quicker onset.

Urological consultation

- Urgent referral for urosepsis or ARF
- Outpatient referral indicated for stones >5mm, or failure to pass stone within 2 to 4 weeks.
- Current surgical options:
 - ◆ Extracorporeal shock wave lithotripsy (ESWL)
 - ◆ Endoscopic lithotripsy with ultrasonic, electrohydraulic or laser probes
 - ◆ Open pyelolithotomy
 - ◆ Percutaneous nephrostomy.

ESWL

- Treatment of choice in 85% of patients.
- Particularly good for stones in the renal pelvis and upper ureter.
- Employs high energy shock waves which are transmitted through water and focused on stone via fluroscopy.
- Can cause renal injury, not ideal method for large or very hard stones, or in patients with odd anatomy.

ESWL-cost analysis

- In prelithotripsy era, each stone event was estimated to cost \$2000 (more hospitalizations, longer stays, bigger surgeries). Annual costs=\$315 million for white males.
- ESWL is cheaper in case by case basis but the overall costs associated with stone diseases has increased.

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16

ESWL is cheaper in case by case basis but the overall costs associated with stone diseases has increased. An economic analysis of the impact of ESWL carried out in Quebec between 1984 and 1992 confirmed these findings. A 59 percent increase in patients treated with renal stones was noted over the study period. Despite shortened lengths of stay and lower costs associated with the use of ESWL compared with surgical, percutaneous and retrograde procedure, a much higher intervention rate was noted and a marked increase in the overall cost associated with stone disease was observed. Likely, reflects a greater willingness of urologists to intervene.

ESWL-complications

- Most common=persistent stone fragments.
- May reversibly damage all parenchymal components.
- May raise blood pressure.
- However, all observations suggesting such complications have limitations (i.e. only studied acute effects, failed to consider the “bilateral” nature of kidney function etc.)

Other surgical techniques

- Open stone surgery: done rarely (<1%) for complex stones
- Percutaneous nephrostolithotomy
 - ◆ Reserved for extremely large or complex calculi or in pts with some anatomic abnormalities
 - ◆ Good for cystine stones which are fairly resistant to ESWL.

Rigid and Flexible ureterorenoscopy

- Treatment of choice for the majority of middle and distal uretral stones.
- Procedure: Ureter is dilated, scope is passed throughout ureter and renal pelvis. Small stones are extracted intact with baskets.
- “Intracorporeal lithotripsy” (with pneumatic pressure, or laser, or ultrasound) can be used to break up larger stones.

Evaluation and subsequent treatment

- Retrieve stones and send for analysis.
- Subsequent therapy depends on stone and biochemical abnormalities that are present.
- **ALL** patients should increase fluid intake to > 2L/day, including drinking at night

What to do after the first stone?

- There remains disagreement as to whether a complete metabolic evaluation is indicated in all patients.
- Three approaches to consider: Limited evaluation, complete evaluation and targeted approach.
- Most would agree that a complete metabolic evaluation is indicated in patients with multiple stones or in those with “active” ongoing stone disease.

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21

Active stone disease is defined as recurrent stone, enlargement of old stones or the passage of gravel.

Limited evaluation

- Includes: blood chemistries, including multiple measurements of serum Ca. Further work-up depends on findings.
- At minimum, patients should be advised to drink at least 2L per day of fluids.

Complete evaluation

- Recommended by many due to the potentially high rate of recurrence and potential morbidity.
- Includes: chemistries, 24 hour urine collections.
- Be “patient centered”—a complete evaluation may not be reasonable in patients who will not complete the work-up and monitoring thereafter or take medications.

Targeted approach

- Do a complete evaluation in patients with moderate to high risk:
 - ◆ Middle-aged, white males with +FH
 - ◆ Patients with chronic diarrheal states and/or malabsorption, pathological fractures, osteoporosis, UTIs, or gout.
 - ◆ Patients with stones composed of cystine, uric acid, calcium phosphate or struvite.

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24

Cystine or Calcium phosphate stones: hard

Struvite: @ risk for staghorn calculi

Complete metabolic evaluation

- Blood tests: routine chemistries + serum Ca + uric acid.
- For increased Ca obtain iPTH.
- Urinalysis:
 - ◆ Ph > 7 + phosphate crystals suggests calcium phosphate or struvite calculi
 - ◆ Hexagonal cystine crystals is diagnostic for cystinuria
 - ◆ Uric acid crystals and calcium oxalate crystals are often normal.

24 hour urine collections

- Obtain the measurement of urine volume, pH, and excretion of Ca, uric acid, citrate, oxalate, and creatinine
- Because of the daily variations in dietary intake, it is recommended that 2 or 3 24 hr collections be obtained.
- Collections should be obtained in the outpatient setting and approx. 2-3 months after a stone event.

Treatment of recurrent calcium stones

- Dietary modifications:
 - ◆ Increase fluid intake to greater than 2L per day.
 - ◆ Minimize soft drinks, grapefruit juice.
 - ◆ Reduce protein intake to about 1g/kg (a high protein causes a high acid load to kidneys which favors stone formation).
 - ◆ Limit sodium intake

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27

Recall that 80% of patients with nephrolithiasis form calcium stones, most of which are composed primarily of CALCIUM OXALATE or less often calcium phosphate. Other main types include uric acid, struvite (magnesium ammonium phosphate) and cystine stones.

Limit sodium intake: Calcium is reabsorbed passively in the proximal tubule down the favorable concentration created by the reabsorption of sodium and water. Thus a low sodium diet can enhance proximal sodium and calcium reabsorption.

Treatment-dietary

- Calcium intake:
 - ◆ Limiting calcium intake is not recommended
 - ◆ The decrease in free intestinal calcium leads to overabsorption of dietary oxalate and enhanced oxalate excretion.
 - ◆ A low calcium diet may have secondary bad effects!

Drug therapy

- Indicated if the stone disease remains active (as evidenced by the formation of new stones, enlargement of old stones or passage of gravel) *despite dietary modifications over a 6 month period.*

Drug therapy (cont.)

- Idiopathic hypercalciuria: treated with normal calcium, low animal protein and low salt diet plus a **thiazide** diuretic (at 12.5 to 25 mg/d)
- Net effect may be a 90% reduction in the incidence of new stones.
- Urinary calcium and sodium excretion should be monitoring after institution of therapy.

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30

Idiopathic hypercalciuria: I.e not due to primary hyperparathyroidism, sarcoid.

Drug therapy (cont.)

- Hyperuricosuria: uric acid crystals can act as a nidus for calcium stone formation. Tx with allopurinol.
- Hypocitraturia: Increasing urinary citrate excretion is the goal since citrate inhibits stone formation by forming soluble complex with calcium. Citrate excretion can be enhanced by alkalination of the urine with potassium citrate or potassium bicarbonate.

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31

Hyperuricosuria: usually due to increased protein diet

Hypocitraturia: can be marked in patients with chronic metabolic acidosis.

Drug therapy (cont)

- Enteric hyperoxaluria (I.e short bowel syndrome, malabsorption problems): goal is to diminish intestinal oxalate absorption. Tx with potassium citrate and calcium carbonate.
- Patients with no metabolic abnl: minority. Make dietary changes, could still consider HCTZ.

Case

- HPI: A 30 year old Caucasian male and physician resident presents to your office with a 2 day h/o left flank pain and gross hematuria. The pain comes and goes, lasts about 20-30 min and is at times, quite severe. He has had no nausea, or vomiting and is tolerating p.o.'s well.
- PMH: None
- Meds: None
- FH: Father with h/o kidney stones.

Case (cont.)

- Social: Nonsmoker. Alcohol: 1-2 glasses of wine/week. He works long arduous hours as an intern. He admits to minimal fluid intake while he is on call. "There's just not time" he laments! He requires lots of "caffeine" while on call and loves diet Dr. Pepper. Despite his schedule, he recently completed the Seattle City Marathon and currently runs about 20-25 miles a week. Diet: "Atkins" diet x 3 weeks.

Case continued

- What test are you going to order first?
- What radiologic study are you going to choose?

Case (cont)

- A helical CT reveals one 7mm stone in the left proximal ureter.
- You refer the patient for urological evaluation.
- The patient undergoes ESWL and tolerates the procedure well.

Case (cont)

- The patient represents to your office 2 months later completely asymptomatic. He is still concerned however and would like a “complete” work-up?
- Is this reasonable?
- What do you order?

Case (cont)

- Blood chemistries X 2 reveal a total calcium of 9.9 and 10.1.
- A 24 hour urine study x 2 reveals >300 mg/day of calcium.
- What is your diagnosis?
- What are your recommendations and interventions?

Case (cont)

- Dx: idiopathic hypercalciuria
- TX: Increase fluid intake (esp. in light of marathon training) D/C Atkins diet. Limit soft drink intake.
- A followup U/S at 6 months reveals a new small 2mm asymptomatic stone. You therefore decide to initiate: HCTZ 12.5 mg p.o. qd

Review-take home points

- 5mm stones are not likely to pass and require surgical evaluation.
- Non contrast helical CT remains the gold standard for diagnosis.
- Work-up after the 1st stone=different approaches, be patient centered!
- ESWL can tx 85% of kidney stones that need surgical intervention and ureterorenoscopy often treats the rest (i.e the more distal stones).