Pathology lab

Rola Alwaheidi, MD

Cystic kidney diseases

Simple cysts

Description

- Very common in the general population
- Most common renal masses
- Thin wall and only water-like fluid inside

Clinical features

Usually asymptomatic

In the case of enlargement:

-Dull pain (back, side, or upper abdomen)

-Changes in urinary habits (e.g., impaired urinary flow)

Diagnostics

Usually a benign, incidental finding during CT or ultrasound examinations

Treatment

- Not indicated in most cases
- Indication for surgery: symptomatic cysts (e.g., impaired urinary flow, pain, bleeding) or risk of further complications (e.g., infection, malignancy)

Complications (Complications are rare).

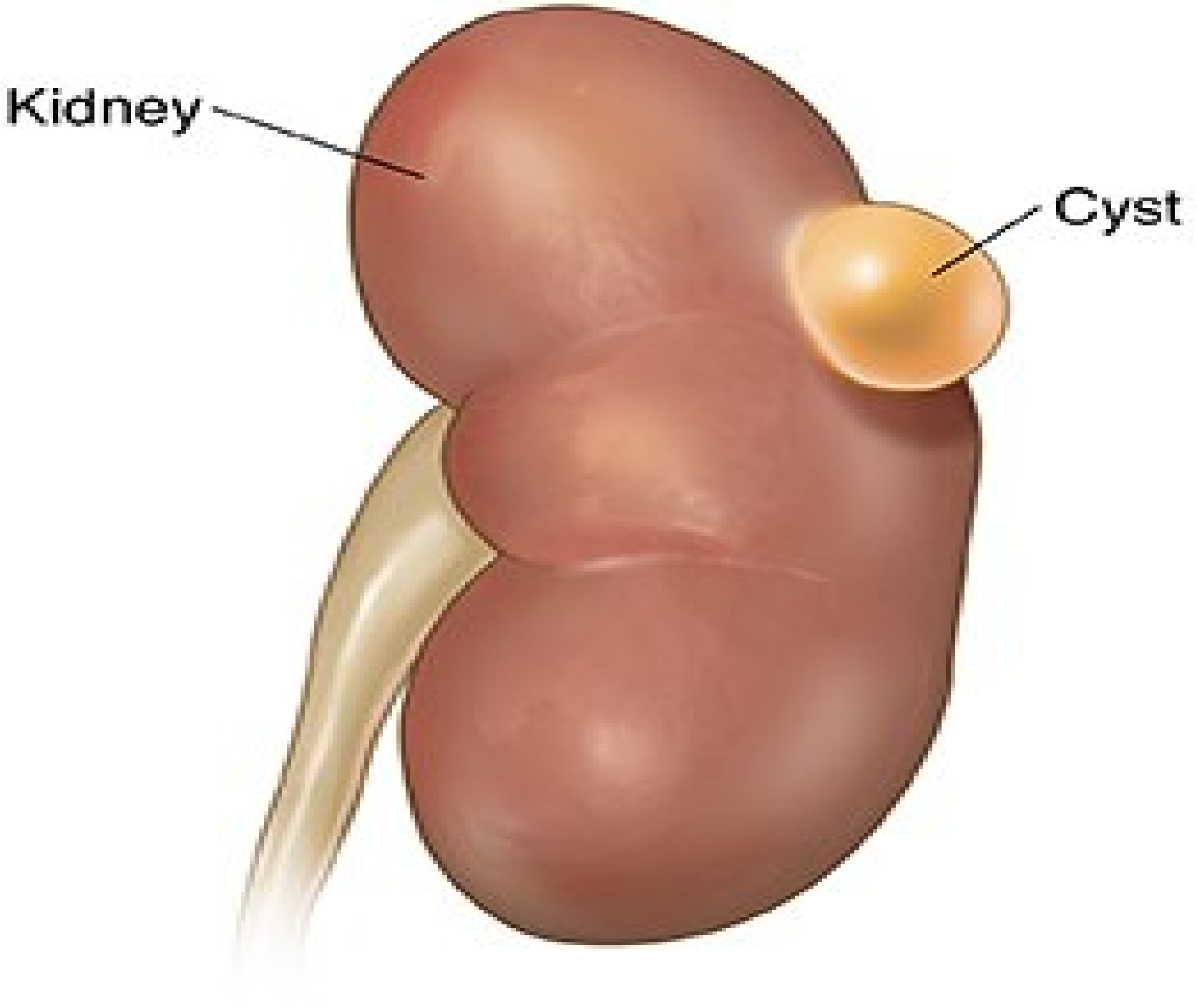
- Cyst rupture
- Cyst infection
- Compression of adjacent tissue (e.g., of the ureter causing impaired urinary flow)

Simple cysts are generally not harmful lesions that occur as multiple or single cystic spaces of variable size. Commonly, they are 1 to 5 cm in diameter; translucent; lined by a gray, glistening, smooth membrane; and filled with clear fluid.

On microscopic examination, these membranes are seen to be composed of a single layer of cuboidal or flattened cuboidal epithelium, which in many instances may be completely atrophic. The cysts usually are confined to the cortex. Rarely, massive cysts as large as 10 cm in diameter are encountered.

Simple cysts constitute a common postmortem finding that has no clinical significance. The main importance of cysts lies in their differentiation from kidney tumors, when they are discovered either incidentally or during evaluation of hemorrhage and pain

Radiographic studies show that in contrast with renal tumors, renal cysts have smooth contours, are almost always vascular, and produce fluid rather than solid tissue signals on ultrasonography.


Kidney
Cyst

Polycystic kidney disease

Polycystic kidney disease (PKD) is an inherited disorder characterized by the development of multiple cysts in the kidneys.

It is classified into two distinct disorders: autosomal recessive PKD (ARPKD) and autosomal dominant PKD (ADPKD).

Early diagnosis and treatment may prevent or delay end-stage renal disease in both conditions, but kidney transplantation is the only curative treatment option.

Epidemiology

Incidence

ADPKD: ~ 1/1,000

The most common inherited cause of chronic kidney disease

Responsible for 5–10% of end-stage renal disease (ESRD)

ARPKD: ~ 1/20,000

Etiology

ADPKD

Autosomal dominant inheritance

Mutation in: PKD1 on **chromosome 16** (85% of cases), the gene that encodes polycystin-1 OR

PKD2 on **chromosome 4** (15% of cases), the gene that encodes polycystin-2

Positive family history

ARPKD

Autosomal recessive inheritance

Mutation in PKHD1 gene on chromosome 6, the gene that encodes for fibrocystin, a protein involved in the maintenance of primary cilia of the renal collecting duct and biliary epithelial cells

Pathophysiology

ADPKD Two-hit hypothesis

- Inherited mutation in one allele of **PKD1** (polycystin-1) or **PKD2** (polycystin-2) genes
  - Polycystin-1: involved in cell-cell and/or cell-matrix interactions
  - Polycystin-2: a nonselective cation channel transporting Ca^{2+}
- Additional second somatic acquired mutation in tubule epithelial cells

Abnormal cilia-mediated signaling pathways → formation and expansion of cysts in the renal cortex and medulla → compression of renal vessels with activation of the renin-angiotensin-aldosterone system (RAAS), ischemia, and destruction of the kidney parenchyma

ARPKD: inherited mutation in the PKHD1 gene → defective fibrocystin (also called polyductin) → cystic dilation of collecting ducts and bile ducts (intrahepatic and extrahepatic bile ducts)

Clinical Features

ADPKD

Symptom onset

Symptoms usually occur after 30 years of age, but the disease may also manifest during childhood.

Symptoms are less severe and tend to manifest later in individuals with the PKD2 mutation compared to those with the PKD1 mutation.

Renal manifestations

Gross hematuria

Flank or abdominal pain

Recurrent urinary tract infections

Nephrolithiasis

Kidneys might be palpable and enlarged on abdominal exam (they are usually normal at birth)

Signs of chronic kidney disease (e.g., hypertension, fluid overload, uremia)

Extra renal manifestations

- Multiple benign **hepatic cysts** (prevalence increases with age)
- Cysts may also occur in the **pancreas**, spleen, ovary, and testicles.
- **Cerebral** **berry aneurysm** (~8%) The risk is higher in patients with a family history positive of ADPKD.
  - May rupture and cause subarachnoid hemorrhage (the risk for growth and rupture is the same in patients with ADPKD as in the general population)
- Cardiovascular
  - Signs of **arterial hypertension** (e.g., morning headaches) through increased renin production
  - Heart valve defects (particularly mitral valve prolapse)
  - Left ventricular hypertrophy
  - Potential association with coronary artery aneurysm and aortic aneurysm
- Colon diverticula (diverticulosis), abdominal or inguinal hernias

ARPKD

Symptom onset: Symptoms most commonly manifest in infancy or childhood.

Renal manifestations

- Protruding abdomen (nontender abdominal mass) due to **bilateral renal enlargement** and/or hepatomegaly
- **Chronic renal failure** : frequently hematuria, proteinuria, and oliguria
- Severe in-utero renal impairment → oliguria in utero → maternal **oligohydramnios** → **Potter sequence**
  - Craniofacial abnormalities (retrognathia, low-set ears, flat nose) and clubbed feet
  - Pulmonary hypoplasia → respiratory insufficiency in neonates

Extra renal manifestation

Hypertension

- Early manifestation
- Often not responsive to monotherapy
- Can result in complications if inadequately controlled (e.g., cardiac hypertrophy, heart failure, cerebrovascular diseases, progressive renal impairment)

Liver involvement: **congenital hepatic** and portal fibrosis → progressive liver failure and **portal hypertension**

Medullary Cystic Kidney Disease

- Autosomal dominant
- Cysts in collecting ducts of medulla
- Name is misnomer
- Most patients DO NOT have cysts
- Kidney fibrosis occurs → small, shrunken kidneys
- Contrast with ADPKD (enlarged kidneys)
- Often have early onset (adolescent)
- Renal failure

Nephrolithiasis

Nephrolithiasis encompasses the formation of all types of urinary calculi in the kidney, which may be deposited along the entire urogenital tract, from the renal pelvis to the urethra

Overview of kidney stones

Calcium oxalate stones ~ 75%

Uric acid stones~ 10%

Struvite stones~ 5–10%

Calcium phosphate stones< 5%

Cystine stones< 5%

Calcium oxalate stones

Etiology

Hypercalciuria: presence of elevated calcium levels in the urine

(Either idiopathic Hypercalciuria or due to hypercalcemia (e.g., due to hyperparathyroidism)

Dietary Sodium

↑Na

↑ECV

↓RAAS

↓Na Reabsorption Proximal Tubule

↓Ca Reabsorption Proximal Tubule

More Na = More Ca Urine

High Na diet = Stone formation

Low Na diet = Treatment stones

Hyperoxaluria: presence of elevated oxalate levels in the urine

- Increased intake of dietary oxalate
- Increased intestinal absorption of oxalate, e.g., due to fatty acid malabsorption (e.g., Crohn disease, ulcerative colitis, short bowel syndrome)
  - Calcium normally binds oxalate to form calcium oxalate, which is excreted via feces.
  - In conditions associated with fatty acid malabsorption due to impaired bile acid reabsorption, calcium preferentially binds free fatty acids, leading to excess free oxalate and, therefore, to increased oxalate absorption.
- Vitamin C supplements
- Ethylene glycol poisoning

Hypocitraturia: decreased level of citrate in the urine

Hyperuricosuria: increased urinary excretion of uric acid (Associated with decreased solubility of calcium oxalate.)

Develop in persistently acidic urine

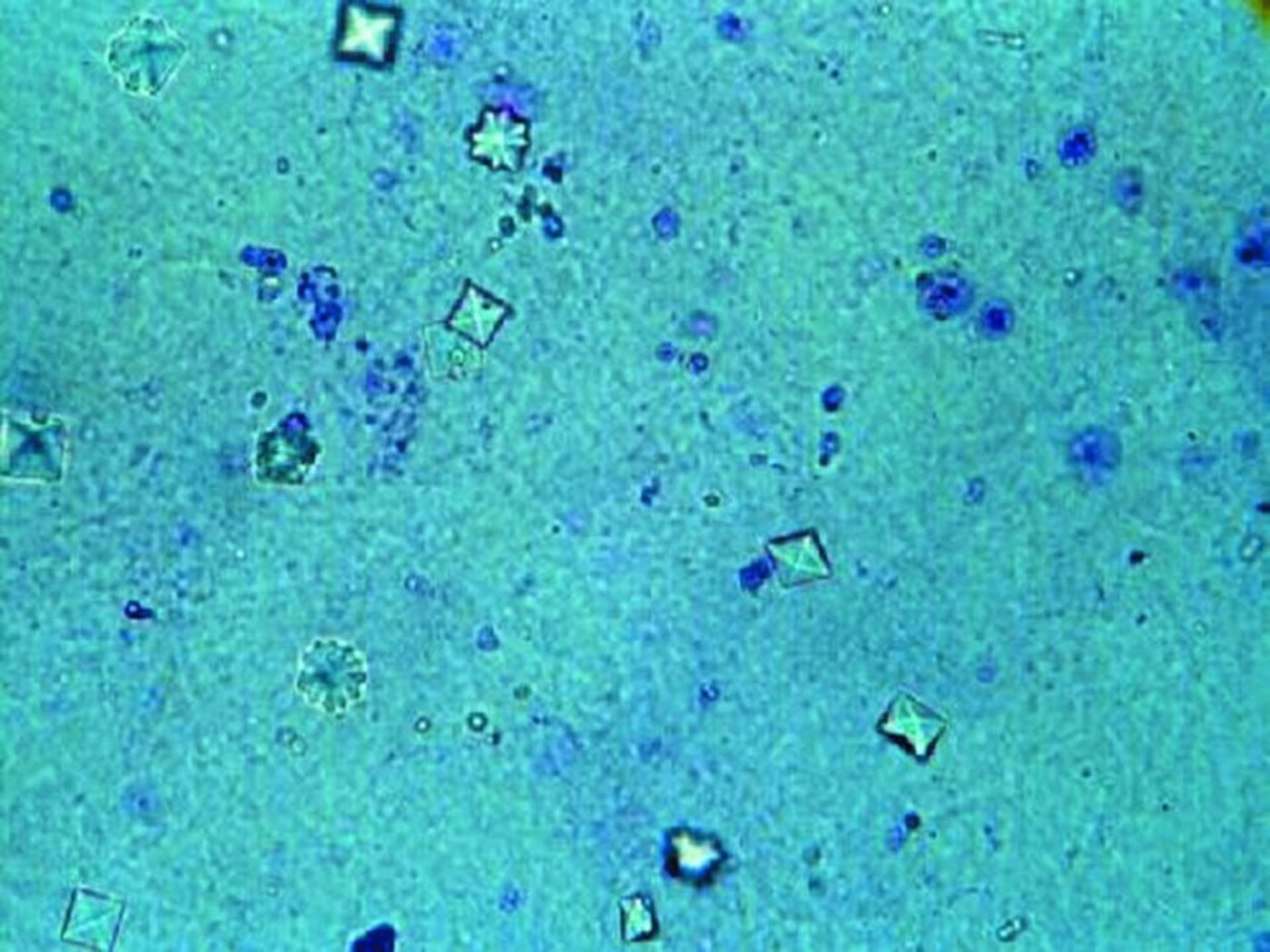
Classic case

- Patient drinking less water
- Flank pain, hematuria
- Calcium stone on imaging
- Normal Ca level in plasma
- Increased calcium level in urine

Diagnosis

Urine microscopy: dumbbell-shaped or octahedron-shaped crystals

X-ray (or CT): **radiopaque** stones



Treatment

- Most stones pass on their own
- Large stones that do not pass require surgery
- Recurrent stone formers may take medication

Thiazides

- Decrease Ca in urine

Citrate (Potassium citrate)

- Binds with calcium but remains dissolved
- Lowers urinary Ca available for stones
- Inhibits of stone formation

Uric acid stones

Etiology

Hyperuricemia and hyperuricosuria

Gout

High cell turnover (e.g., tumor lysis syndrome,etc)

↓ Urine volume, e.g., due to dehydration

Develop in persistently acidic urine

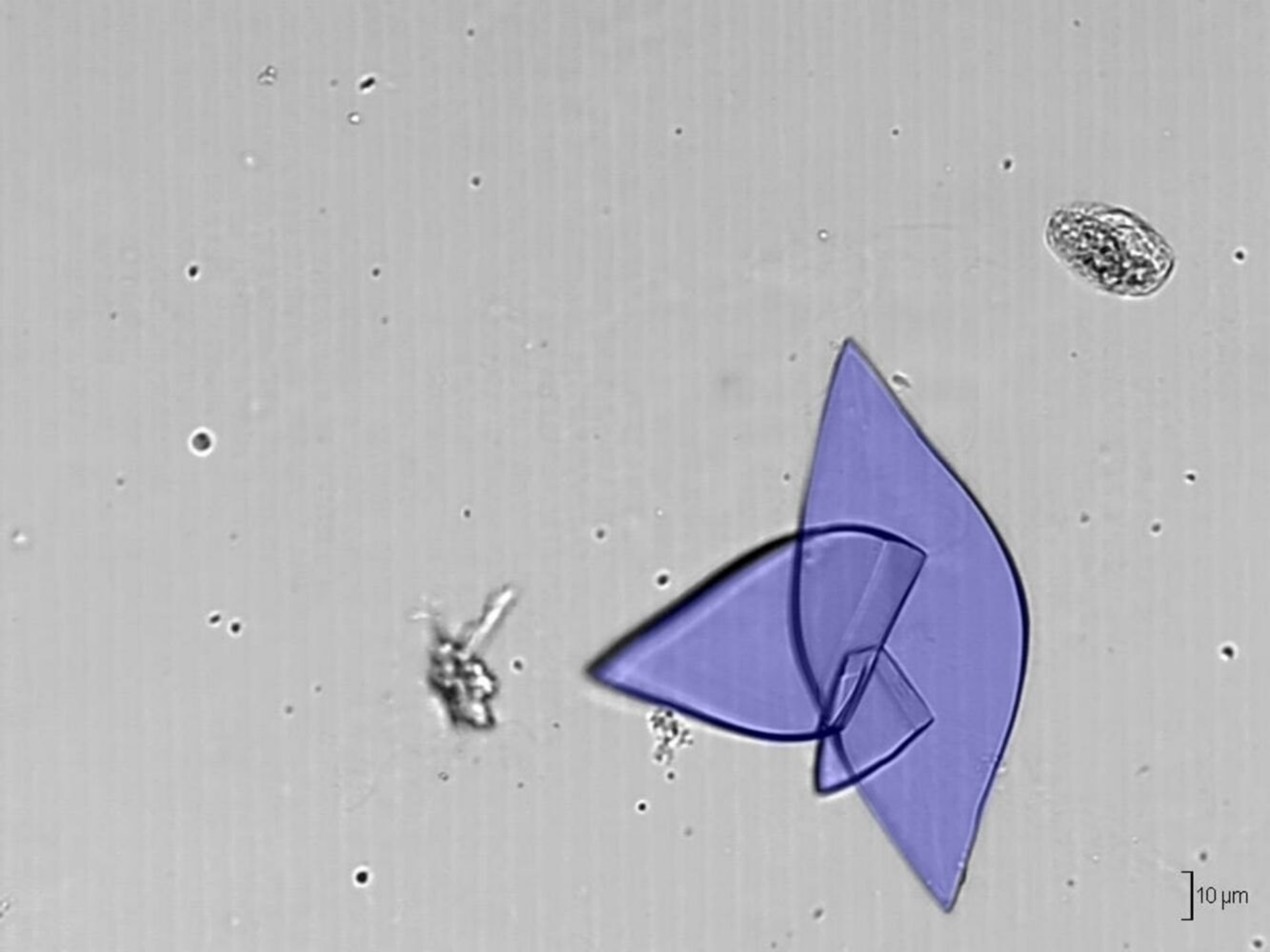
- Classic case
- Flank pain, hematuria
- No stone on x-ray

Diagnosis

Urine microscopy: rhomboid/needle-shaped crystals (Diamond shaped)

X-ray: **radiolucent** stones

CT: can be visible but are usually only minimally visible (not as visible as calcium stones)


10 µm

Treatment

- Hydration
- Alkalization of urine
- Potassium bicarbonate
- Rarely allopurinol
  - Xanthine oxidase inhibitor
  - Reduces uric acid production
- Medical therapy often effective
- Usually does not require surgery

Struvite stones (magnesium ammonium phosphate stones)

Etiology

- Upper UTI with **urease-producing bacteria** such as Proteus mirabilis, Klebsiella, Staphylococcus saprophyticus, and/or Pseudomonas
  - These bacteria convert urea to ammonia → elevated ammonia causing alkaline urine → precipitation of the ammonium magnesium phosphate salt → crystal and stone formation
  - Can form very large stones that fill the entire renal pelvis and calyces (staghorn calculi)
- Use of indwelling catheter increases risk
- Develop in persistently alkalic urine

- Classic presentation
- UTI symptoms (dysuria, frequency)
- Mild flank pain
- Hematuria
- Large, branching staghorn stone on imaging

Diagnosis

Urine microscopy: rectangular prisms (coffin lid-appearance) indicate struvite stones

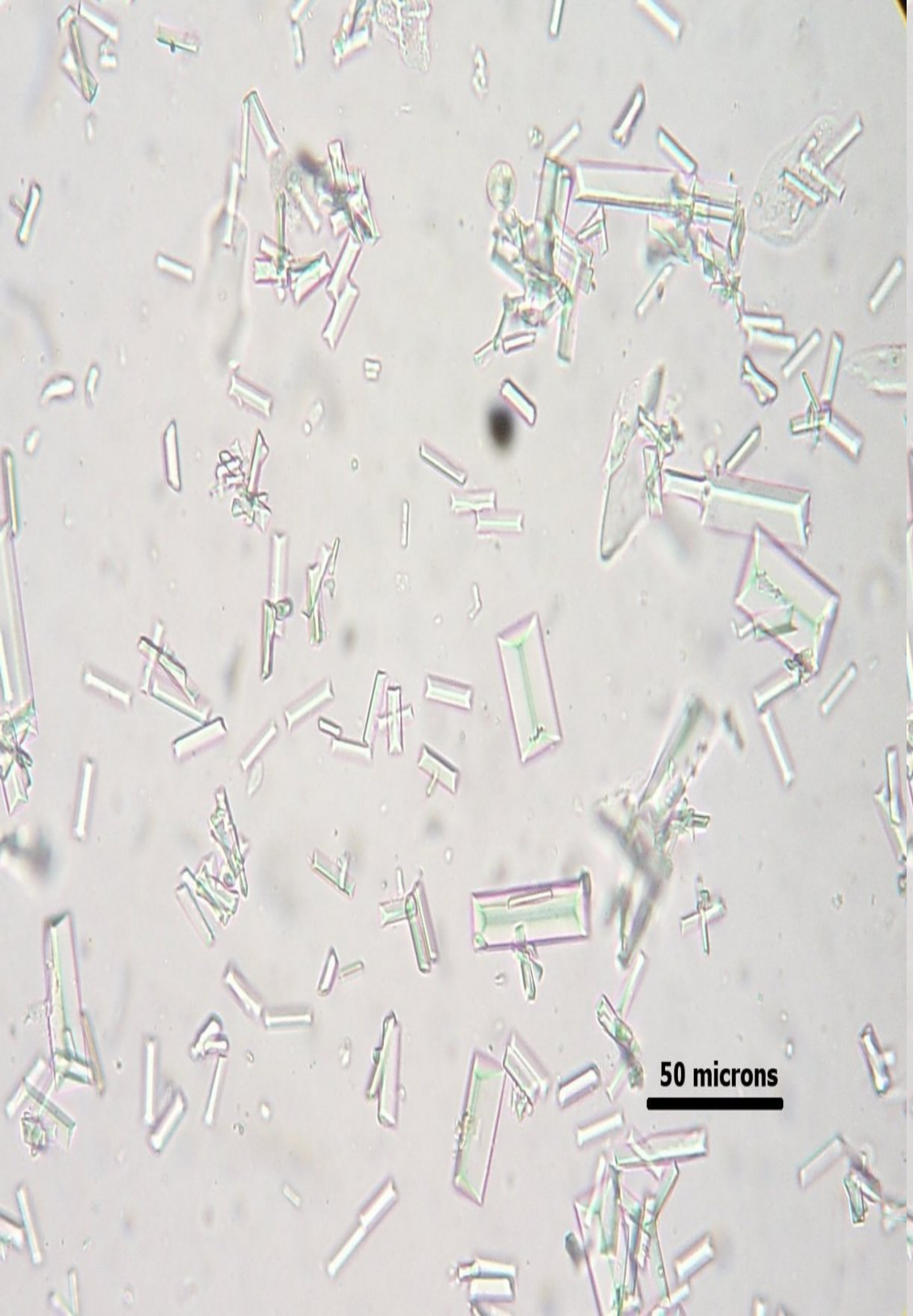
X-ray (or CT)

Weakly **radiopaque** stones

Possibly staghorn calculi

Treatment:

- Surgery
- Antibiotics


50 microns


50 microns

Calcium phosphate stones

Etiology

- Hyperparathyroidism
- Type 1 renal tubular acidosis
- Upper urinary tract infections
- Develop in persistently alkalic urine

Diagnosis

- Urine microscopy: wedge-shaped crystals
- X-ray (or CT): **radiopaque** stones

Cystine stones

Etiology

Autosomal recessive defect in cystine-reabsorbing PCT transporter → impaired proximal renal tubular absorption of dibasic amino acids → cystinuria → cystine stone formation (as cystine is poorly soluble)

Develop in persistently acidic urine

Clinical features : recurrent kidney stones (manifesting with e.g., flank pain) starting in childhood

Diagnosis

Urine microscopy: hexagonal crystals

X-ray (or CT)

Weakly **radiopaque** stones

Possibly staghorn calculi

- Classic case
- Child
- No history of UTI (contrast with Struvite)
- Large, staghorn stone
  - Treatment:
- Hydration
- Alkalization of urine

Clinical features

Stones usually form in the collecting ducts of the kidneys but may be deposited along the entire urogenital tract from the renal pelvis to the urethra. Their localization and size determine the specific symptoms. Small kidney stones may also be asymptomatic and detected incidentally.

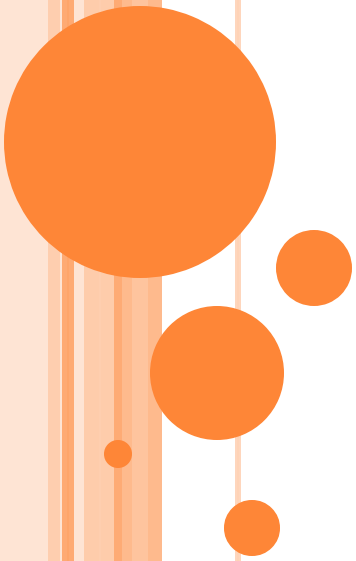
Severe unilateral and **colicky flank pain** (renal colic)

- Radiates anteriorly to the lower abdomen, groin, labia, testicles, or perineum
- Paroxysmal or progressively worsening
- The area around the kidneys may be tender on percussion (costovertebral angle tenderness)

Hematuria

Nausea, vomiting, and reduced bowel sounds

Dysuria, frequency, and urgency



Thank you