



**Brigham and Women's Hospital**

Founding Member, Mass General Brigham

# **MUST KNOW CLINICAL IMAGES IN NEPHROLOGY**

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Associate Physician  
Nephrology Division  
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Instructor  
Harvard Medical School



## Annie Liu DO, MS, MPH



University of New England College of Osteopathic  
Medicine

Medicine Residency @ Maine Medical Center

Nephrology Fellowship @ Massachusetts General  
Hospital and Brigham and Women's Hospital

Instructor @ HMS

- Clinical focus: Geriatric Nephrology
- Research focus: Supportive care of older adults with prevalent end stage kidney disease

# DISCLOSURES

None



# OBJECTIVES

1. Recognize classic clinical and histopathologic images associated with common and high-yield diseases in nephrology
2. Interpret key radiologic, urinalysis, and biopsy findings

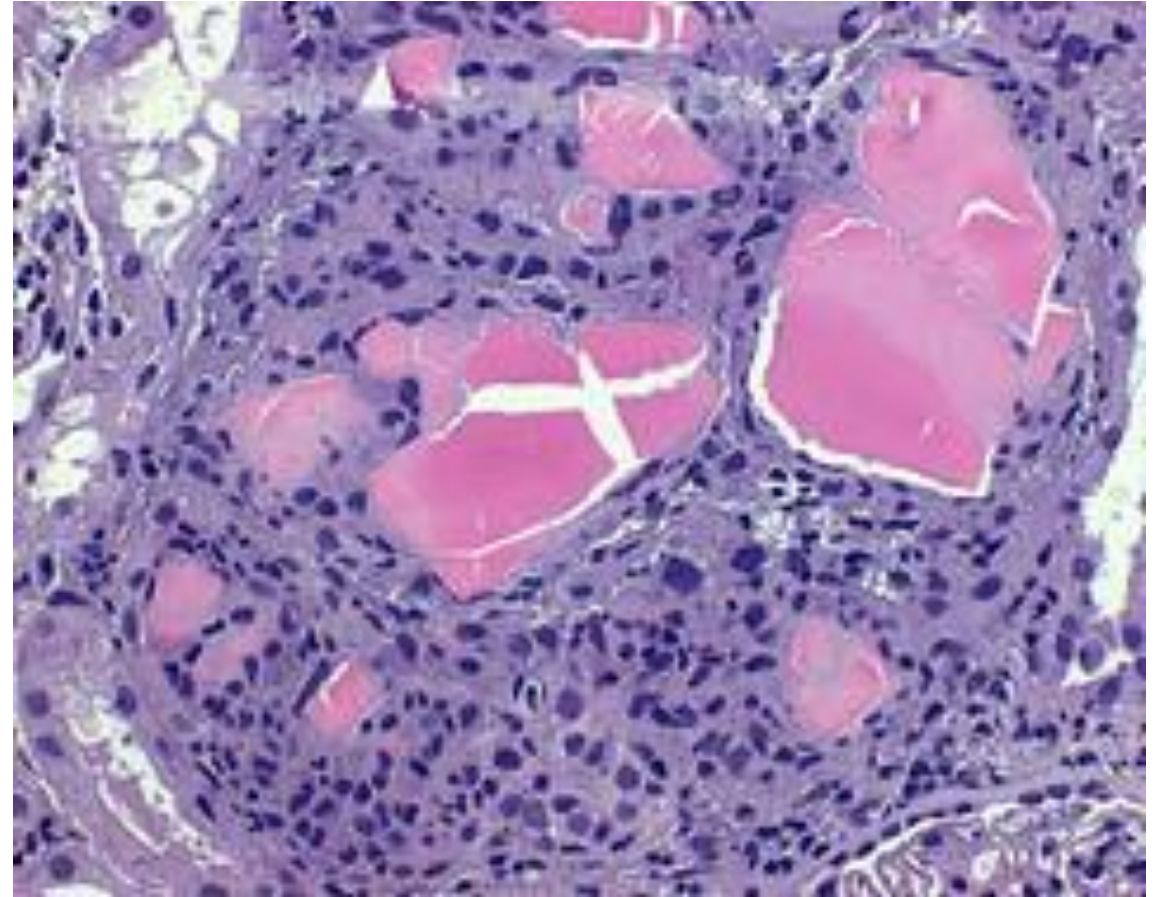


# Case 1

A 69 year old woman with malaise, generalized pain, and weakness for the past 3 months. Laboratory studies reveal: serum creatinine 3.8 mg/dL (baseline 1.2 mg/dL a year ago), hemoglobin 8.9 g/dL, serum albumin 3.0 g/dL. A renal biopsy is performed.

What's the diagnosis?

- A. Light chain deposition disease
- B. Phosphate nephropathy
- C. Uric acid nephropathy
- D. Cast nephropathy
- E. Fibrillary glomerulonephritis

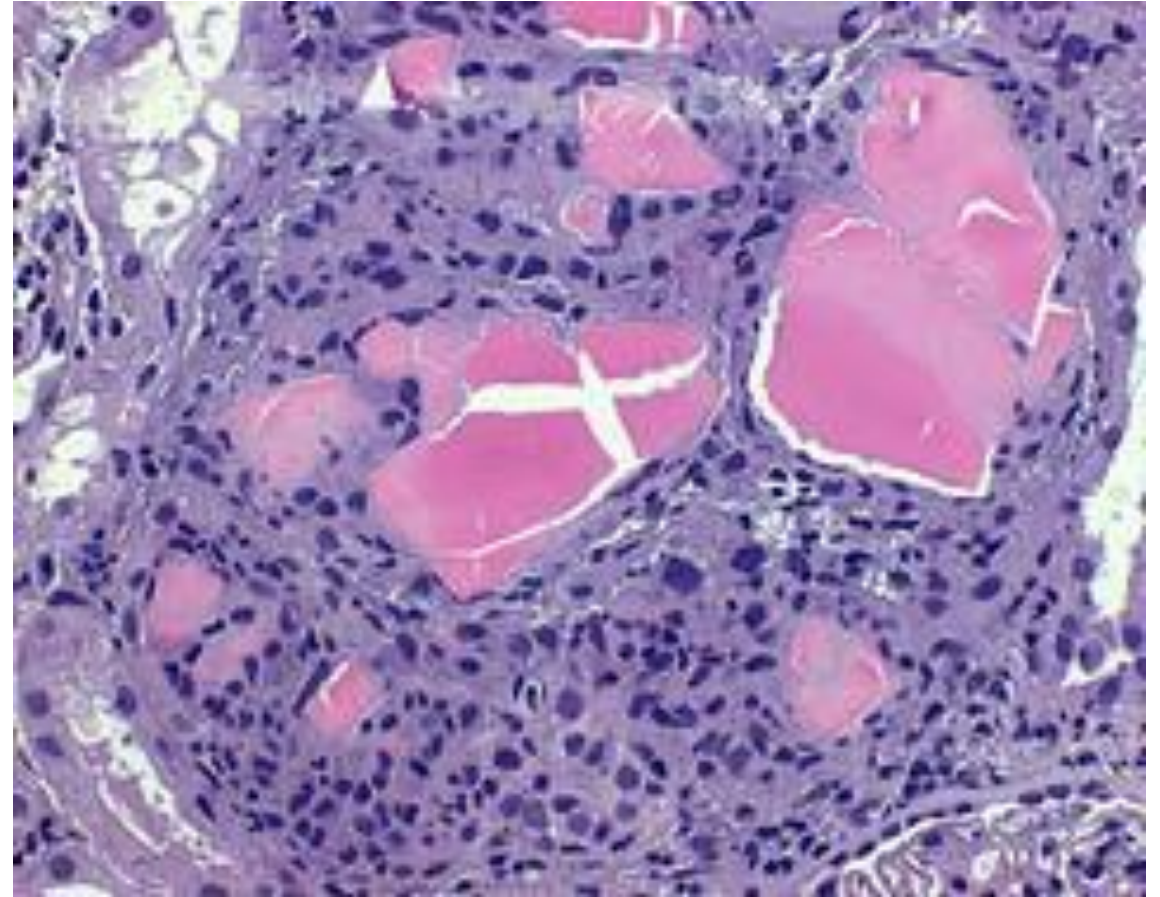


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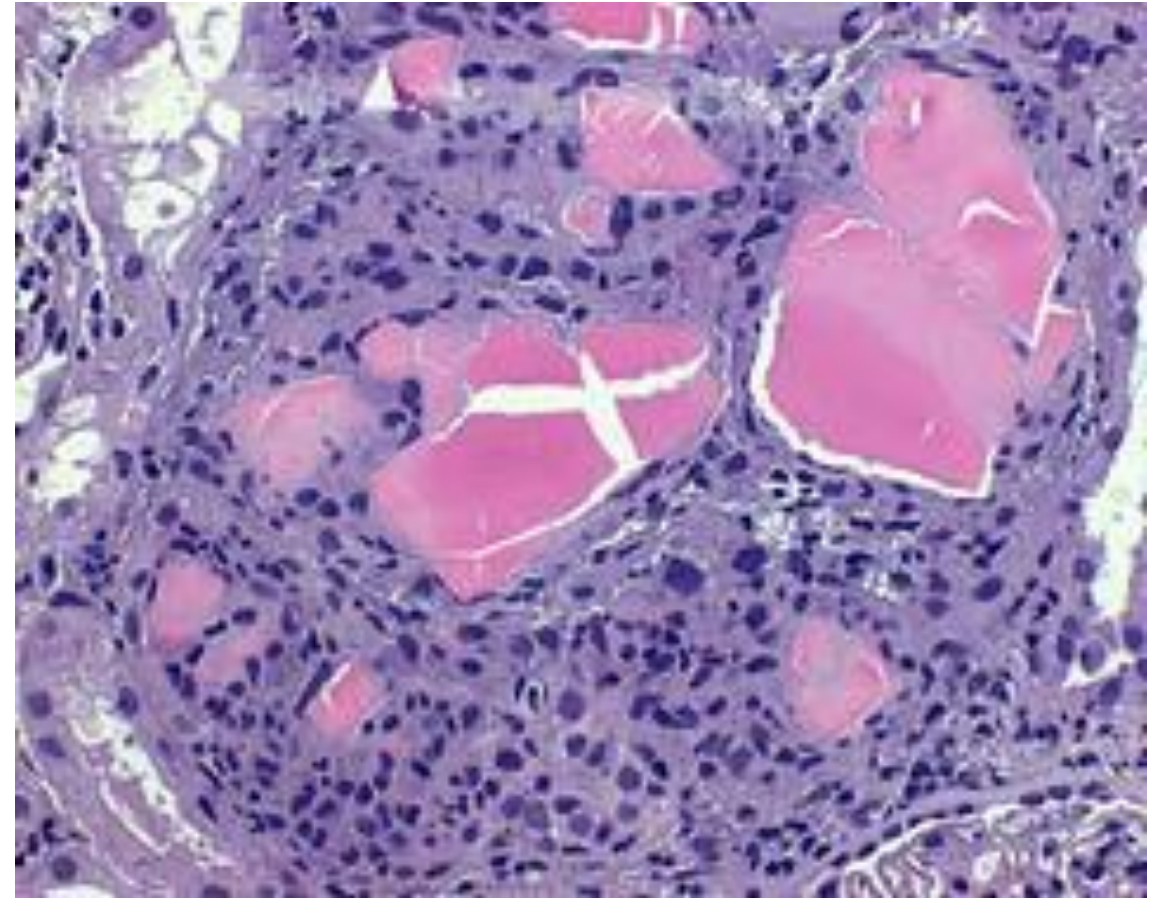
## D. Cast Nephropathy

- Multiple myeloma is the malignant proliferation of plasma cells involving more than 10 percent of the bone marrow.
- Bone pain related to multiple lytic lesions is the most common clinical presentation.
- Up to 30 percent of patients are diagnosed incidentally while being evaluated for unrelated problems; 1/3<sup>rd</sup> of patients are diagnosed after a pathologic fracture, commonly of the axial skeleton.



# Cast Nephropathy

- Overproduction of light chains → tubular capacity for reabsorption is exceeded
- Filtered light chains and immunoglobulins then bind Tamm-Horsfall glycoprotein in the distal nephron
- Cast formation causing tubular obstruction in the distal nephron that elicits an inflammatory response
- Gold standard for diagnosis: kidney biopsy



Kidney biopsy: hypereosinophilic fractured casts within tubules

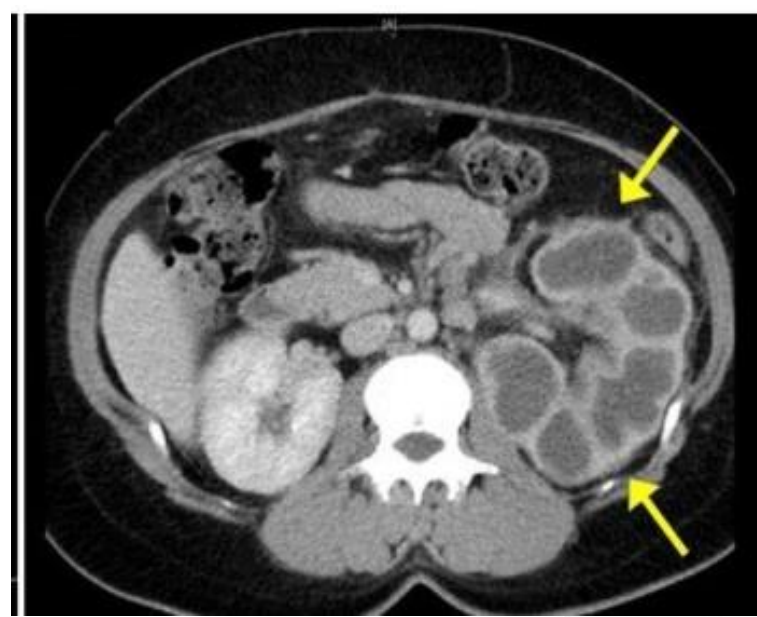


## Case 2

A 44 year old woman with a history of recurrent kidney stones and UTIs, presented with left flank pain, fatigue, and fever. She had previously undergone percutaneous nephrolithotomy and extracorporeal shock wave lithotripsy one year ago for left staghorn calculi. A CT abdomen/pelvis was obtained.

What is the most likely diagnosis?

- A. Renal cell carcinoma
- B. Xanthogranulomatous pyelonephritis
- C. Renal abscess
- D. Tuberculosis
- E. Angiomyolipoma

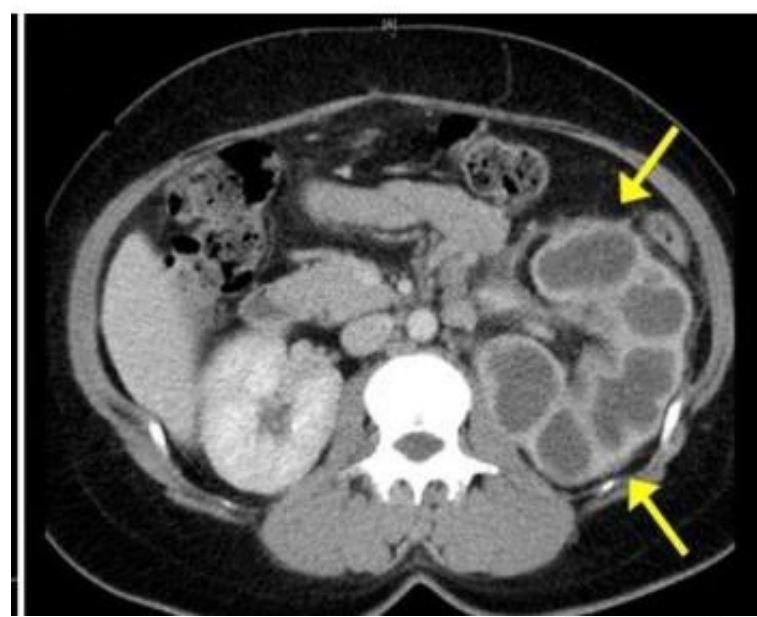


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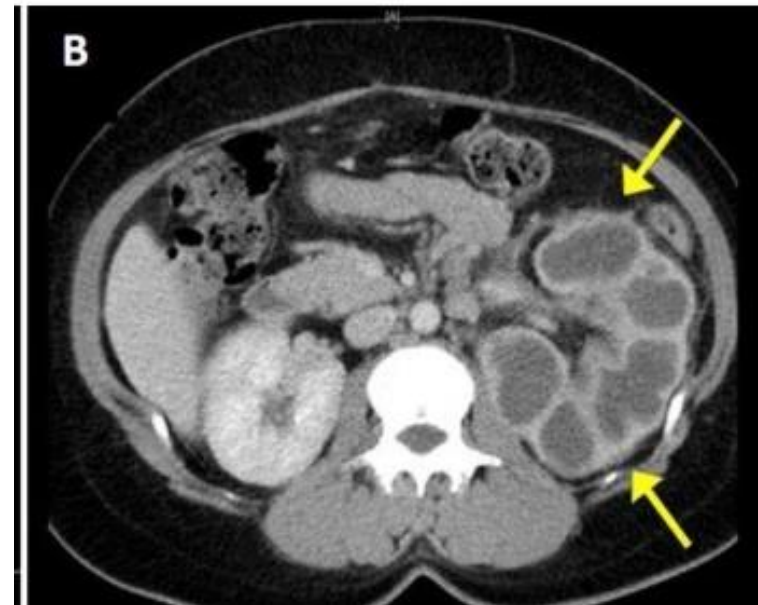
## B. Xanthogranulomatous pyelonephritis

- First described in 1916 as a rare destructive granulomatous inflammation of renal parenchyma
- Accounts for 0.6% of all chronic pyelonephritis cases
- More prevalent in women
- Causes: calculus or non-calculus urinary obstruction, urosepsis, chronic renal ischemia, lymphatic obstruction



## B. Xanthogranulomatous pyelonephritis

- Presentation: flank pain, fever, weight loss, anorexia
- On CT: enlarged segment of the kidney, poor or no excretion of contrast into the collecting system, low attenuation collection representing dilated, debris-filled calyces, and xanthoma collections
- Dilated and enlarged renal pelvis and calyces gives a multiloculated appearance (e.g. bear paw sign)

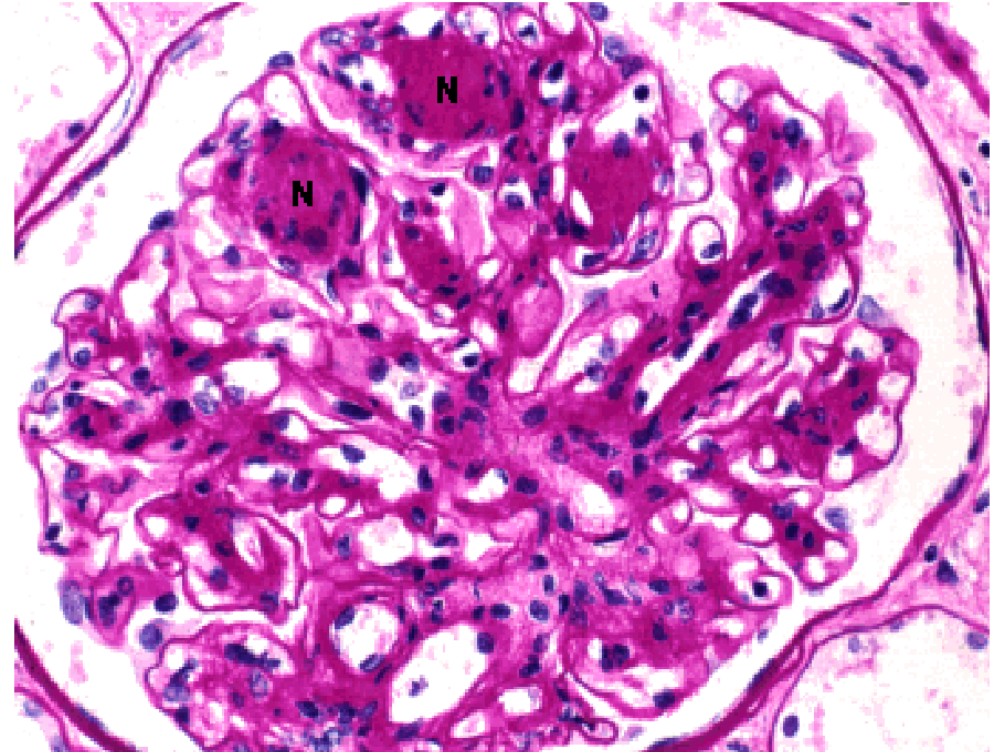


# Case 3

A 58 year old man with a 12-year history of T2DM (HbA1C of 8.2), HTN, HLD, and CKD3B with urine albumin to creatinine ratio of 0.5 g/g. Currently managed with lisinopril 40 mg/d, amlodipine 10 mg/d, and furosemide 40 mg/d. On exam: BP 132/60 mmHg, HR 70 bpm. Trace to 1+ edema.

Which of the following is the most appropriate next step in management?

- A. No changes to therapy are needed other than optimizing glycemic control
- B. Initiate an SGLT2 inhibitor and consider adding a non-steroidal mineralocorticoid receptor antagonist
- C. Referral for kidney transplant evaluation
- D. Perform another kidney biopsy to confirm the diagnosis
- E. Add an angiotensin receptor antagonist to his current regimen



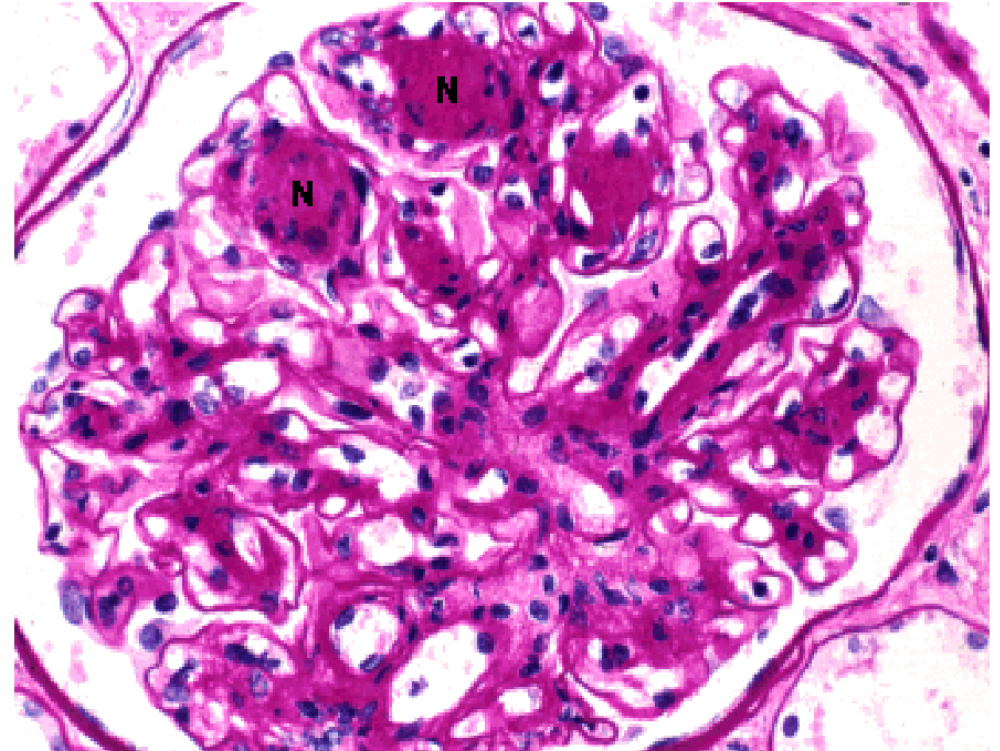


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# Question stem breakdown

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## Hints

- Longstanding history of T2DM
- Uncontrolled T2DM
- Hypertension and hyperlipidemia
- Moderate albuminuria
- On max dose of lisinopril



# Diabetic Kidney Disease (DKD)

- First line therapy for DKD with albuminuria
  - Maximally dosed ACEi or ARB
  - Combination of ACEi and ARB are associated with increased risk of hyperkalemia and AKI
- SGLT2i (e.g. empagliflozin, dapagliflozin) are strongly recommended in DKD with albuminuria ( $\geq 200$ -300 mg/g), regardless of glycemic control (EMPA-KIDNEY and DAPA-CKD)
- Nonsteroidal MRAs (e.g. finerenone) offer additional renal and cardiovascular protection in patients with T2DM and DKD (FIDELIO-DKD and FIGARO-DKD)



# SGLT2 inhibitors

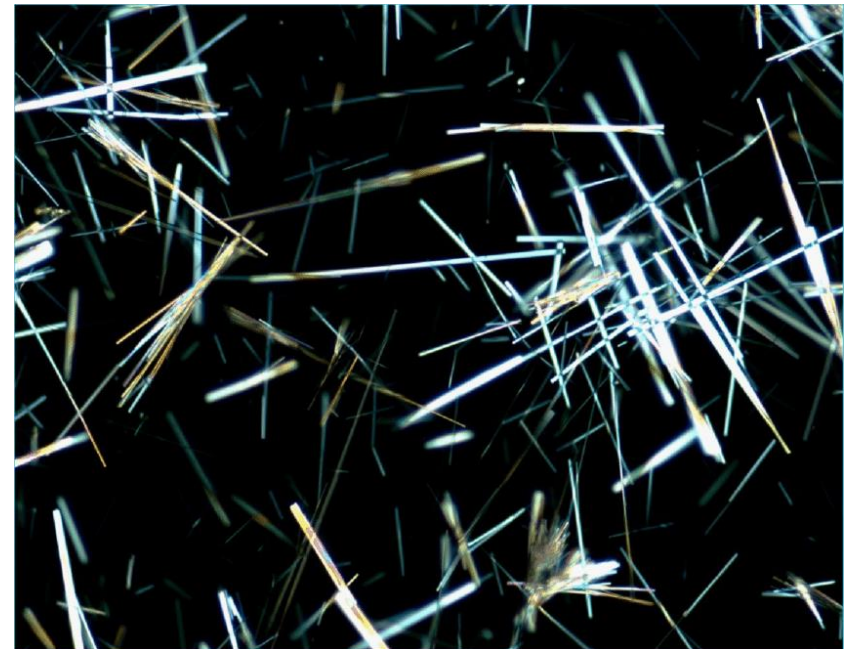
- Recommendation 3.7.2: We recommend treating adults with CKD with an SGLT2i for the following (1A):
  - eGFR  $\geq$  20 mL/min per 1.73 m<sup>2</sup> with UACR  $\geq$  200 mg/g or
  - Heart failure, irrespective of level of albuminuria
- Recommendation 3.7.3: We suggest treating adults with eGFR 20 to 45 mL/min per 1.73 m<sup>2</sup> with UACR < 200 mg/g with an SGLT2i (2B)



## Question 4

A 62-year-old man with T2DM and HTN is hospitalized for disseminated herpes zoster and is started on intravenous acyclovir. On hospital day 2, he develops nausea and right flank discomfort. Vital signs are stable. Urine output has decreased. Repeat labs show serum creatinine of 2.4 mg/dL (baseline creatinine is 1.0 mg/dL). A urine sample is sent for microscopy. Which of the following is the most likely cause of this patient's acute kidney injury?

- A. Acute interstitial nephritis
- B. Acute tubular necrosis
- C. Obstructive crystal-induced tubulopathy
- D. Pre-renal azotemia due to volume depletion
- E. Uric acid nephropathy

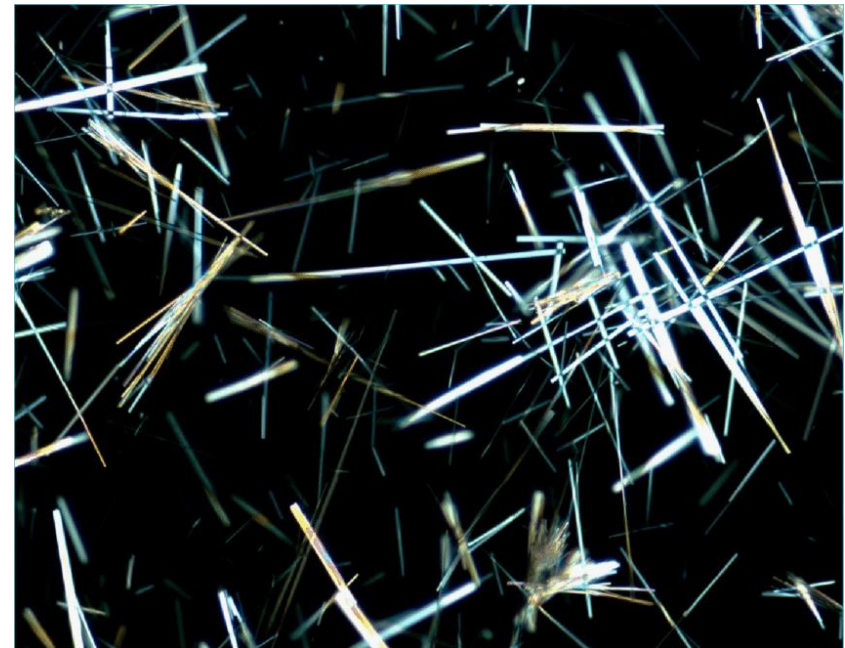




## Question 4

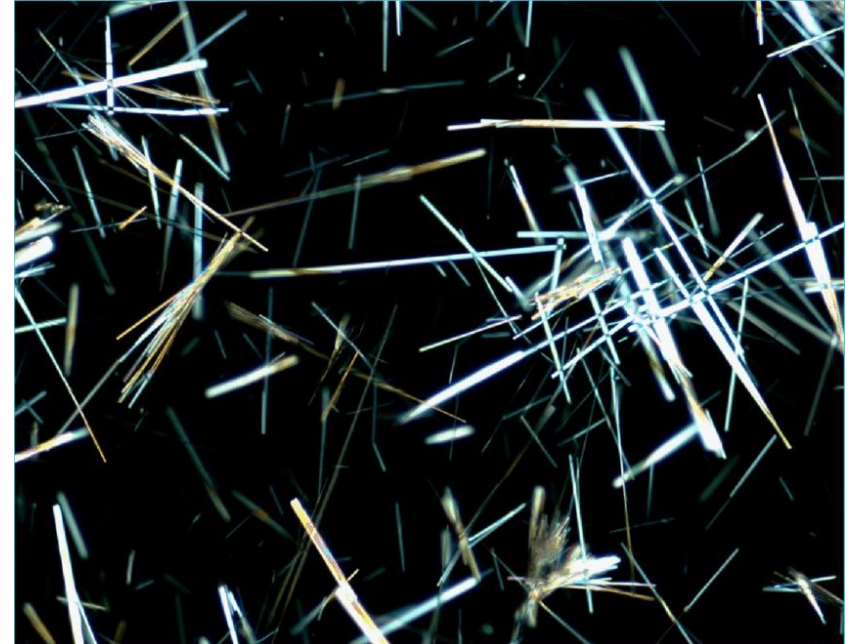
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# Acyclovir induced nephropathy

- Acyclovir is renally excreted (65-91%) via glomerular filtration and tubular secretion
- With low urine flow or volume depletion, the drug can precipitate as needle-shaped crystals leading to tubular obstruction and AKI





## Case 5



A 39-year-old man with ESKD experiencing homelessness presents to the emergency department with anorexia, nausea, fatigue, oliguria, and pruritus. Five months earlier, he had stopped attending his regular hemodialysis sessions. On exam, BP 167/80 mm Hg, lethargic, slowed speech and LE edema; breath has a urine-like odor.

What of the following is the MOST likely diagnosis?

- A. Retention keratosis
- B. Uremic frost
- C. Eczematous dermatitis
- D. Postinflammatory desquamation



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# Uremic frost

- First described by Hirschsprung in 1865
- Manifestation of severe azotemia
- Presents as tiny, yellow-white urea crystals deposited on the skin = frosted appearance
- Common on areas with eccrine glands (e.g. scalp, neck, face, forearms, chest)
- Can be easily wiped away
- Less common given availability of dialysis
- Among 9 cases of uremic frost published, mean BUN 199 mg/dL and mean creatinine 17.5 mg/dL

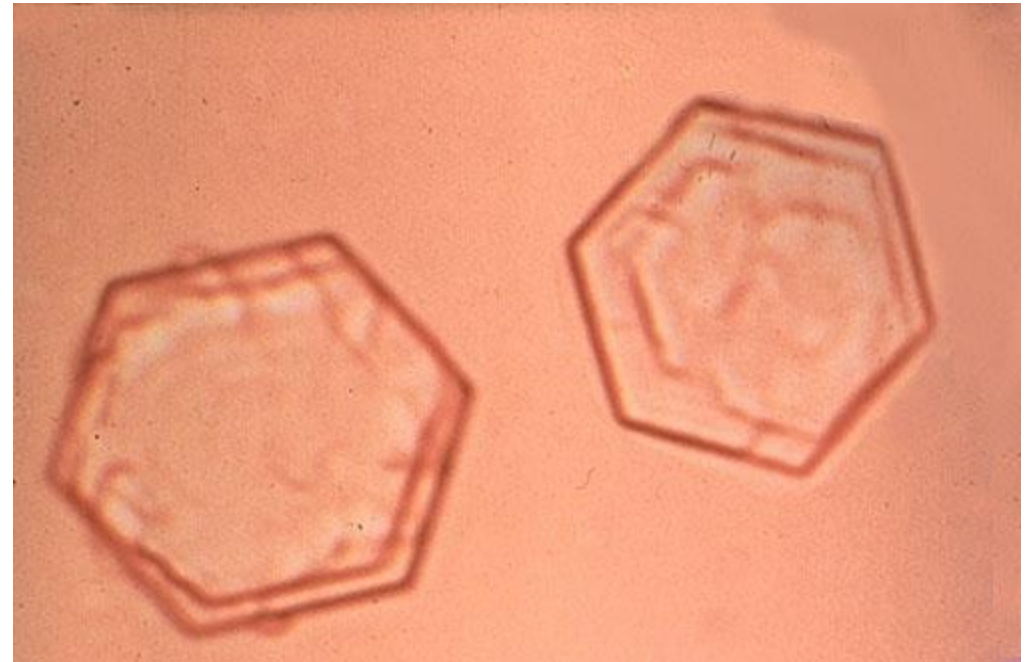




## Case 6

The urine sediment shown is associated with which genetic mutation?

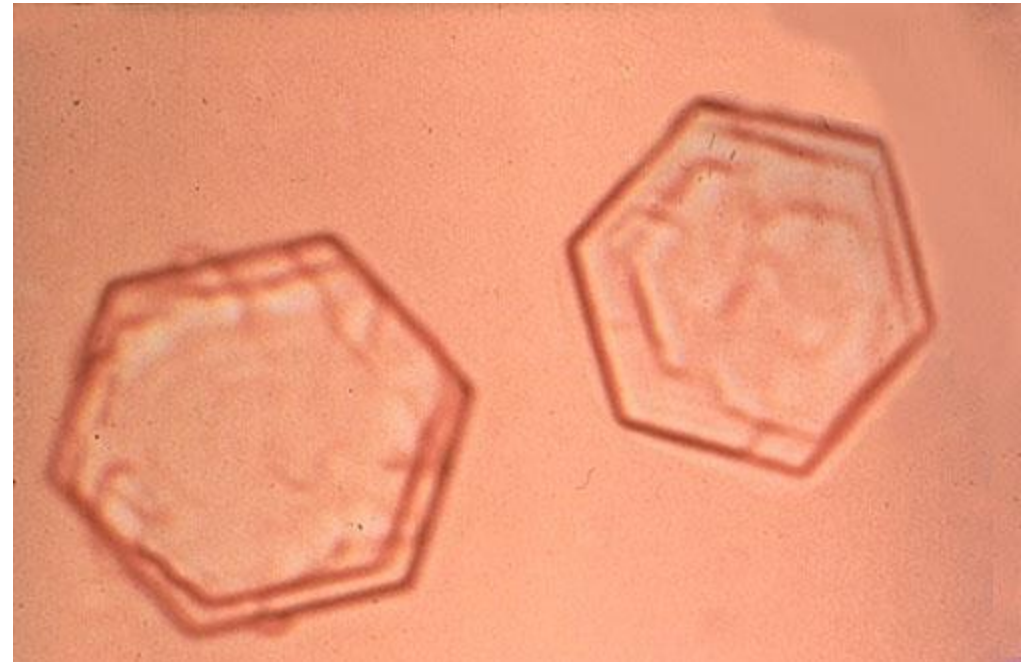
- A. SLC3A1
- B. PKD
- C. COL4A5
- D. NPHS2
- E. UMOD



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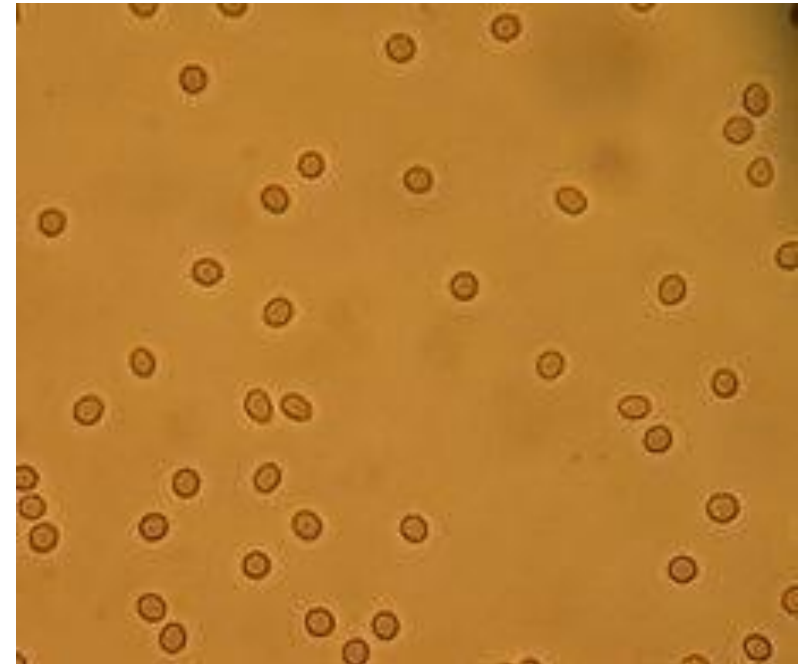
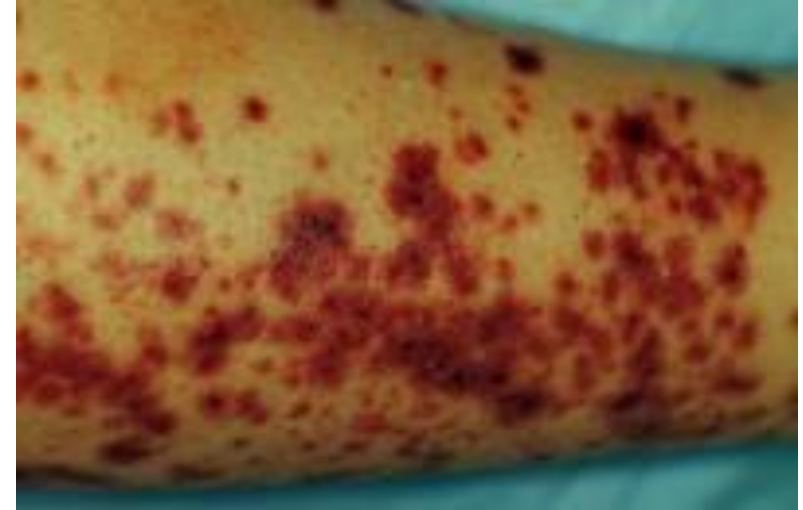
## A. SLC<sub>3</sub>A



- Cystine crystals are usually hexagonal, translucent, white.
- Cystinuria is a rare disorder but common genetic cause for nephrolithiasis
- Autosomal recessive is the most common pattern caused by mutations in the [SLC3A1](#) or [SLC7A9](#) genes.
- These genes encode two parts of a transporter controlling renal tubular reabsorption of dibasic amino acids (e.g. cystine) in the kidneys.
- The genetic defect results in urinary wasting of cystine, poorly soluble in urine at typical pH → cystine stones.

# Case 7

A 22-year old woman presents with arthralgias, abdominal pain and a rash on her lower extremities. Vital signs are stable, and serum creatinine 0.8 mg/dL. Urinalysis shows: 2+ blood, 1+ protein with microscopy (shown). A fecal occult blood test is positive.



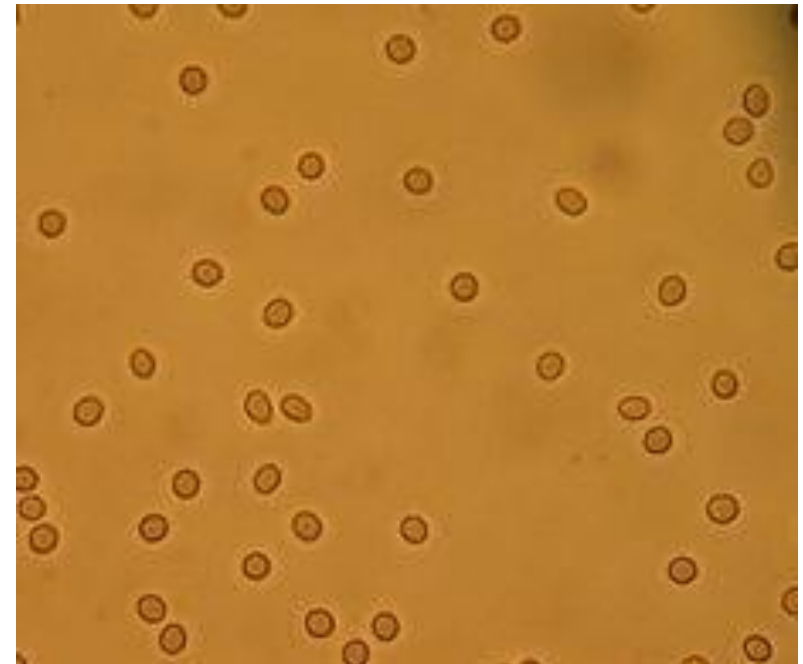
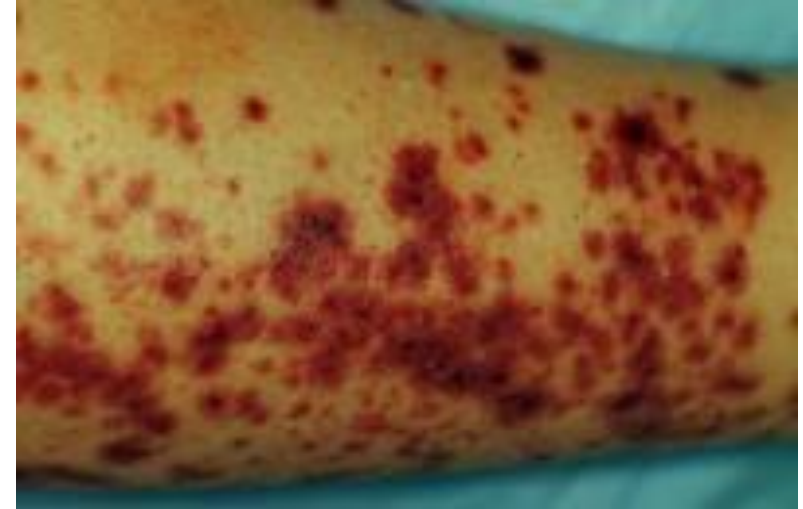
What is the MOST likely diagnosis?

- A. Renal cell carcinoma
- B. Renal infarction
- C. Nephrolithiasis
- D. Anti-GBM disease
- E. IgA vasculitis



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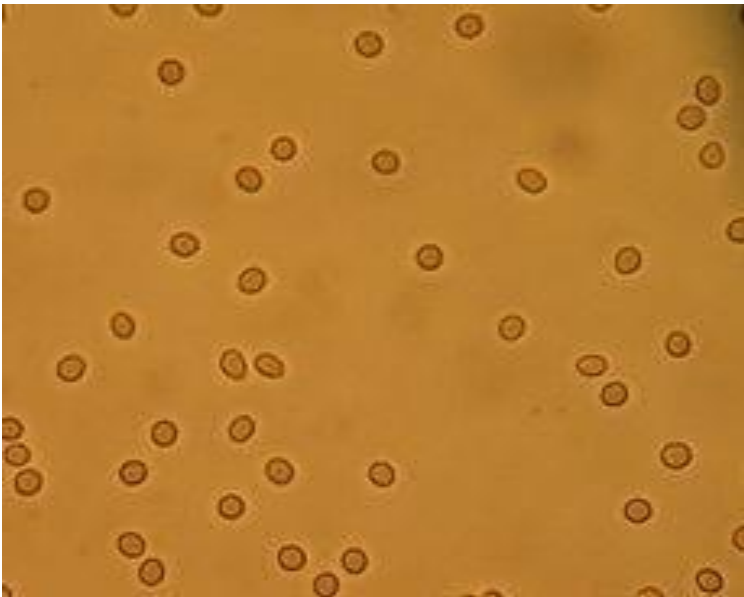
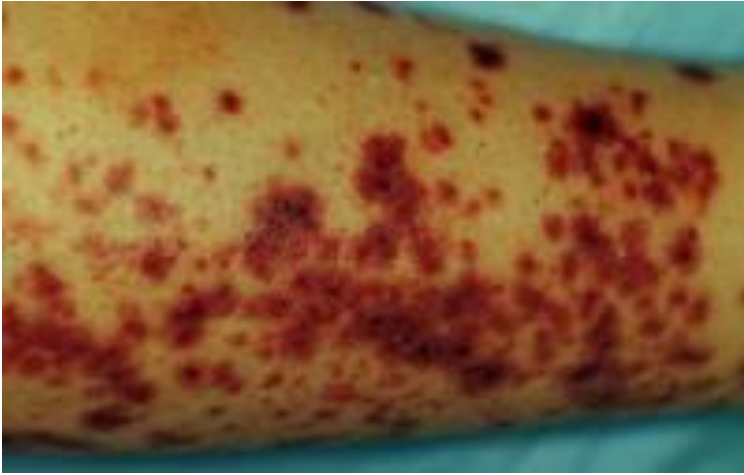
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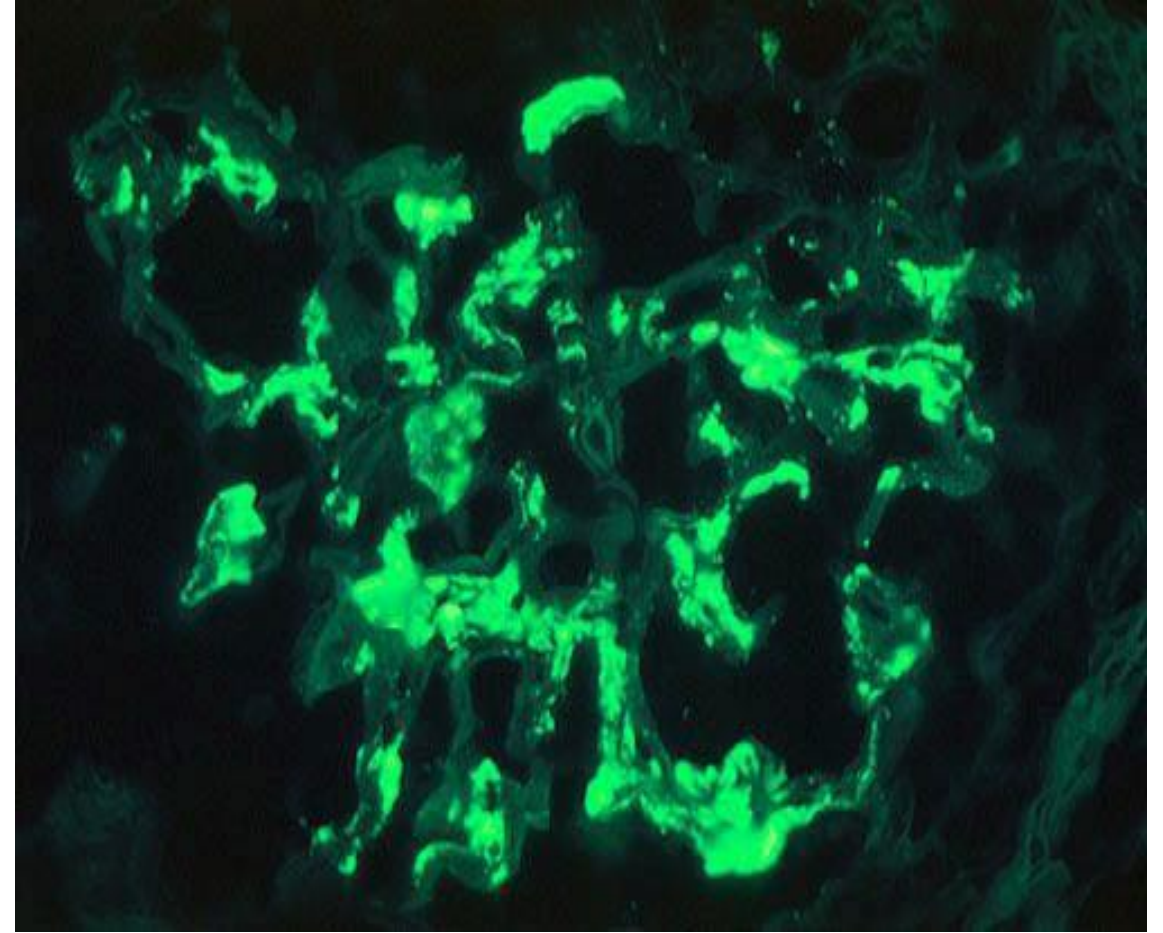
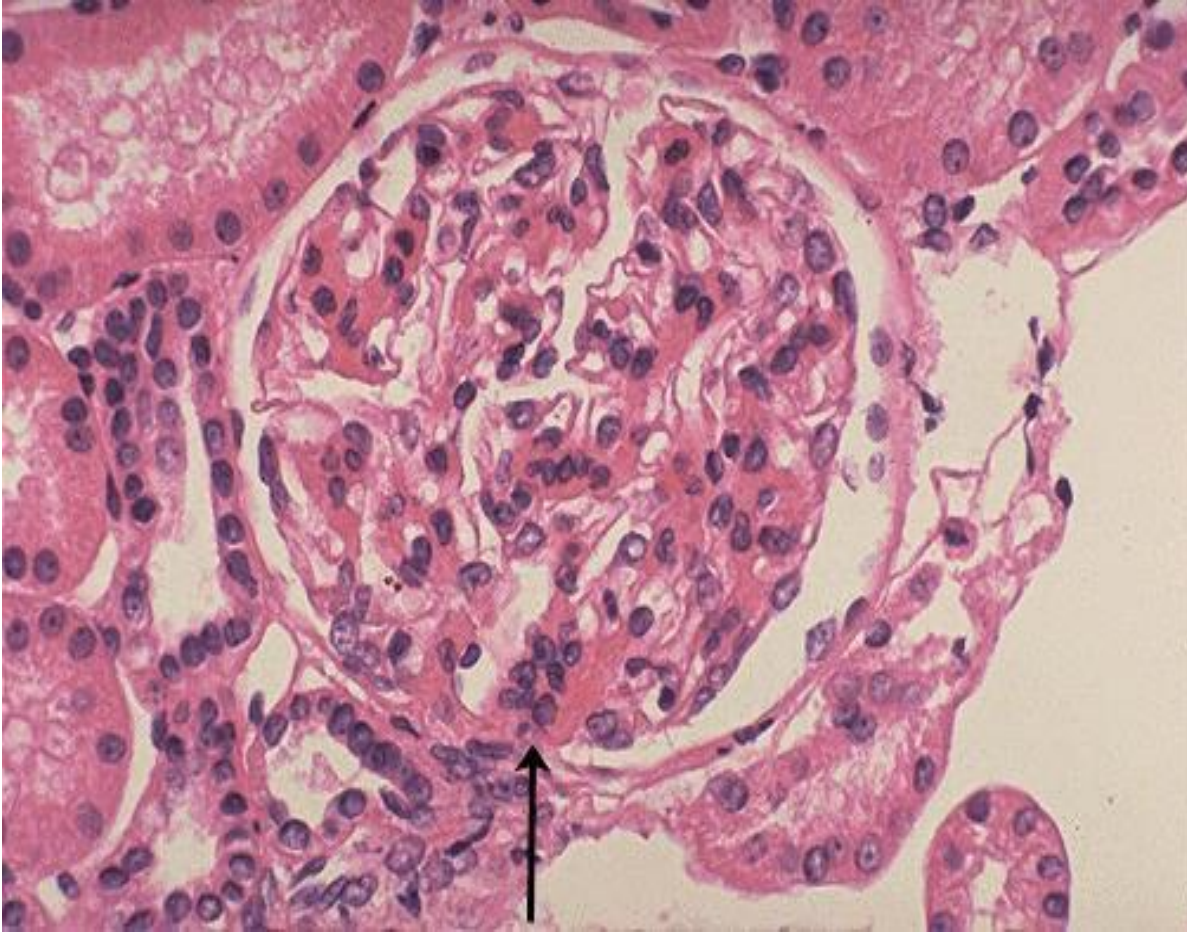


## E. IgA Vasculitis



- Formerly known as Henoch-Schonlein Purpura
- Hints:
  - Palpable purpura
  - Hematuria -- red cells appear crenated - dysmorphic red cells
  - Arthralgia
  - GI involvement

# Pathology of IgA Nephropathy



## Case 8



**What is the most likely diagnosis?**

- A. Renal tubular acidosis**
- B. Primary hypoparathyroidism**
- C. Familial hypocalciuric hypercalcemia**
- D. Salicylate overdose**
- E. Paget's disease**

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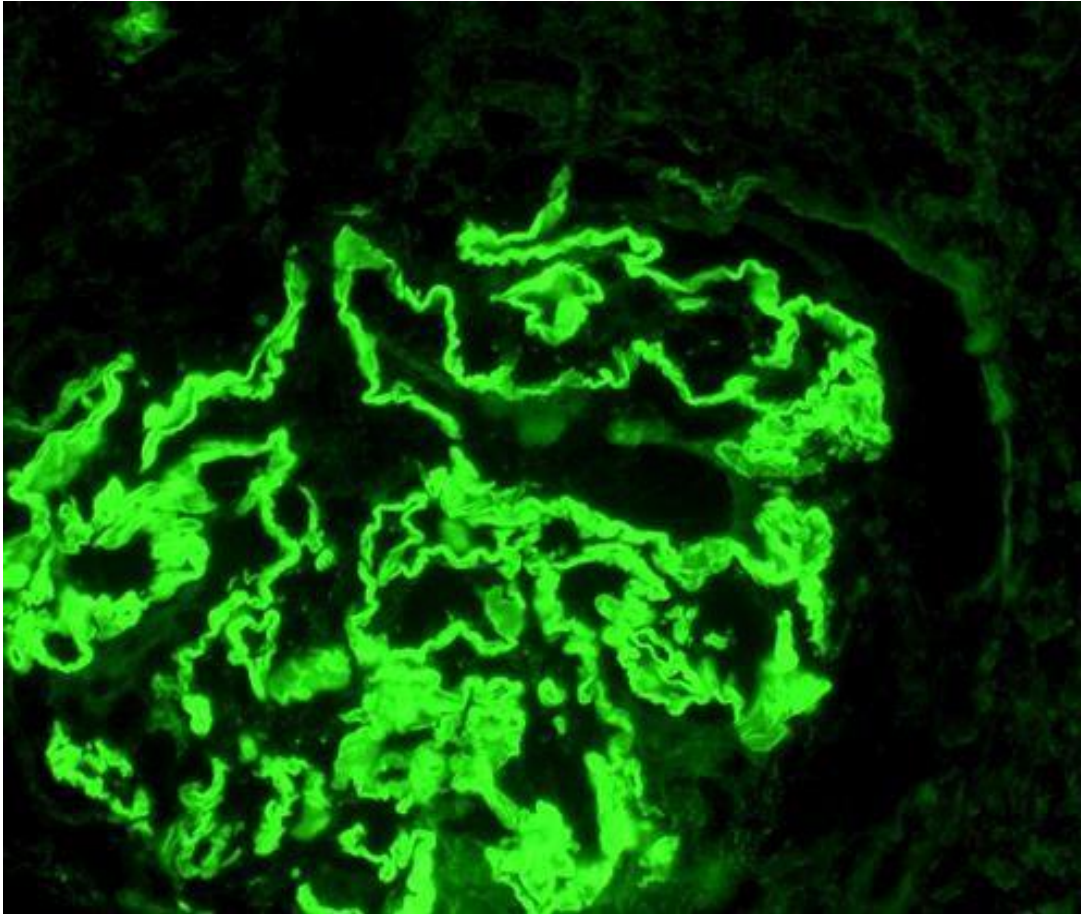
## A. Renal Tubular Acidosis



**The film reveals bilateral symmetric calcification of the renal parenchyma, sparing only the renal pelvis. This patient had been diagnosed with renal tubular acidosis at 9 years of age, but did not undergo medical follow-up for 20 years. The other listed choices are not common causes of nephrocalcinosis.**



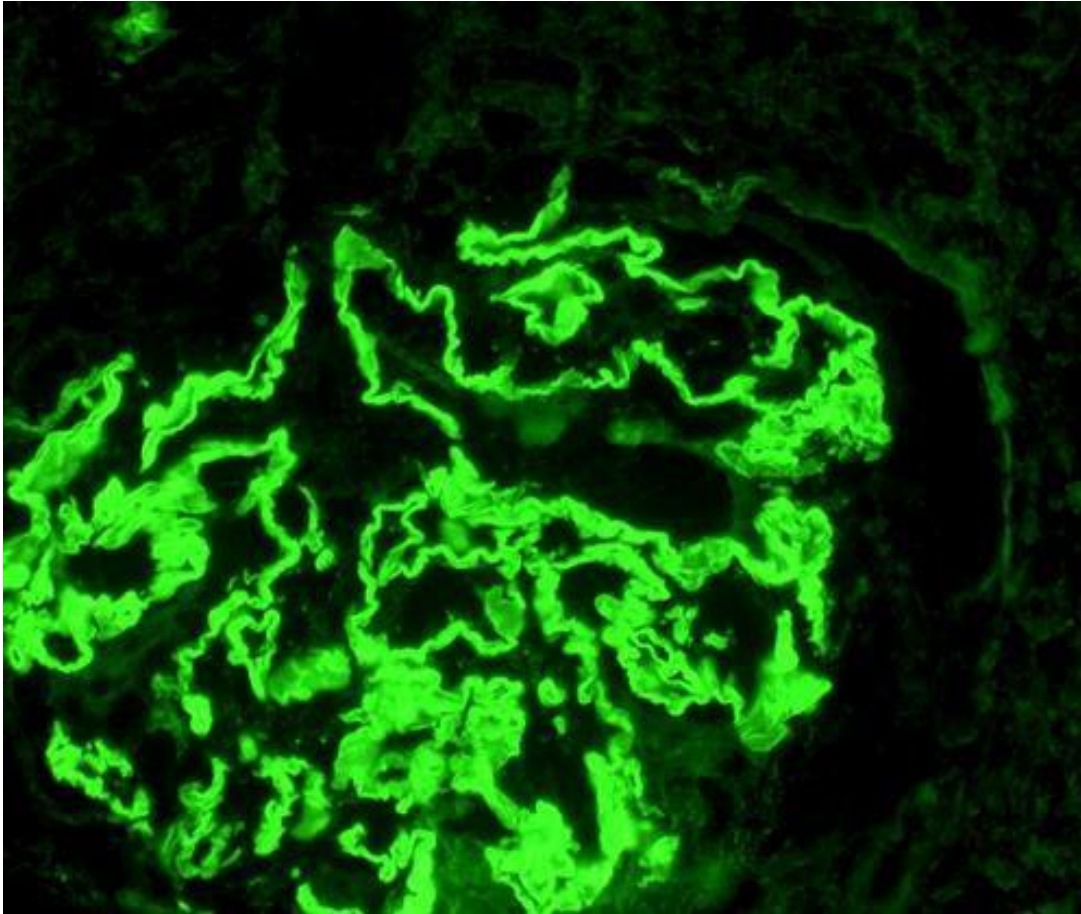
## Case 9



The most likely diagnosis is

- A. Idiopathic focal segmental glomerulosclerosis
- B. Diabetic nephropathy
- C. Membranoproliferative glomerulonephritis
- D. Microscopic polyangiitis
- E. Anti-GBM nephritis

## Case 9



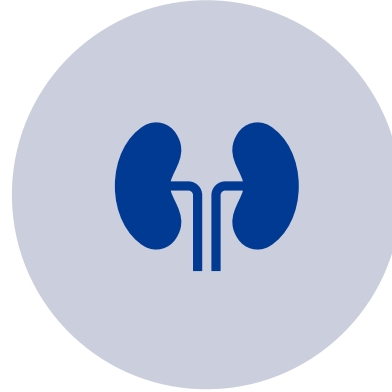
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## E. Anti-GBM antibody glomerulonephritis



DR. ERNEST GOODPASTURE,  
RESIDENT OF THE MGH PATH  
DEPARTMENT, MOONLIGHTING AT  
THE CHELSEA NAVAL HOSPITAL,  
REPORTED AUTOPSY FINDINGS IN  
YOUNG SAILORS (AM J MED SCI,  
1919)



1958, STANTON AND TANGE  
USED THE TERM  
GOODPASTURE'S SYNDROME:  
HEMORRHAGE AND  
GLOMERULONEPHRITIS (AUST  
ANN MED, 1958)



1964, SCHEER AND  
GROSSMAN REPORTED  
LINEAR STAINING ON IF (ANN  
INTERN MED, 1964)

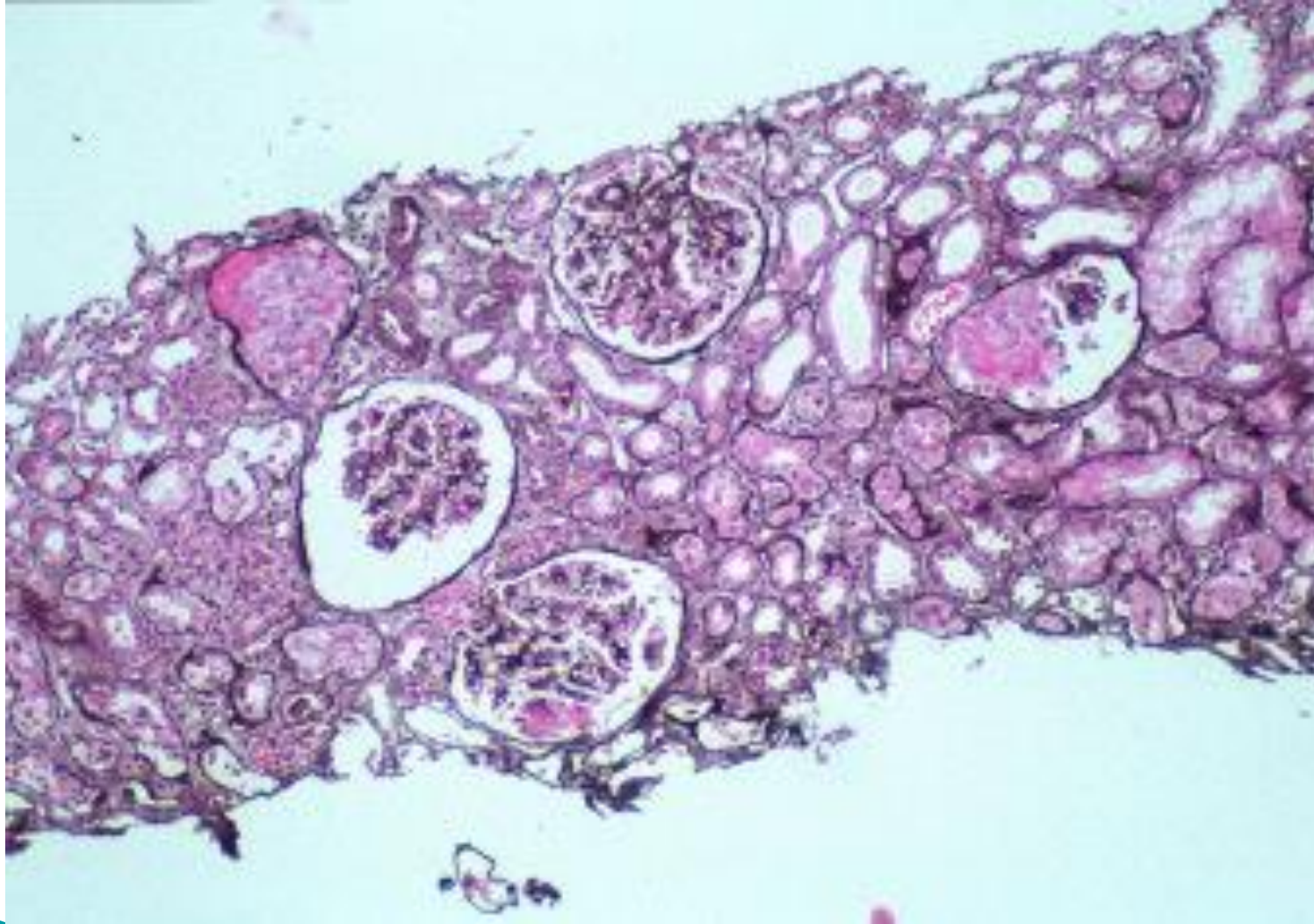
# Anti-GBM antibody glomerulonephritis

- Incidence 1 case/million per year in the U.S.
- 1-2% of renal biopsy specimens
- Bimodal age distribution: late teens to 20s and 50-70 years old)
- Slight predominance in males
- Presentation:
  - 50-75% have upper respiratory prodrome (e.g. hemoptysis, cough, dyspnea), anemia
  - Severe kidney injury in a manner of RPGN
  - Microscopic hematuria

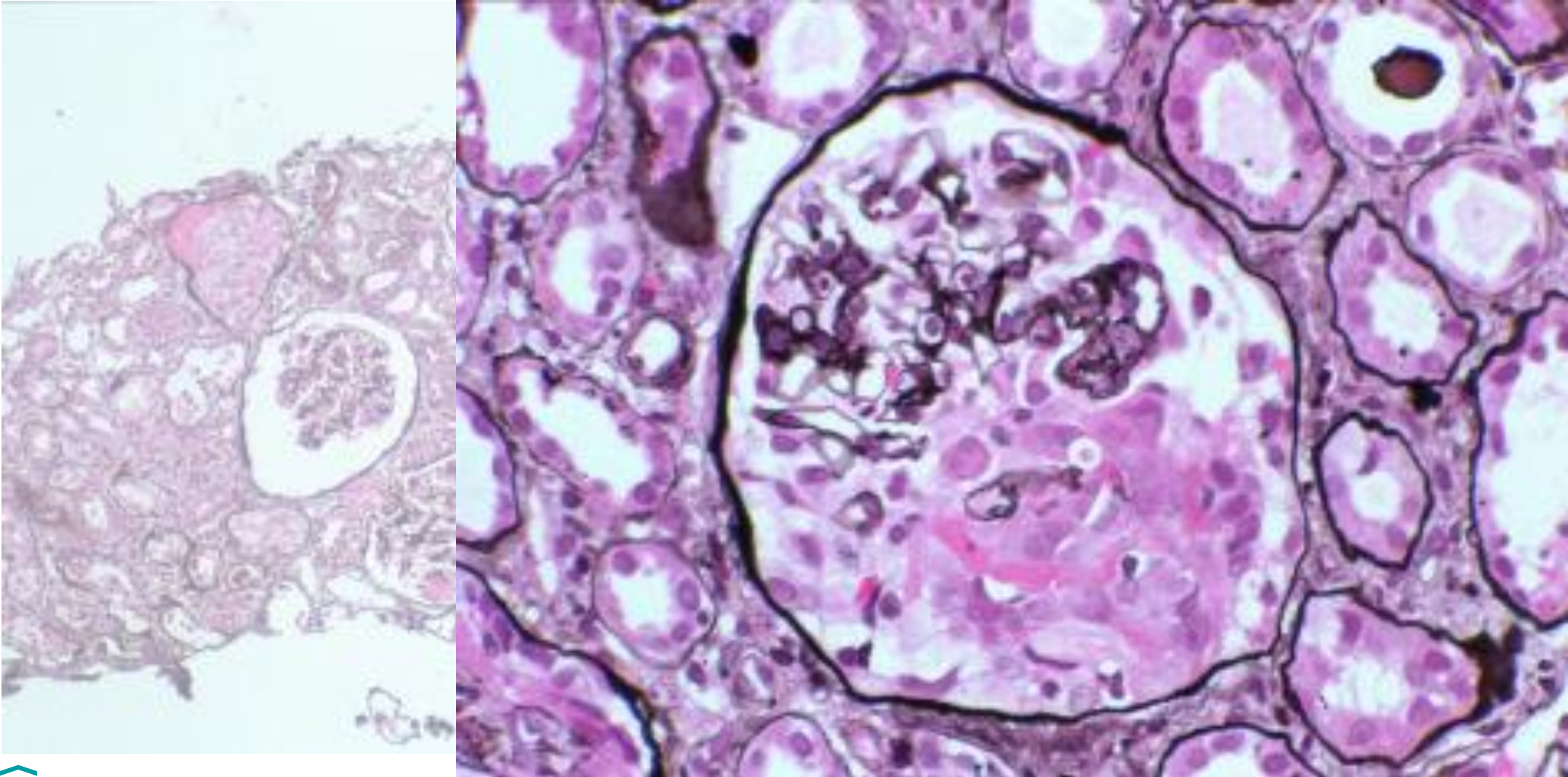




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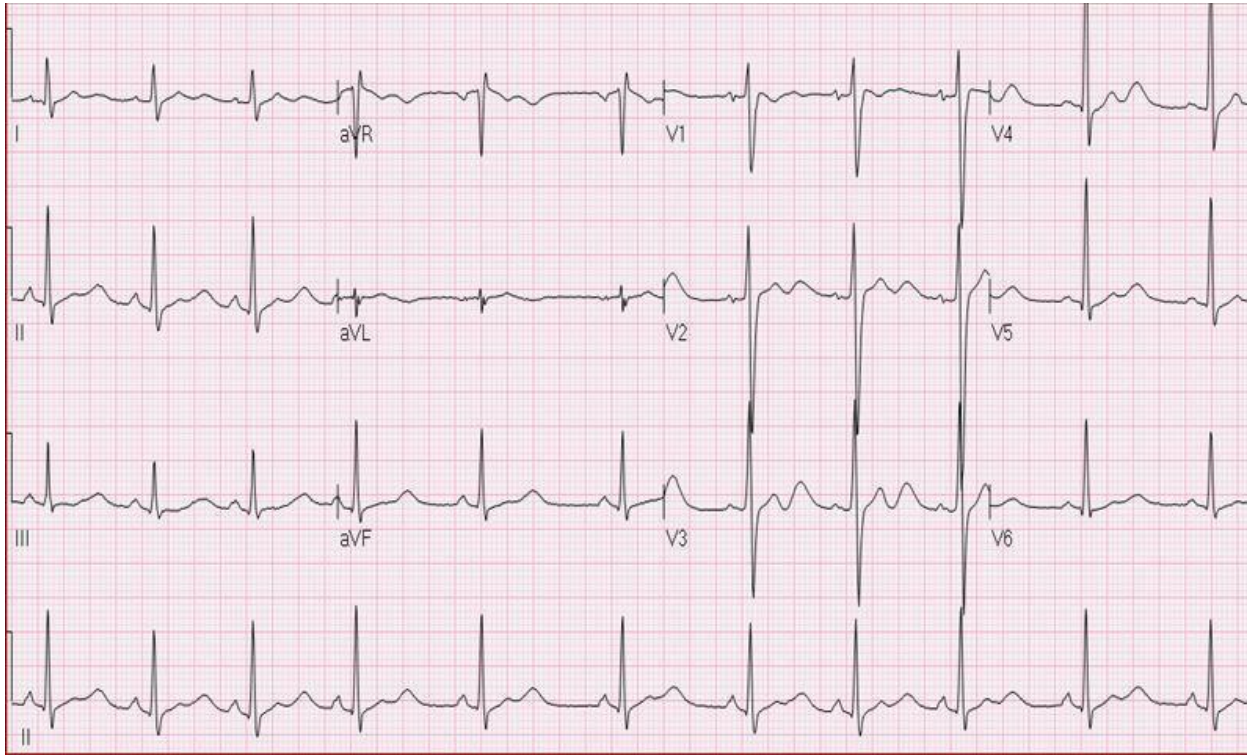


# Anti-GBM antibody glomerulonephritis





## Case 10

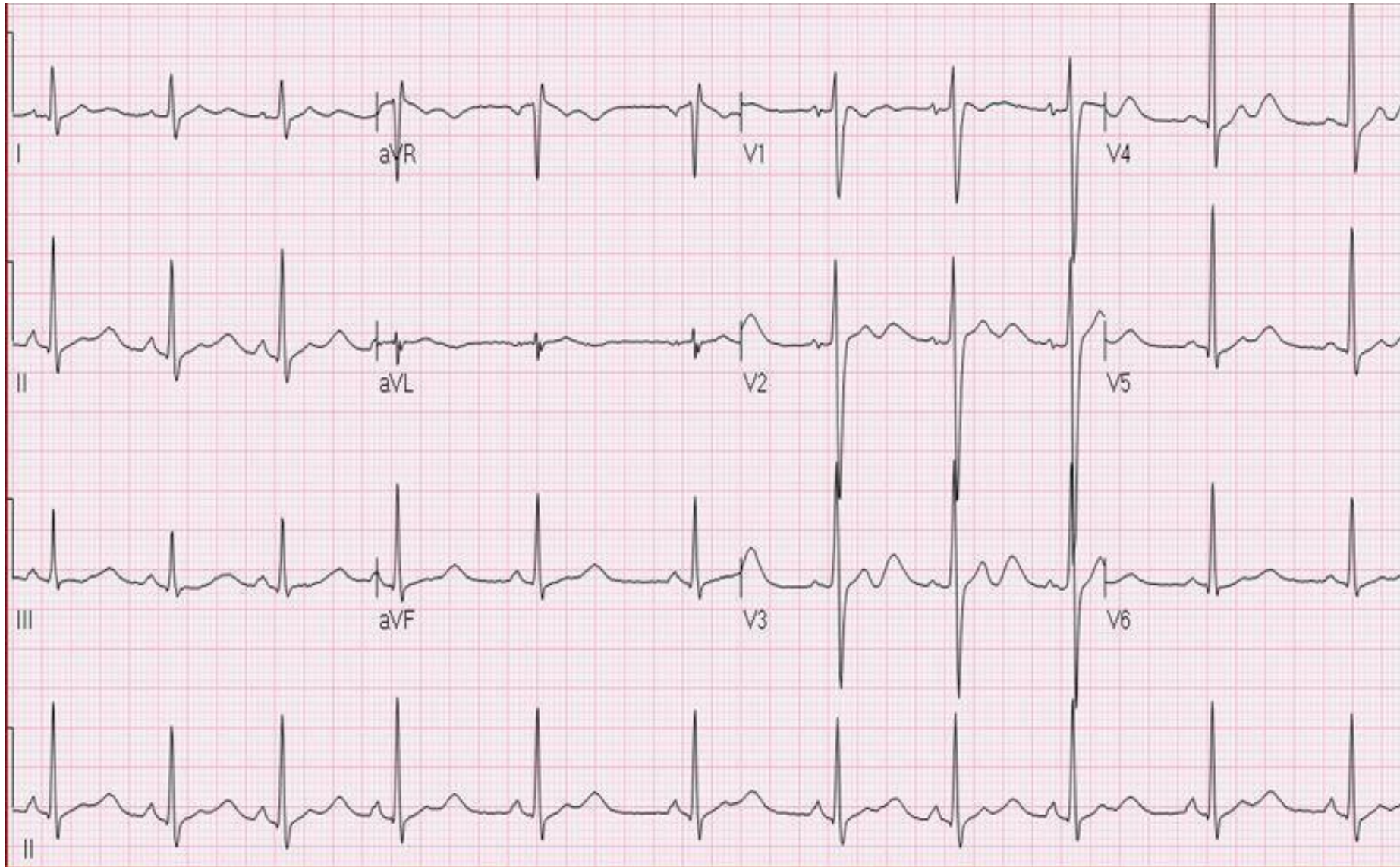


A 48 year old man with CKD (baseline creatinine of 1.5 mg/dL) presents with weakness, fatigue and an episode of palpitations. His medications include furosemide 40 mg BID, lisinopril 20 mg QD, atorvastatin 20 mg QD and aspirin 81 mg QD.

Based on the ECG, what is the most likely diagnosis?

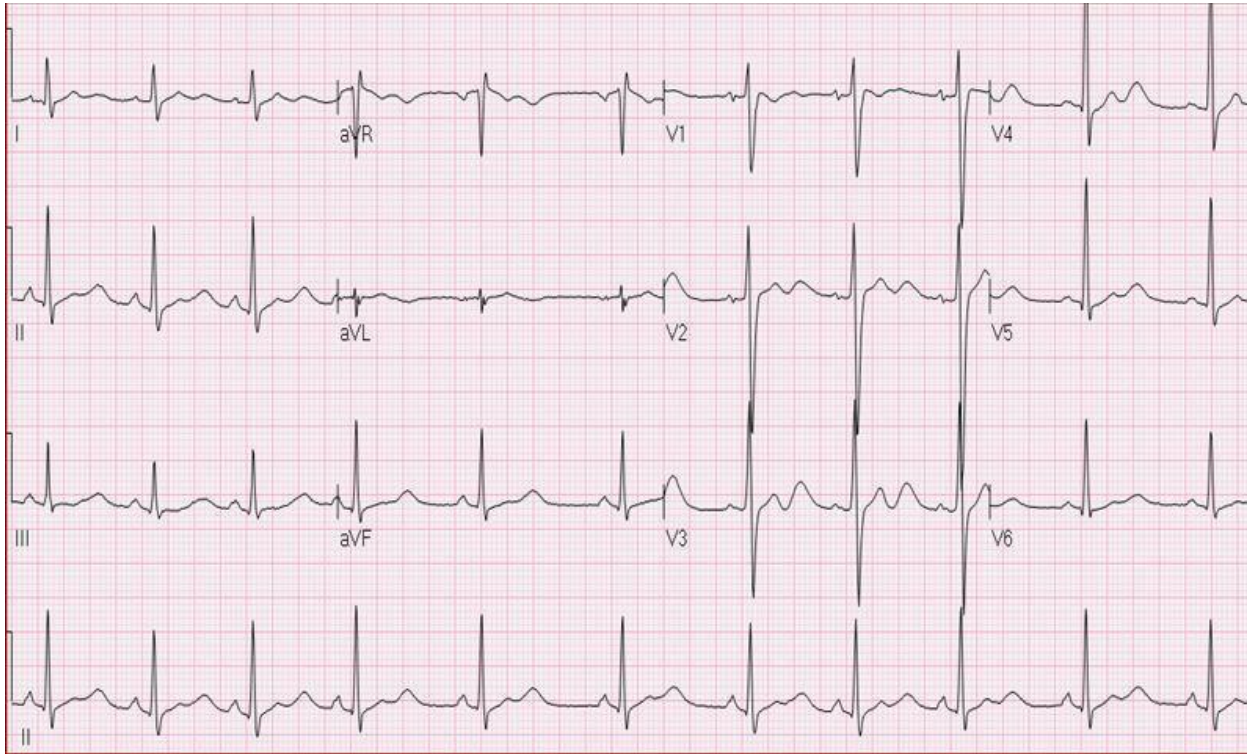
- A. Hypomagnesemia, Mg 1.4 mg/dL
- B. Hypokalemia, K 2.0 mEq/L
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## Case 10





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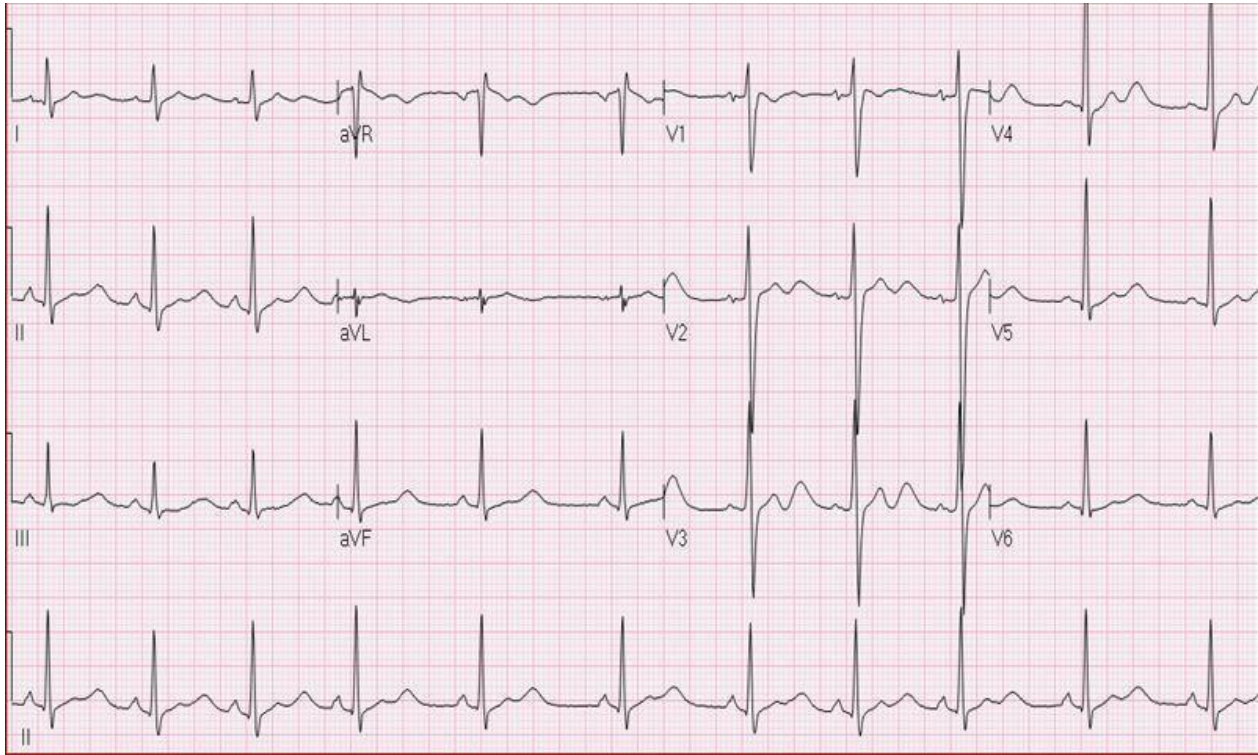


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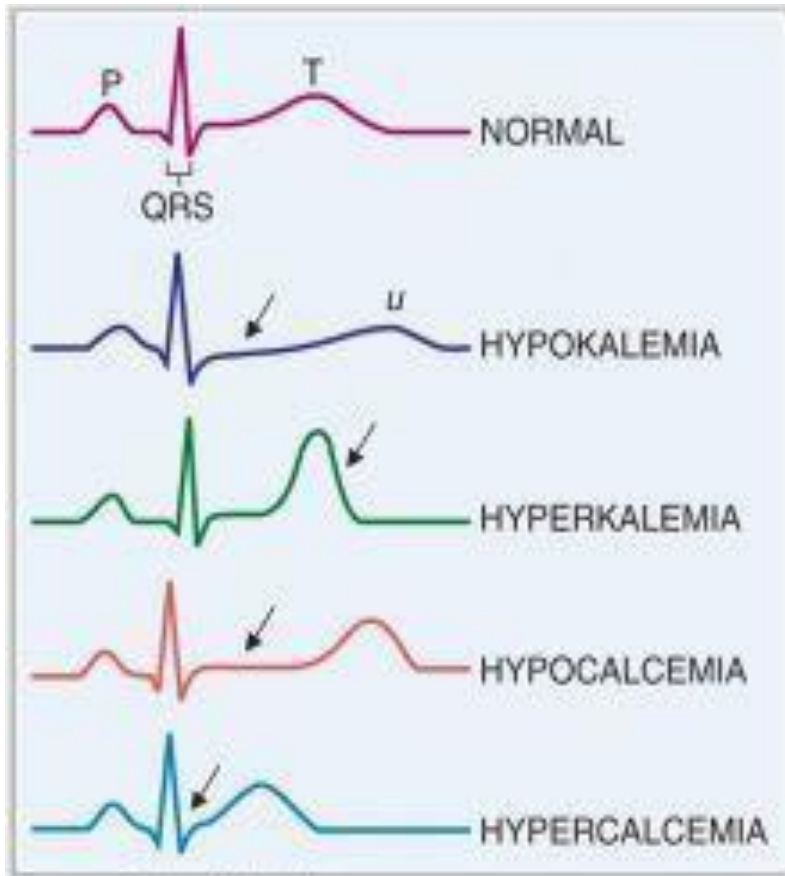
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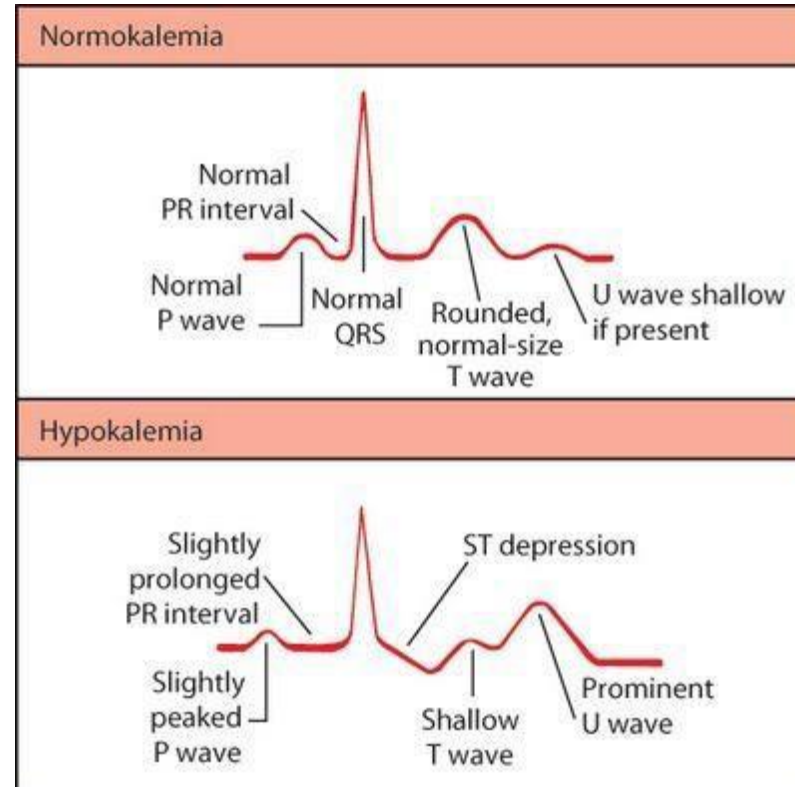
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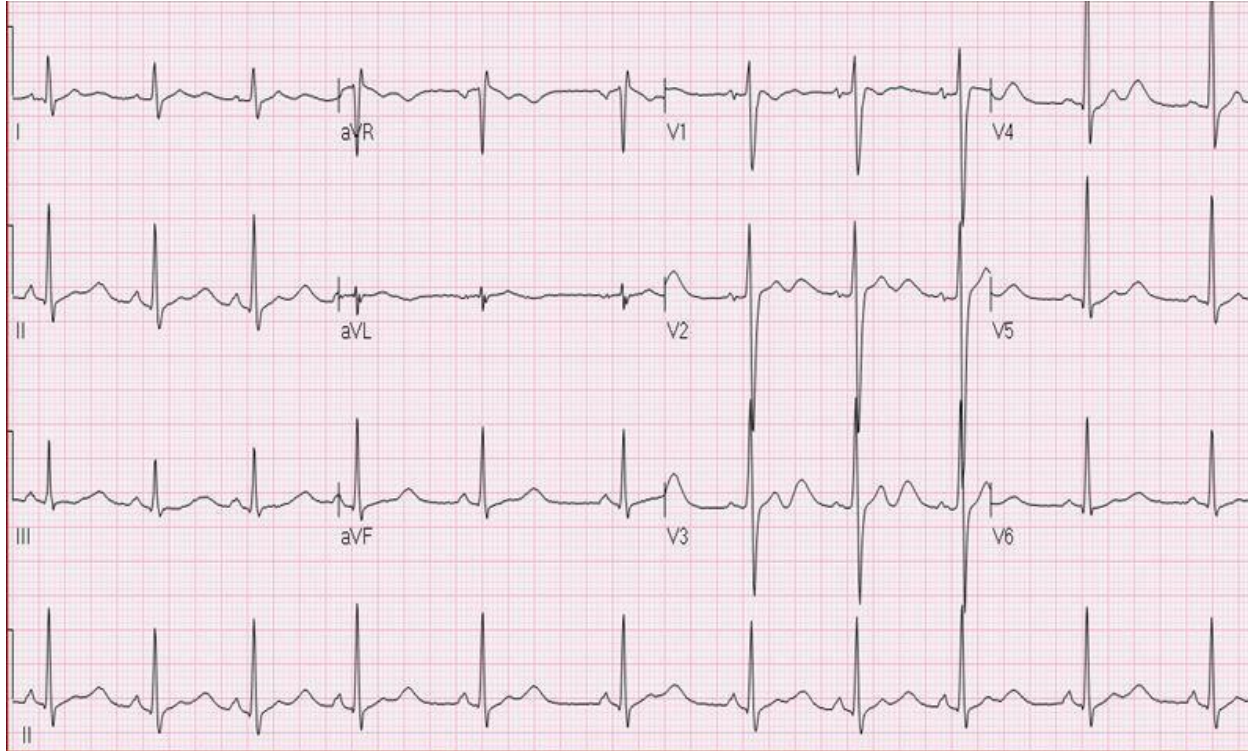


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## B. Hypokalemia



- T wave flattening
- Increase in amplitude of U wave
- ST segment depression
- Associated with increased risk for premature ventricular contractions and supraventricular and ventricular tachyarrhythmias



## Case 11



**This 64-year old woman with ESKD on iHD presents with a painful ulcerative skin lesion on her thigh. She reports it began as a reddish rash and ulcerated over a few weeks.**

**Which of the following is the most appropriate next step to confirm the diagnosis?**

- A. MRI of the affected limb**
- B. Wound swab for bacterial culture**
- C. Skin biopsy**
- D. Serum protein C and S levels**
- E. Lupus serologies**

## Case 11

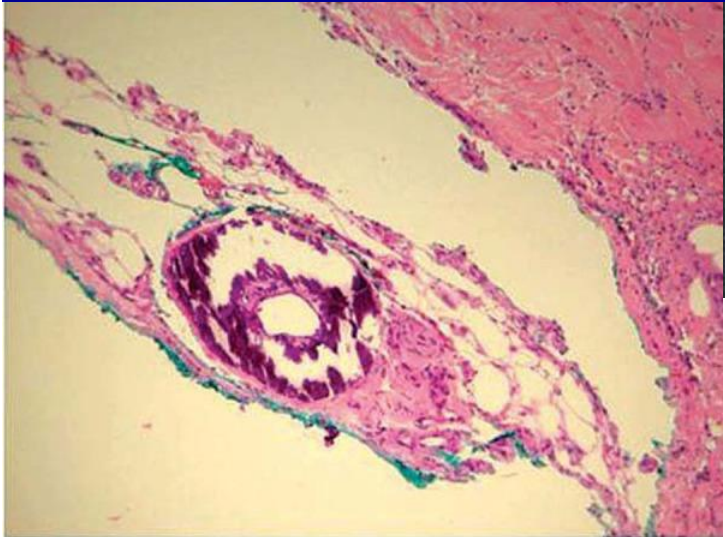


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## C. Skin biopsy



### Calcific uremic arteriolopathy (CUA)

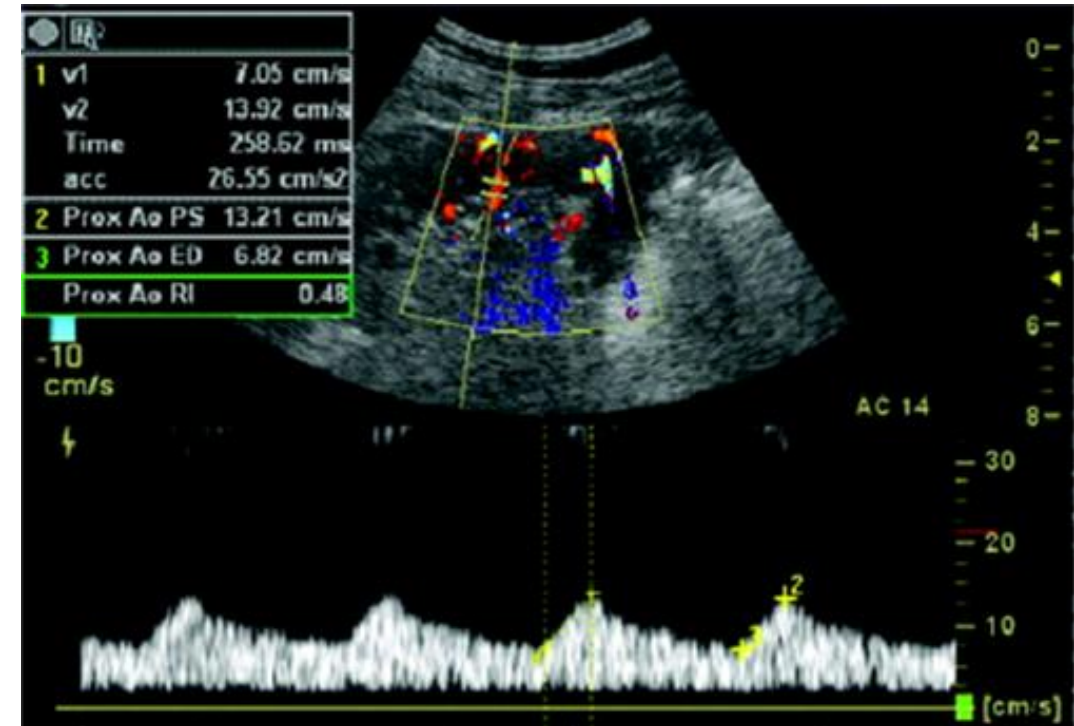
- 1% to 4.5% of patients in dialysis
- Classical presentation: initial skin lesion, livedo reticularis-like on the lower limbs, which progress to violaceous, painful, plaque or subcutaneous nodules, followed by ischemic/necrotic ulcers of reticular pattern.
- DDx:
  - Necrotizing fasciitis
  - Pyoderma gangrenosum,
  - Coumadin necrosis
  - SLE
- 1-year mortality 40-80%
- Skin biopsy confirming arteriolar calcification and mural thrombosis associated with septal panniculitis.

## Case 12

A 68 year old man with a history of HTN, type 2 diabetes, and CAD presents for follow up. His current medications include amlodipine and lisinopril (initiated 4 weeks ago). On exam, BP 162/94, serum creatinine 1.7 mg/dL (1.3 mg/dL two weeks ago), potassium 4.8 mEq/L, urinalysis shows 1+ protein, no hematuria or casts. Renal duplex ultrasonography is shown.

Which of the following is the most appropriate next step in management?

- A. Discontinue lisinopril and initiate hydralazine
- B. Continue lisinopril and add thiazide diuretic
- C. Refer for immediate renal artery stenting
- D. Add spironolactone for improved blood pressure control
- E. Discontinue lisinopril and initiate clonidine



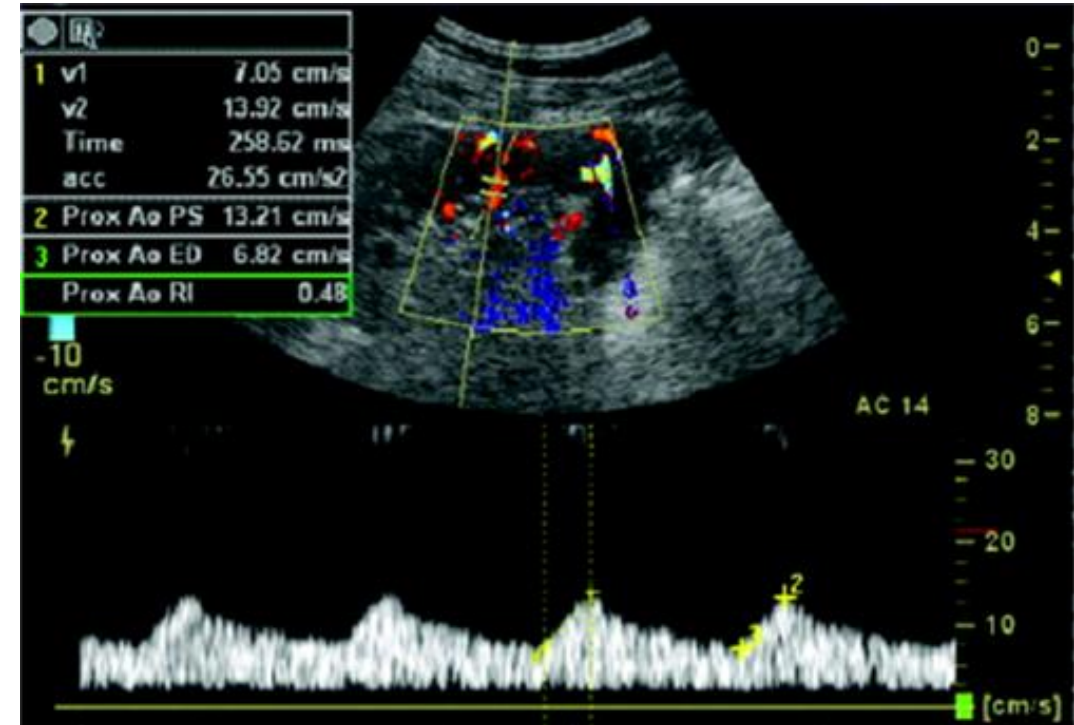


## Case 12

A 68 year old man with a history of HTN, type 2 diabetes, and CAD presents for follow up. His current medications include amlodipine and lisinopril (initiated 4 weeks ago). On exam, BP 162/94, serum creatinine 1.7 mg/dL (1.3 mg/dL two weeks ago), potassium 4.8 mEq/L, urinalysis shows 1+ protein, no hematuria or casts. Renal duplex ultrasonography is shown.

Which of the following is the most appropriate next step in management?

- A. Discontinue lisinopril and initiate hydralazine
- B. Continue lisinopril and add thiazide diuretic
- C. Refer for immediate renal artery stenting
- D. Add spironolactone for improved blood pressure control
- E. Discontinue lisinopril and initiate clonidine





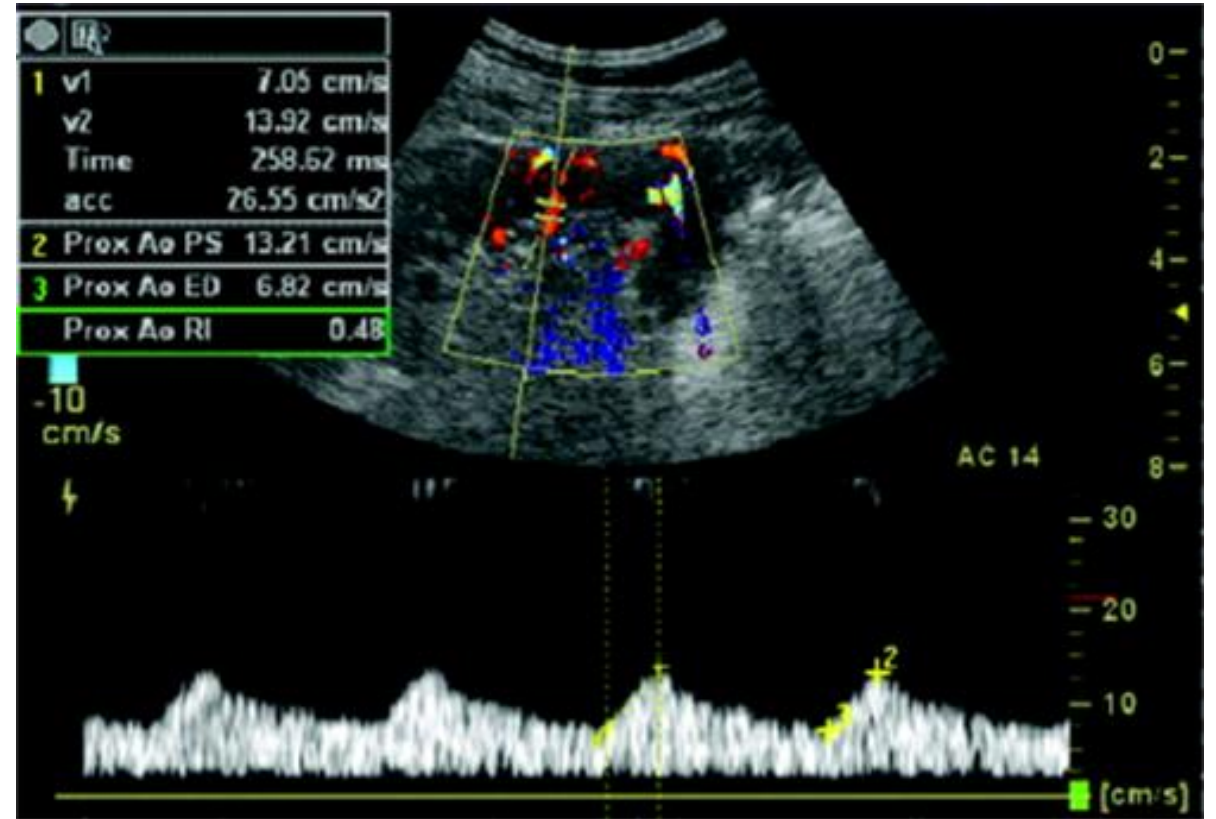
# Resistant Hypertension

- Definition: BP is not at goal despite 3 different classes of antihypertensives at the highest tolerated dose with one being a diuretic
- Patients with resistant HTN are nearly 50% more likely to have a cardiovascular event and 25% more likely to develop kidney failure than those with HTN that is not resistant



# Renal artery stenosis (RAS)

- RAS is common among those with resistant HTN, especially older adults with known vascular disease, smoking history, diabetes, and CKD
- Duplex ultrasound imaging is the most common initial imaging test performed in those with a high pretest probability of a RAS diagnosis
- Elevated peak systolic velocity is the most sensitive and specific ultrasound criterion for a RAS diagnosis
  - Most common abnormality is a tardus-parvus waveform



# Revascularization in atherosclerotic renovascular disease

- In 1960s, surgical revascularization of the kidney became standard therapy for selected patients with renovascular hypertension
- Later expanded in the 1980s to endovascular revascularization with stent implantation
- Three RCTs (STAR, ASTRAL, and CORAL) directly compared stent placement with medical therapy vs. medical therapy alone.
  - Result: renal revascularization did not consistently lower blood pressure, restore kidney function, or prevent CV outcomes more effectively than optimal medical therapy alone over 3-5 years
  - Limitation: under-enrollment of the most hemodynamically significant renal artery stenoses



# TAKE HOME MESSAGES

1. Images in question stems are helpful adjunct to narrow the answer choices
2. Know the classic urine microscopy findings





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# CLINICAL TRIALS

Clinical Trials	Change in Management
DAPA-CKD (2020) EMPA-KIDNEY (2022)	Established and confirmed that SGLT2i improve renal and cardiovascular outcomes in patients with CKD and albuminuria, regardless of diabetes status
Effects of empagliflozin on progression of chronic kidney disease: a prespecified secondary analysis from the EMPA-KIDNEY trial. Lancet Diabetes Endocrinol. 2024. doi: 10.1016/S2213-8587(23)00321-2	Secondary analysis of EMPA-KIDNEY, empagliflozin reduced progression of CKD in different subgroups of patients with CKD, including patients without albuminuria <b><i>Use of SGLT2i for patients with heart failure or CKD (eGFR &lt;45) without albuminuria</i></b>

