Kidney Stone (Nephrolithiasis) — Classification, Symptoms and Treatment

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Nephrolithiasis is a clinical condition characterized by the presence of calculus in the urogenital tract. Calcium oxalate stones are the most common stones. Clinical presentation involves acute presentation with flank pain, which occasionally radiates to the groin. Non-contrast CT is the investigation of choice in nephrolithiasis and can diagnose all types of stones. Management depends on the location and size of the stone. Smaller stones have a greater chance to pass spontaneously, while stones larger than 5 mm need surgical management with percutaneous nephrolithotomy, ureteroscopy and extracorporeal lithotripsy.

Definition of Nephrolithiasis

Nephrolithiasis - The Kidney Stone
The formation of stones in the nephrons due to supersaturation and crystallization of inorganic and organic phosphates and acids is called nephrolithiasis. It’s also known as kidney stones.

Epidemiology of Nephrolithiasis

Nephrolithiasis as a Common Disorder

Nephrolithiasis is one of the most common urological disorders with a prevalence of 13% in males and 7% in females. Struvite stones are more common in females, than in males, because there is an increased predisposition of urinary tract infection in females. Cystine stones are seen in children who have defective transporter in the proximal tubule.

Classification – Types of Stones

Calcium Stones

Calcium stones form the major part of all the stones, which are seen clinically. Calcium oxalate stones are the most common calcium stones. The types of calcium stones are:

- Calcium oxalate
- Calcium phosphate stones

Magnesium Ammonium Phosphate Stones (Struvite Stones)

These are most commonly seen in urinary tract infections. Staghorn calculus is the characteristic type of stone seen in patients with Proteus infections.
Uric Acid Stones

These are characteristically seen in patients who produce an excess amount of uric acid or show an under-secretion of uric acid.

Cystine Stones

These stones are seen in patients who have a defective absorption of cystine. It leads to the increased concentration of cystine in the urine, leading to a stone (hexagonal in shape) formation.

Pathophysiology of Nephrolithiasis

Supersaturation and crystallization are the two primary factors being responsible for calculus formation.

Calcium Stones

The following factors are responsible for the formation of calcium stones:

1. Hypercalciuria

The majority of the patients having hypercalciuria do not have any primary disorders, while some have primary hyperparathyroidism.

The most likely contributions for higher urinary calcium excretion are:

- Increased intestinal absorption
- Increased bone resorption
- Increased renal loss

2. Hyperoxaluria

Increased urinary oxalate excretion causes more predispositions to stones when compared to the increased urinary calcium levels. Increased intestinal oxalate absorption predisposes to calcium oxalate stones. A decreased calcium intake is not indicated in nephrolithiasis. Normally, intestinal calcium binds to the oxalates and prevents the absorption of oxalates into the circulation. Decreased calcium leads to an increased
absorption of oxalates, which further predisposes calcium oxalate stones.

This mechanism is specifically seen in the following clinical conditions:

- Malabsorption syndromes
- Surgical bowel resection
- Bariatric surgery (ileojejunal surgery)

3. Hypocitraturia

Citrates are the principal substances which prevent the formation of stones. The mechanism of action involves binding with calcium in the renal tubules. In the absence of citrate, there will be supersaturation of the calcium in the urine, resulting in the formation of stones. Clinical conditions resulting in chronic metabolic acidosis (renal tubular acidosis and chronic diarrhea) lead to hypocitraturia.

Uric Acid Stones

Urate salts are soluble in the urine with a pH of 7. Clinical conditions which increase the uric acid production will precipitate uric acid stones. Conditions leading to increased uric acid production are:

1. Inherited condition
   - Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) deficiency
   - Glucose-6-phosphatase deficiency

2. Conditions with increased uric acid production
   - Myeloproliferative disorders
   - Lymphoproliferative disorders
   - Hemolytic disorders
   - Glycogen storage disorders (type III, V, VII)
   - Alcoholism
   - Increased dietary intake of purines

Struvite Stones

Composition of Struvite Stones

Magnesium ammonium phosphate and calcium carbonate

Staghorn Calculus
These are usually branched stones that are commonly composed of magnesium ammonium phosphate and are present in the renal pelvis. They’re resulting in the partial or complete obstruction of the renal pelvis.

**Mechanism of Formation of Struvite Stones**

Increased production of ammonia is the primary step involved in the formation of struvite stones. This is usually secondary to infection with urease producing bacteria, such as Proteus and Klebsiella. Normal urine has very low levels of ammonium phosphate. Infection with Proteus and Klebsiella breaks down urea into ammonia. The presence of ammonia increases the pH (more alkaline) and reduces the solubility of phosphates. These insoluble phosphates will form magnesium ammonium phosphate stones.

**Cystine Stones**

It is a hereditary condition in which there is a defect in the absorption of cystine by the proximal convoluted tubule. The solubility of cystine is very low, resulting in the formation of cystine stones. It is predominantly seen in children.

**Clinical Examination and Symptoms of Nephrolithiasis**

**Pain** is the presenting feature of the nephrolithiasis. The pain can be moderate to severe in intensity and is colicky and paroxysmal in nature. Pain is often associated with nausea and vomiting. Location of the pain is dependent on the site of obstruction. Presence of flank pain, radiating to the groin, is due to the presence of a stone in the lower ureter, while the presence of constant flank pain indicates the presence of a stone at the upper ureter or at ureteropelvic junction. The patients are usually restless and agitated.
Diagnosis & Laboratory Investigations

Urine Examination

It shows characteristic crystals in the urine examination. Crystals are formed as a result of supersaturation of the inorganic salts present in the urine. Almost all the stones are formed in alkaline urine, except uric acid stones.

- **Calcium stones**: Envelope or dumbbell shaped oxalate crystals
- **Struvite stones**: Coffin lid crystals
- **Uric acid stones**: Rhomboid or rosette shaped stones are seen

**Cystine stones**: Hexagonal stones

**Urine dipstick test** helps in aetiologic differentiations: check the pH, erythrocytes, leukocytes, bacteria and protein. The **Urine cyanide-nitroprusside test** is positive for identification of cystinuria.

Radiological Investigations

1. **Plain X-ray**: A plain abdominal X-ray helps in the identification of radio opaque stones. However, uric acid stones cannot be diagnosed on X-ray as they are radiolucent.
2. **Ultrasound**: It helps in the identification of the renal stones and the presence, or absence, of hydronephrosis.
CT scan: A non-contrast CT scan is the investigation of choice in the diagnosis of the nephrolithiasis. It helps in the diagnosis of all kind of stones (including radiolucent uric acid stones), along with the accurate size and location.

Image: “3 mm stone in the ureter” by James Heilman, MD. License: CC BY-SA 3.0

Stone Analysis

Straining of the urine analysis of the stones is recommended.

Treatment of Nephrolithiasis

Acute pain management involves the administration of NSAIDS and opioids.

The management depends on the extent, nature and site of location of the calculus. It usually involves a combined medical and surgical approach. Medical therapy involves the administration of oral alpha adrenergic blockers. The tone of the urethral muscle is reduced by the utilization of alpha adrenergic blockers. This will facilitate the smooth passage of the stone.

Smaller stones < 5 mm have an increased chance of responding to the medical treatment, whereas those > 5 mm have a less chance of falling spontaneously.

Surgical Management

- Percutaneous nephrolithotomy
- Ureteroscopy
- Extracorporeal lithotripsy

Specific Treatment of Uric Acid Stones

Medical therapy is usually effective in the treatment of uric acid stones. The treatment includes:

- Increased fluid intake
- Xanthine oxidase inhibitors (decrease the uric acid production)
- Alkalinization of the urine
Specific Treatment of Struvite Stones

Percutaneous nephrolithotomy (PNL) is the treatment of choice.

- Extracorporeal lithotripsy (ECL) is recommended with PNL in some situations. It usually requires the placement of the stent and to facilitate the adequate passage of stones postoperatively.
- Administration of antibiotics is required to cover the acute infection and maintenance of sterile tract following nephrolithotomy.
- Periodic monitoring is required for every 6 to 12 months to check the recurrence of further formation.

Specific Treatment of Cystine Stones

- Increased fluid intake
- Increased alkalinization of the urine
- Low methionine diet

Prognosis of Nephrolithiasis

The majority of stones pass spontaneously. Hospitalization is required in conditions where obstruction is associated with urinary tract infection. Emergent surgical drainage is required in the presence of urosepsis and pyelonephritis. There is an increased chance of recurrence in patients with nephrolithiasis. Increased fluid intake along with metabolic evaluation is recommended.
Review Questions

The solutions are located below the sources.

1. What are the most characteristic features of the cystine stones?
   
   A. Envelope or dumbbell shaped crystals
   B. Coffin lid crystals
   C. Rhomboid or rosette shaped stones
   D. Hexagonal stones
   E. Conical crystals

2. Which of the following is the investigation of choice for the diagnosis of nephrolithiasis?

   A. CT scan
   B. Ultrasound
   C. Plain X-ray
   D. Stone analysis
   E. Acoustic microscopy

3. The composition of struvite stones is...

   A. magnesium ammonium phosphate
   B. calcium only
   C. calcium oxalate
   D. phosphate only
   E. uric acid

References


Diagnosis and acute management of suspected nephrolithiasis in adults via upToDate.com

Cystine stones via upToDate.com

Uric acid nephrolithiasis via upToDate.com

Correct answers: 1D, 2A, 3A

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