Stone Diseases

Renal stones: are polycrystalline aggregate composed of varying amounts of crystalloid and organic matrix

Epidemiology: they are the 3rd most common affliction of urinary tract preceded by UTI and prostatic pathologies.

•10% of Caucasian men will develop a kidney stone by the age of 70. Within 1 year of a calcium oxalate stone, 10% of men will form another calcium oxalate stone, and 50% will have formed another stone within 10 years.

Etiology

⇒ **Intrinsic factors**

• ***Age***. The peak incidence of stones occurs between the ages of 20-50 years.

• ***Sex.*** Males/ female ratio is 3:1. Testosterone may cause increased oxalate production in the liver (predisposing to calcium oxalate stones) and women have higher urinary citrate concentrations (stone formation inhibitor).

• ***Genetic.*** Kidney stones are relatively uncommon in Native Americans, Black Africans, and US Blacks, and more common in Caucasians and Asians. -25% of patients with kidney stones report a family history of stone disease. Familial renal tubular acidosis (predisposing to calcium phosphate stones) and cystinuria (predisposing to cystine stones) are inherited.

⇒ **Extrinsic (environmental) factors**

Geographical location (climate and season). Renal stone disease is more common in hot climates. Ureteric stones become more prevalent during the summer, presumably because of higher urinary concentration in the summer. Concentrated urine has a lower pH, encouraging cystine and uric acid stone formation. Exposure to sunlight may also increase endogenous vitamin D production, leading to hypercalciuria.

Water intake: Low fluid intake (<1200ml/day) predisposes to stone formation. Increasing water 'hardness' (high calcium content) may reduce risk of stone formation, by decreasing urinary oxalate.

Diet High animal protein intake increases risk of stone disease (high urinary oxalate, low pH, low urinary citrate). High salt intake causes hypercalciuria.

Occupation: Sedentary occupations predispose to stones compared with manual workers.

Types of stones :

Stones may be classified according to composition, X-ray appearance, size and shape.

1. Stone composition

Calcium oxalate 85% , Uric acid 5-10% , Calcium phosphate + calcium oxalate 10% , Pure calcium phosphate Rare , Struvite (infection stones) 2-20% ,Cystine 1%.

Other rare stone types (all of which are radiolucent): indinavir (a protease inhibitor used for treatment of HIV); triamterene (a relatively insoluble potassium sparing diuretic, most of which is excreted in urine); xanthine.

2. Radiodensity on X-ray

Three broad categories of stones are described, based on their X-ray appearance. This gives some indication of the likely stone composition and helps, to some extent, to determine treatment options. However, in only 40% of cases is stone composition correctly identified from visual estimation of radiodensity on plain X-ray.

- ***Radio-opaque***

Opacity implies the presence of substantial amounts of calcium within the stone. Calcium phosphate stones are the most radiodense stones, being almost as dense as bone. Calcium oxalate stones are slightly less radiodense.

- ***Relatively radiolucent***

Cystine stones are relatively radiodense because they contain sulphur j (Fig. 9.1). Magnesium ammonium phosphate (struvite) stones are less' radiodense than calcium containing stones.

- ***Completely radiolucent***

Uric acid, triamterene, xanthine, indinavir (cannot be seen even on CTU).

3. Size and shape

Stones can be characterized by their size, in centimetres. Stones which grow to occupy the renal collecting system (the pelvis and one or more renal calyx) are known as staghorn calculi. They are most commonly composed of struvite— magnesium ammonium phosphate, but may be composed of uric acid, cystine, or calcium oxalate monohydrate.

Stone components :

1-Crystal component: it constitute more than 90%

2- Matrix component: 2-10% of stone weight. It is composed mainly of protein with small amounts of hexose and hexosamine. It may serve as natural glue or a nidus for crystal aggregation.

Mechanisms of stone formation: not fully understood but 2 accepted theories:

1- Nucleation theory: The stone is originated from crystal or foreign bodies immersed in supersaturated urine. Nucleation initiates the stone process and may be induced by a variety of substances, including protienaceouse matrix, crystal, foreign bodies and other particulate tissues. After nucleation there will be growth and aggregation.

Homogenous Nucleation: supersaturated urine of same substance

Heterogeneous Nucleation (Epitaxy):may occurs in less saturated urine and need less energy (uric acid crystal initiate calcium oxalate stone)

2- Crystal inhibitor theory: due to low or absence of natural stone inhibitor including magnesium, citrate, sulfate, pyrophosphate and glycosaminoglycans.

Factors predisposing to specific stone types

- **Calcium oxalate (~85% of stones)**

Hypercalciuria: Excretion of > 4 mg/Kg calcium per day. A major risk factor for calcium oxalate stone formation: it increases the relative supersaturation of urine. About 50% of patients with calcium stone disease have hypercalciuria.

3 types of hypercalciuria:

• Absorptive—increased intestinal absorption of calcium

• Renal—renal leak of calcium

• Resorptive—increased demineralization of bone (due to hyperparathyroidism)

Hypercalcaemia Almost all patients with hypercalcaemia who form stones have primary hyperparathyroidism. Of hyperparathyroid patients, about 1% form stones (the other 99% do not because of early detection of hyperparathyroidism by screening serum calcium).

Hyperoxaluria: Due to:

• Altered membrane transport of oxalate leading to increased renal leak of oxalate

• Primary hyperoxaluria—increased hepatic oxalate production; rare

• Increased oxalate absorption in short bowel syndrome or malabsorption (enteric hyperoxaluria)—the colon is exposed to more bile salts and this increases its permeability to oxalate.

Hypocitraturia: Low urinary citrate excretion. Citrate forms a soluble complex with calcium, so preventing complexing of calcium with oxalate to form calcium oxalate stones.

Hyperuricosuria High urinary uric acid levels lead to formation of uric acid crystals, on the surface of which calcium oxalate crystals form.

- **Uric acid stone: (~5-10% of stones)**

Humans are unable to convert uric acid (which is relatively insoluble) into allantoin (which is very soluble). Human urine is supersaturated with insoluble uric acid. Uric acid exists in 2 forms in urine—uric acid and sodium urate. Sodium urate is 20 times more soluble than uric acid. Uric acid is essentially insoluble in acid urine and soluble in alkaline urine. Human urine is acidic and this low

pH, combined with supersaturation of urine with uric acid, predisposes to uric acid stone formation.~20% of patients with gout have uric acid stones. Patients with uric acid stones may have:
• **Gout.** 50% of patients with uric acid stones have gout.
Myeloproliferative disorders: Particularly following treatment with cytotoxic drugs, cell necrosis results in release of large quantities of nucleic acids which are converted to uric acid.
• **Idiopathic uric acid stones** (no associated condition).

- **Calcium phosphate (calcium phosphate + calcium oxalate stone (10% of stones)**

Occur in patients with renal tubular acidosis (RTA)—a defect of renal tubular H^+ secretion resulting in impaired ability of the kidney to acidify urine. The urine is therefore of high pH, and the patient has a metabolic acidosis. The high urine pH increases supersaturation of the urine with calcium and phosphate, leading to their precipitation as stones.

- **Struvite stone (infection or triple phosphate stones)(MAP stones) (2-20% of stones)**

These stones are composed of magnesium, ammonium, and phosphate. They form as a consequence of urease-producing bacteria which produce ammonia from breakdown of urea (urease hydrolyses urea to carbon dioxide and ammonium), and in so doing alkalinize urine as in the following equation:
$NH_2\text{-}O\text{-}NH_2 + H_2O \rightarrow 2NH_3 + CO_2$
Under alkaline conditions, crystals of magnesium, ammonium, and phosphate precipitate.

- **Cystine stone (1% of all stones)**

Occur only in patients with cystinuria, an inherited (autosomal-recessive) disorder of transmembrane cystine transport, resulting in decreased absorption of cystine from the intestine and in the proximal tubule of the kidney. Cystine is very insoluble, so reduced absorption of cystine from the proximal tubule results in supersaturation with cystine and cystine crystal formation. Cystine is poorly soluble in acid urine (300mg/l at pH 5, 400mg/l at pH 7).

Renal stones: presentation and diagnosis
Kidney stones may present with symptoms or be found incidentally during investigation of other problems. Presenting symptoms include pain and/or haematuria (microscopic or occasionally macroscopic). Struvite staghorn calculi classically present with recurrent UTIs. Malaise, weakness, and loss of appetite can also occur. Less commonly, struvite stones present with infective complications (pyonephrosis, perinephric abscess, septicaemia, xanthogranulomatous pyelonephritis).

Diagnostic tests
• **Plain abdominal radiography (KUB):** calculi that contain calcium are radiodense. Sulphur-containing stones (cystine) are relatively radiolucent on plain radiography.
• Radiodensity of stones in decreasing order: calcium phosphate > calcium oxalate > struvite (magnesium ammonium phosphate) » cystine.
• Completely radiolucent stones (e.g. uric acid, triamterene, indinavir) are usually suspected on the basis of the patient's history and/or urine pH (pH <6—gout; drug history—triamterene, indinavir), and the diagnosis may be confirmed by ultrasound, CTU, or MRU.
• **Renal ultrasound:** its sensitivity for detecting renal calculi is ~95%. A combination of plain abdominal radiography and renal ultrasonography is a useful screening test for renal calculi.
• IVU: increasingly being replaced by CTU.
• CTU: a very accurate method of diagnosing all but indinavir stones. Allows accurate determination of stone size and location and good definition of pelvicalyceal anatomy.and renal function.
• MRU: cannot visualize stones, but is able to demonstrate the presence of hydronephrosis
Differential Diagnosis: Other retroperitoneal pathologies, acute abdomen, peptic ulcer, cholycystitis, aortic aneurysm,……