

Kidney Biopsy: Clinical Correlations

Pre-Session Syllabus



**KIDNEY
WEEK** 20
26

Case 1 from Hae Yoon Grace Choung, MD, Cedars-Sinai Medical Center

A 63-year-old man with hypertension, benign prostatic hyperplasia, hyperlipidemia, asthma, and gout presents to nephrology for routine follow-up for his CKD and is found to have nephrotic-range proteinuria. 24-hour urine shows 8.1 grams of protein. His basic metabolic panel is significant for elevated serum creatinine of 1.4 mg/dL (increased from 1.2 mg/dL). Urine sediment is bland. Blood pressure is 175/97. Otherwise, physical exam is normal, including no peripheral edema. Serologies for antinuclear antibody (ANA) and hepatitis B and C are negative. C3 and C4 are normal. Kappa and lambda free light-chain ratio is normal. He had a kidney biopsy performed more than 10 years ago at an outside institution, but the biopsy report and slides are not available for review. Because of the nephrotic-range proteinuria, a second kidney biopsy is performed.

Biopsy Images

Figure 1. Light microscopy: A. Trichrome, magnification 400x. B. H&E, magnification 200x. C. Jones silver, magnification 400x.

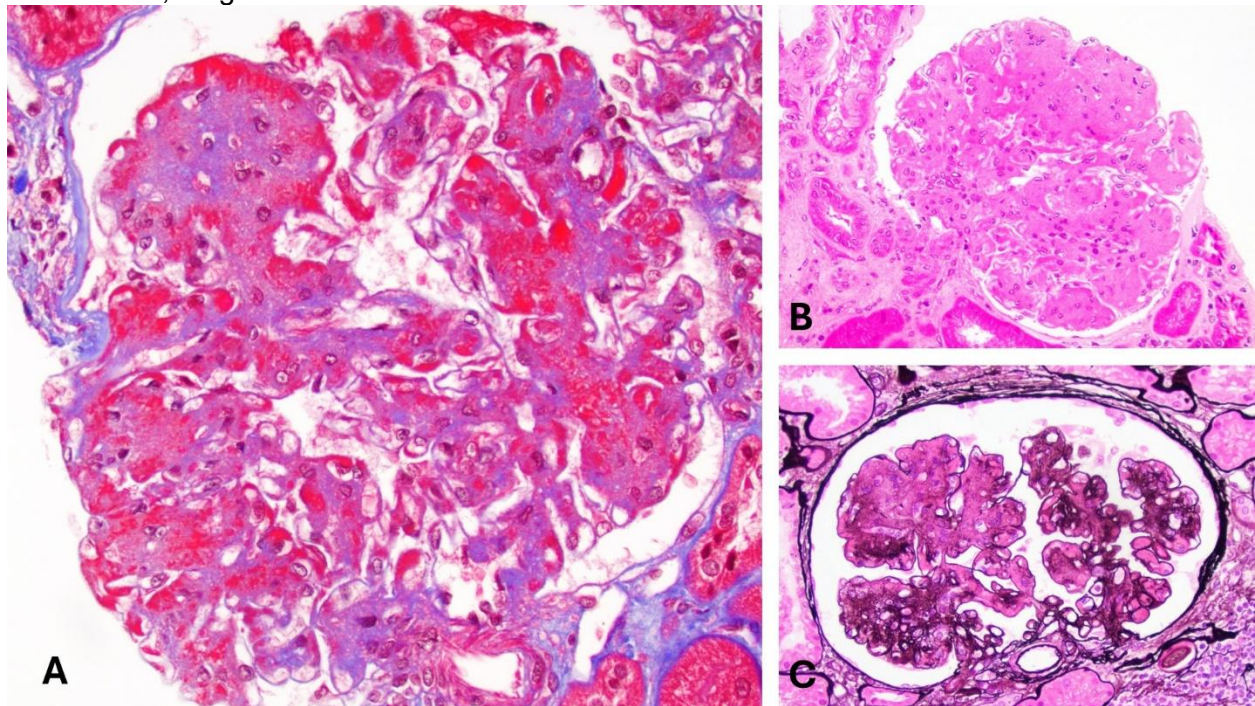


Figure 2. Immunofluorescence microscopy with antifibronectin antibody:

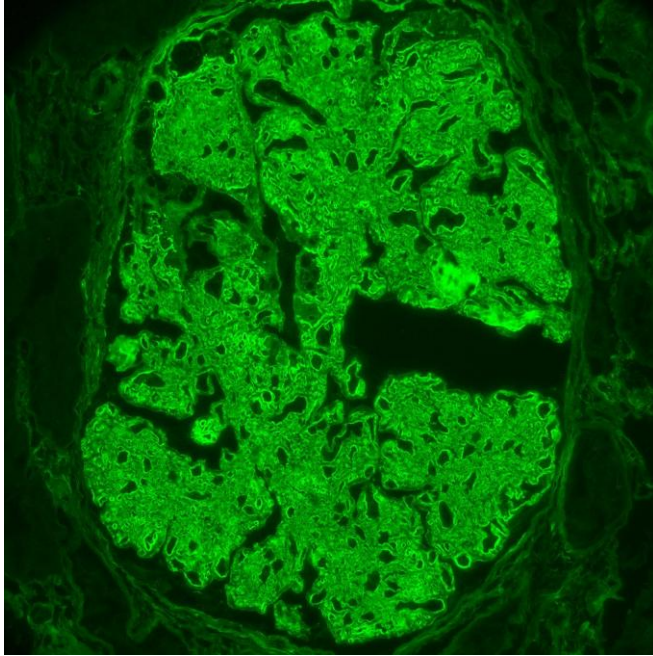


Figure 3. Electron microscopy:

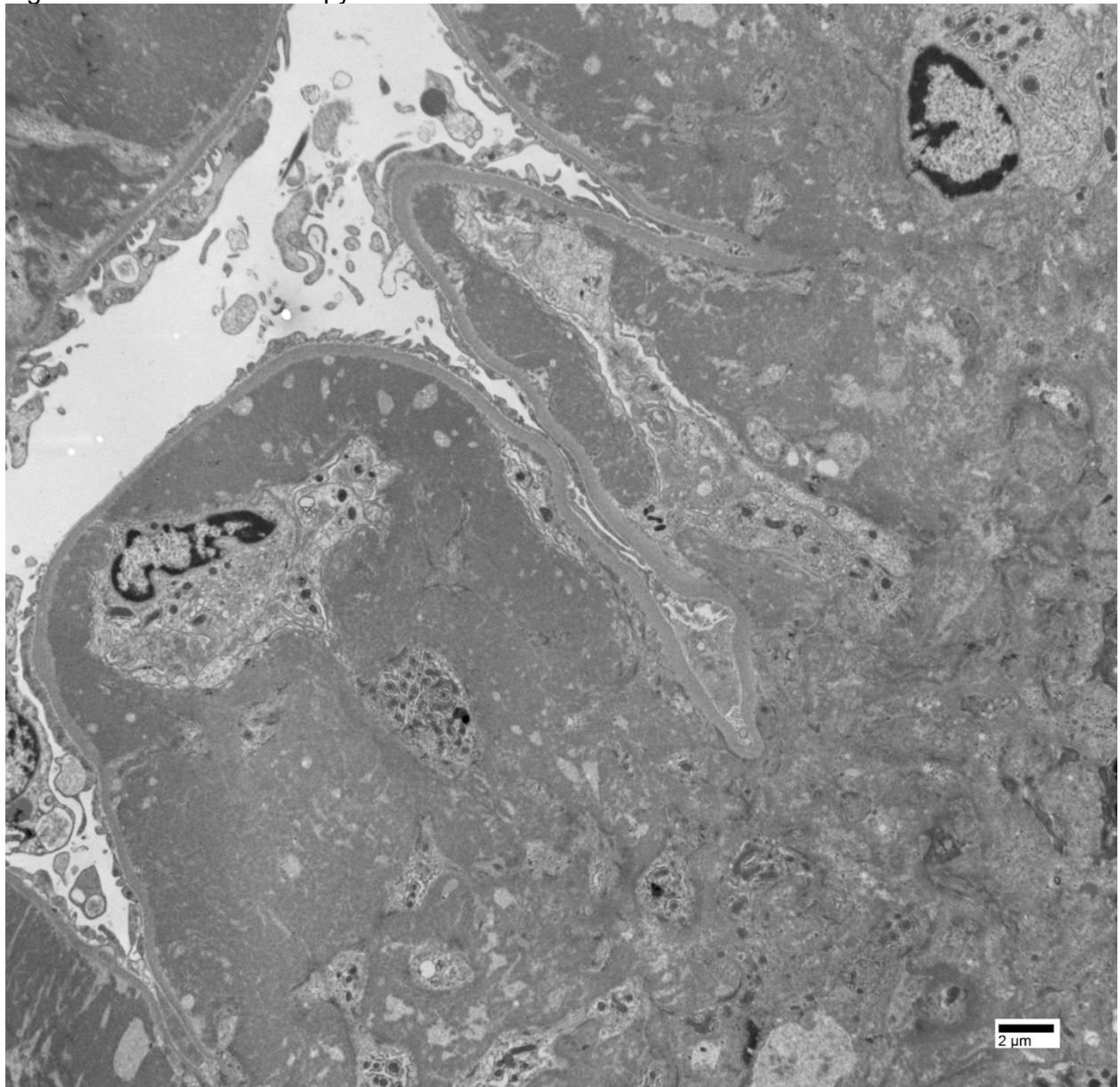
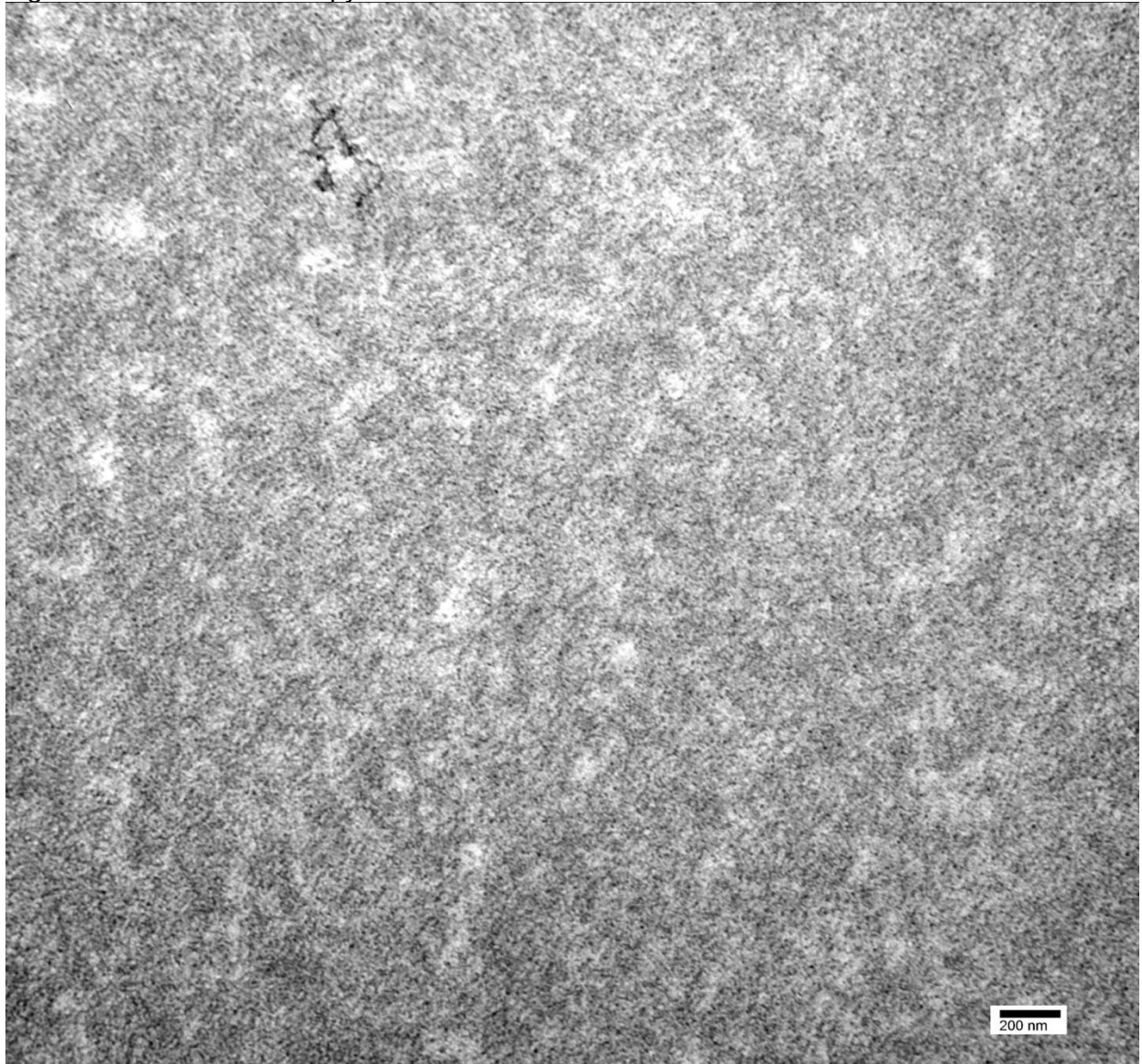


Figure 4: Electron microscopy:



Questions for Case 1

1. A 60-year-old man with hypertension and CKD presents with nephrotic-range proteinuria. Kidney biopsy shows enlarged glomeruli with mesangial and subendothelial expansion by PAS-positive, silver-negative, Congo red-negative material. Immunofluorescence is negative for immunoglobulins and complement. Electron microscopy shows massive mesangial and subendothelial granular electron-dense deposits with rare foci of vague fibril-like substructure, but no well-formed fibrils, microtubules, or punctate powdery deposits are seen. An additional immunohistochemical stain for DNAJB9 is negative.

Which study would be most helpful in establishing the diagnosis?

- A. Immunofluorescence for fibronectin
 - B. Immunohistochemistry for type III collagen
 - C. Immunofluorescence for alpha 5 of type IV collagen
 - D. IgG subclass staining
2. **Which finding would most strongly favor a diagnosis of fibrillary glomerulonephritis over fibronectin glomerulopathy?**
 - A. Congo red positivity
 - B. Mesangial and subendothelial type III collagen fibrils
 - C. DNAJB9 positivity
 - D. Silver-negative deposits by Jones methenamine silver stain
 3. **Fibronectin glomerulopathy is associated with which genetic mutation?**
 - A. Mutation in *COL4A5* gene on chromosome Xq22
 - B. Mutation in *FN1* gene on chromosome 2q34
 - C. Mutation in *WT1* gene on chromosome 11p13
 - D. Mutation in *UMOD* gene on chromosome 16p12.3

Case 2 from Meghan Kapp, MD, MS, Case Western Reserve University and University Hospitals, Cleveland Medical Center

A 68-year-old man presents as a new primary care patient for management of multiple chronic conditions and evaluation of progressively worsening exertional dyspnea over several months. His history includes type 2 diabetes mellitus, dyslipidemia, obstructive sleep apnea, stage 3 CKD, hypertrophic cardiomyopathy without outflow obstruction, heart failure, coronary artery disease, paroxysmal atrial fibrillation, aortic regurgitation, and peripheral artery disease. He has no prior surgical history. He is a former smoker (80 packs/year, quit two years ago). His family history is notable for premature cardiovascular disease on both sides and his father died of myocardial infarction; his mother is alive, and he has no siblings.

Physical examination reveals longstanding, stable bilateral lower extremity edema and multiple violaceous-red papules within the gluteal fold and upper medial thighs. Punch biopsy of a lesion demonstrates angiokeratoma. Laboratory evaluation shows an eGFR of 38 mL/min/1.73 m², consistent with stage 3B CKD. Urinalysis is negative for hematuria but demonstrates 2+ proteinuria (approximately 0.5–1.5 g/day). Given the persistent proteinuria, a kidney biopsy is performed.

[Biopsy Images](#)

Figure 1. Light microscopy:

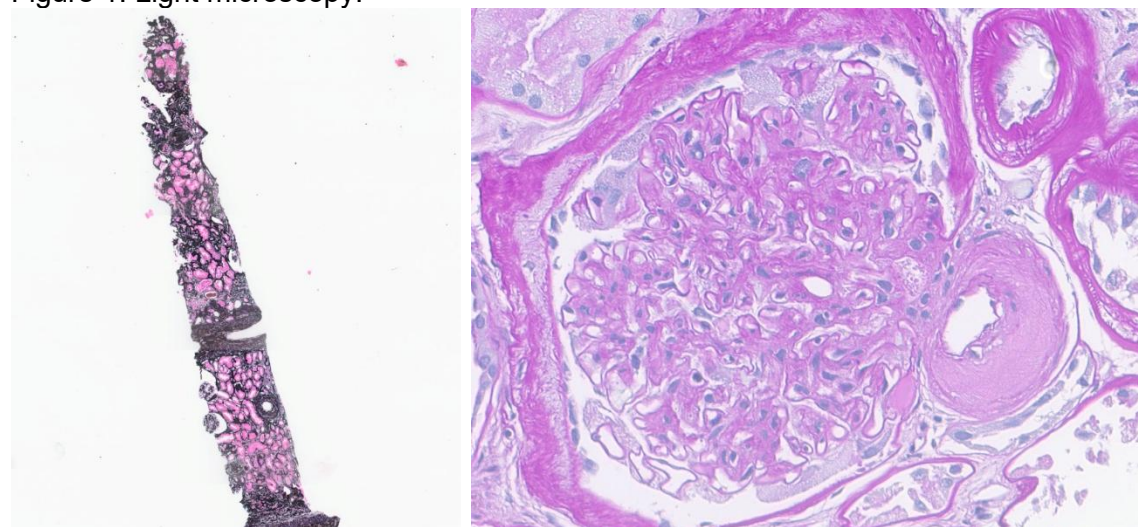
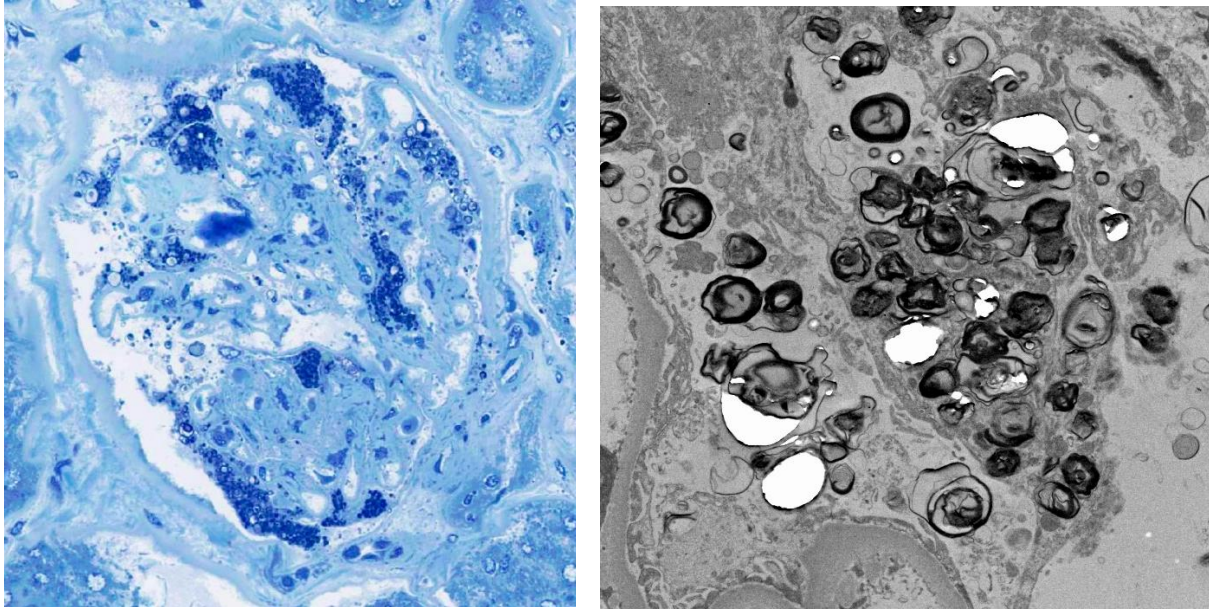


Figure 2. Electron microscopy:



Questions for Case 2

1. A 24-year-old man with genetically confirmed Fabry disease undergoes a kidney biopsy for increased proteinuria despite preserved eGFR.

Which of the following kidney biopsy findings is most characteristic of Fabry nephropathy?

- A. Subepithelial immune deposits ("humps")
 - B. Mesangial IgA deposition
 - C. Lamellated myelin or zebra bodies within podocytes
 - D. Crystalline inclusions within podocytes
2. A 48-year-old woman presents with CKD stage 3 and left ventricular hypertrophy. Her son was recently diagnosed with Fabry disease. Measurement of alpha-galactosidase A (α -Gal A) activity is normal.

Which statement is most accurate?

- A. Normal enzyme activity excludes Fabry disease in women
- B. Women cannot develop Fabry nephropathy
- C. Fabry disease is inherited in an autosomal dominant pattern
- D. Genetic testing for a GLA pathogenic variant is indicated

3. A kidney biopsy from a patient with Fabry disease demonstrates glycosphingolipid accumulation in multiple renal compartments.

Which cell type is generally considered most resistant to clearance of storage material despite treatment and is most closely linked to persistent proteinuria?

- A. Distal tubular epithelial cells
- B. Podocytes
- C. Mesangial cells
- D. Endothelial cells

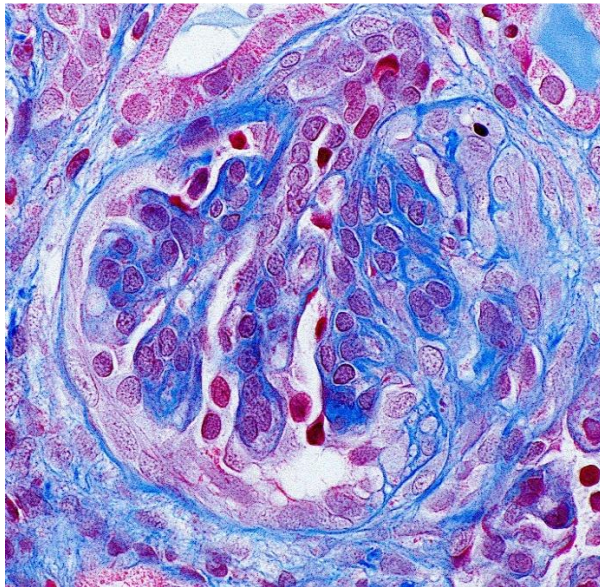
Case 3 from Alexei Mikhailov, MD, PhD, University of North Carolina at Chapel Hill

The patient is a one-year-old male with nephrotic syndrome and lower extremity edema since six months of age. Clinical examination does not reveal developmental abnormalities. A steroid trial demonstrated treatment resistance. His blood pressure is 90/60 mmHg. Laboratory data: serum creatinine 0.3 mg/dL, serum urea nitrogen (BUN) 11, albumin 1.7 g/dL, cholesterol 438 mg/dL. Urinalysis shows with red blood cell casts, 4+ proteinuria. No additional clinical data is available. A kidney biopsy is performed.

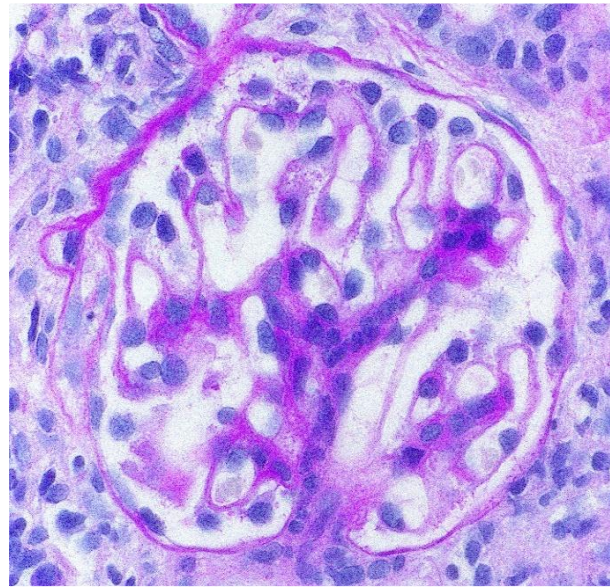
Biopsy Images

Figure 1

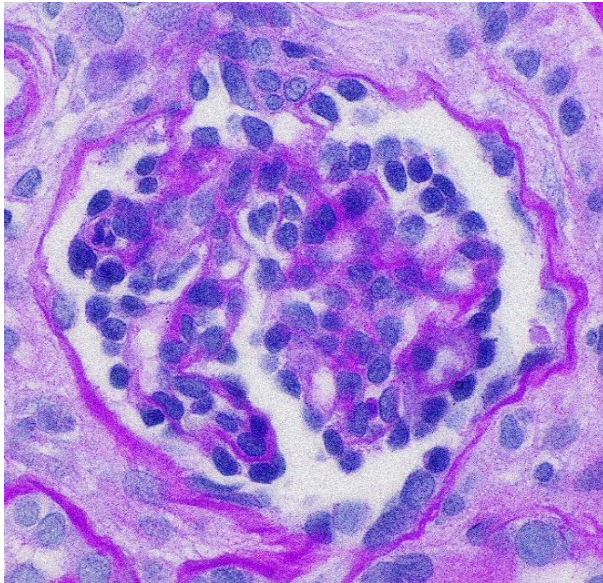
A. Trichrome, 40x:



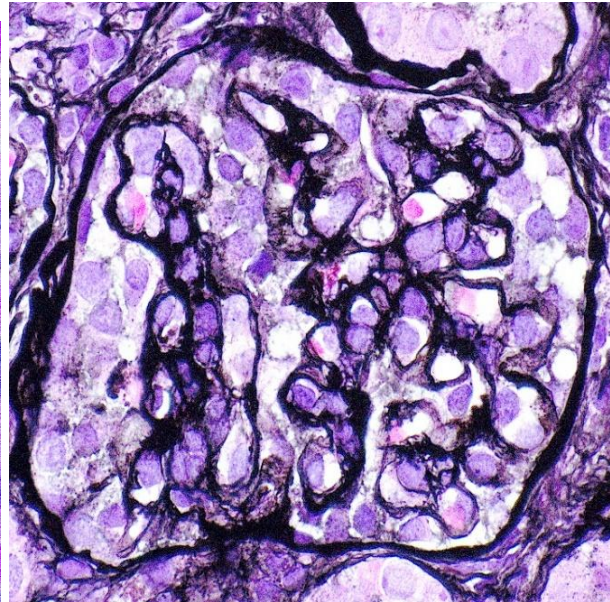
B. Periodic acid-Schiff (PAS), 40x:



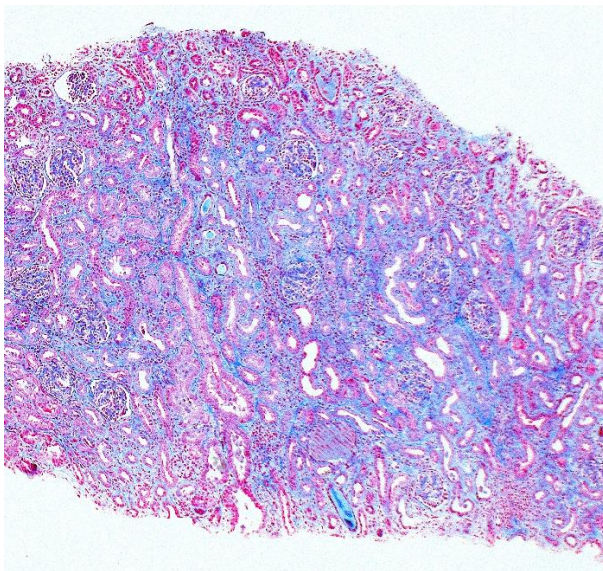
C. PAS, 40x:



D. Periodic acid-methenamine silver (PAMS), 60x:



E. Trichrome, 40x:



F. PAS, 40x:

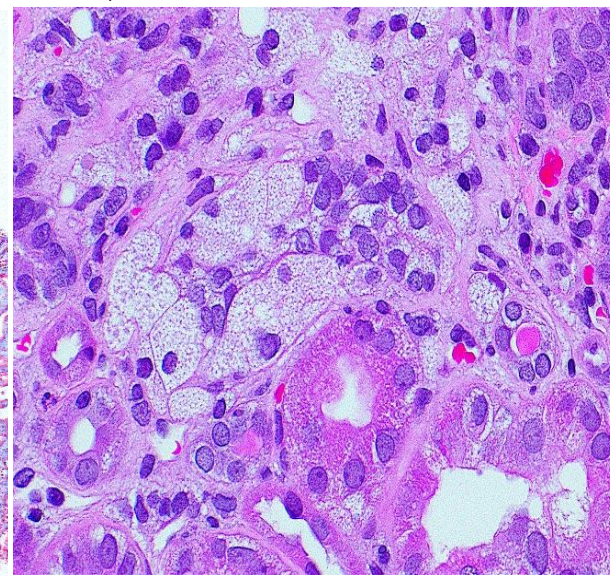
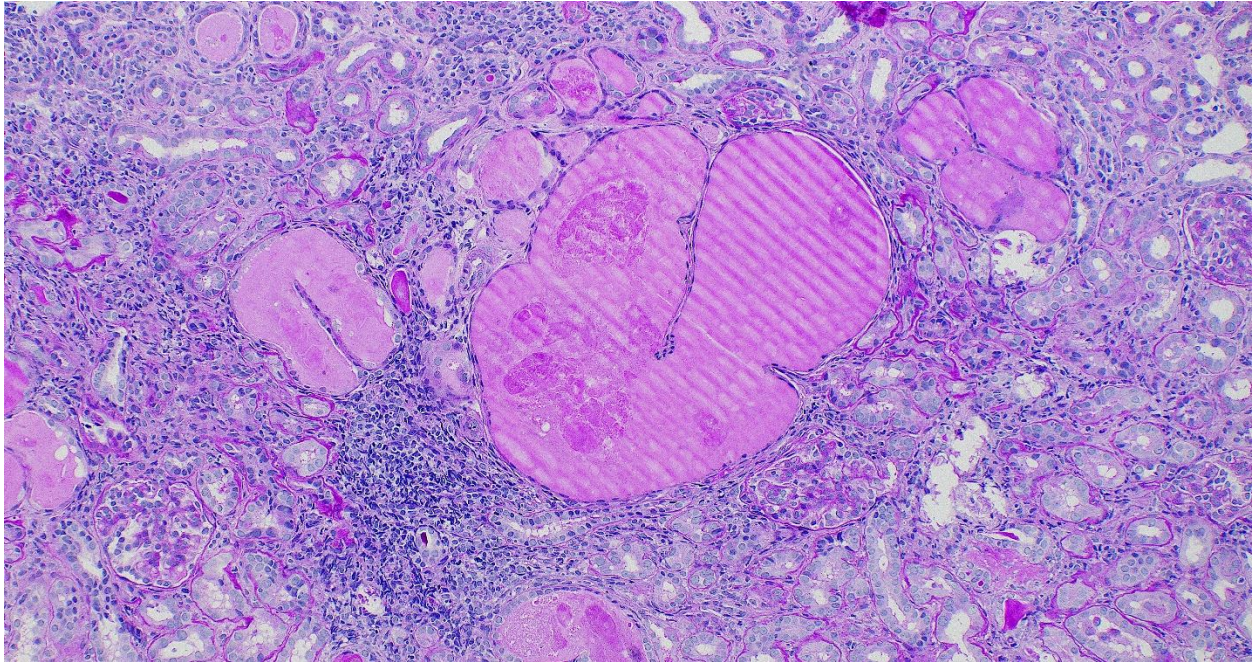


Figure 2

A. PAS, 10x:



B. Trichrome, 10x:

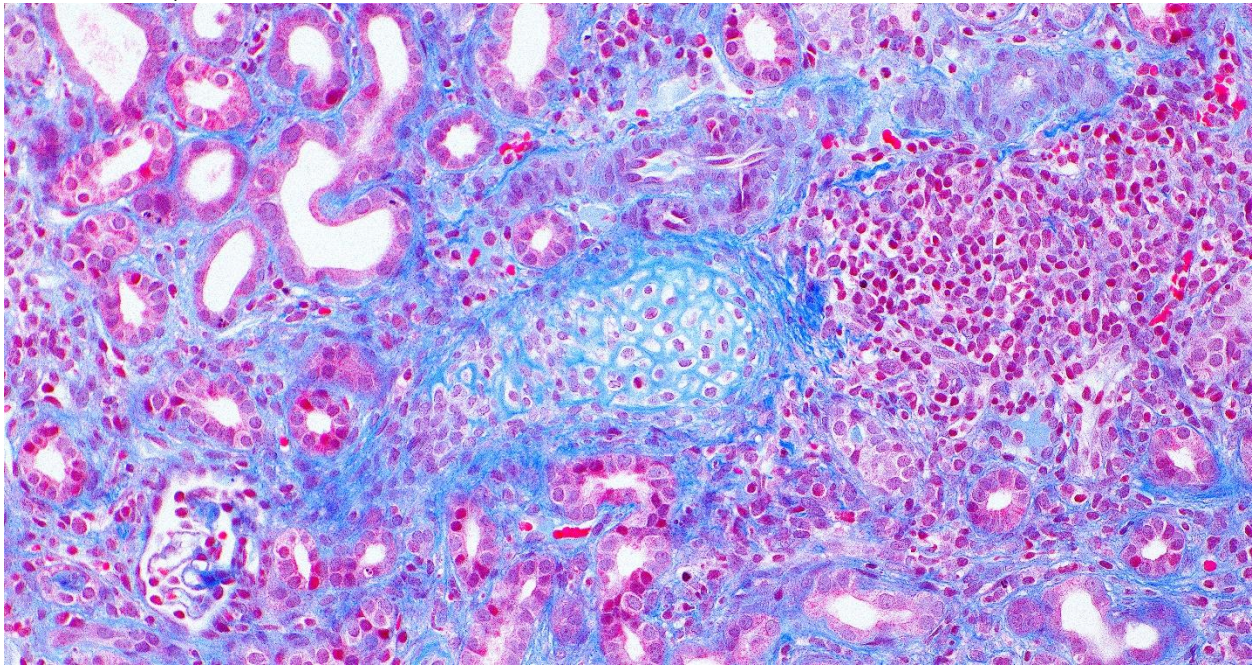
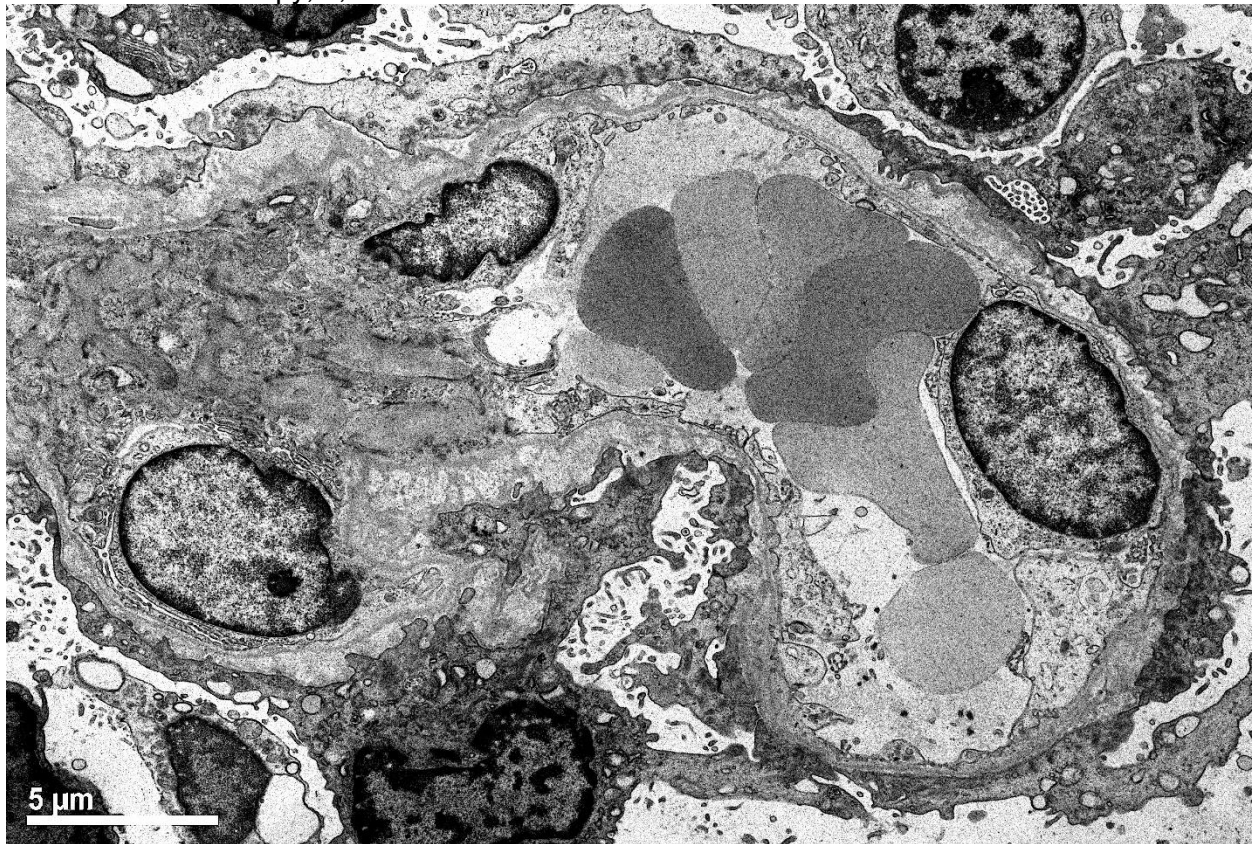
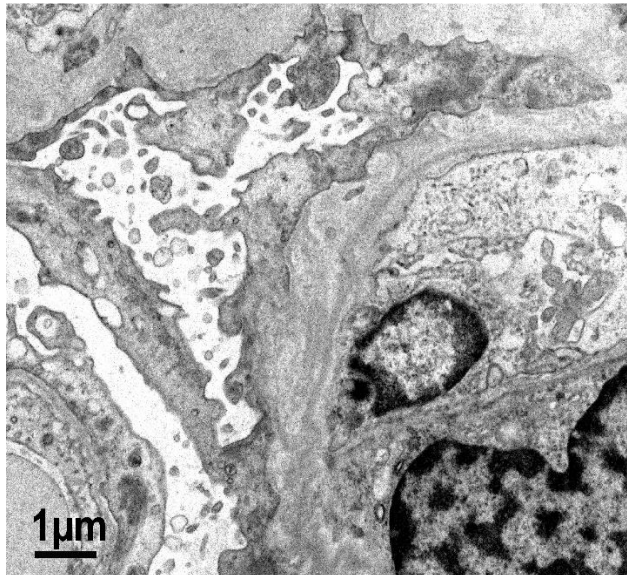


Figure 3

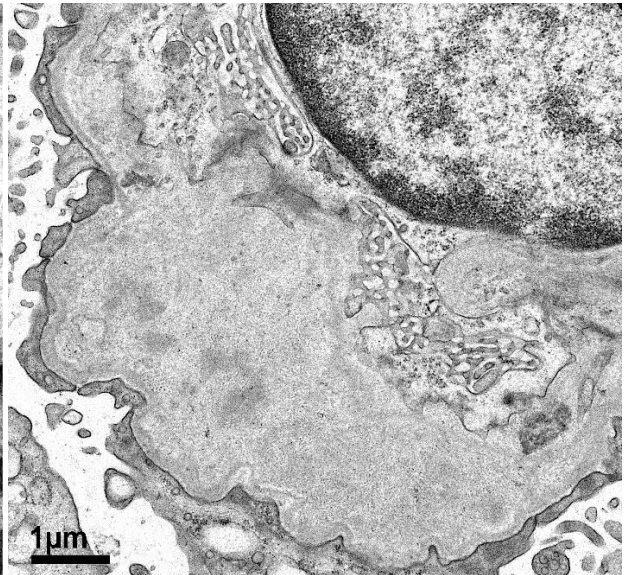
A. Electron microscopy, 6,000x:



B. Electron microscopy, 15,000x:



C. Electron microscopy, 12,000x:



Questions for Case 3

1. Which single feature most strongly prompts a genetic study in a one-year-old patient with persistent proteinuria and preserved kidney function?
 - A. Partial, transient response to corticosteroids with prompt relapse on tapering
 - B. Persistence of immature (fetal) glomeruli distributed throughout the cortex on a well-sampled biopsy
 - C. Diffuse (>80%) podocyte foot process effacement on electron microscopy
 - D. A first-degree relative with biopsy-proven focal segmental glomerulosclerosis (FSGS)
 - E. Granular IgA and IgM along scattered peripheral capillary walls without a mesangial-dominant pattern

2. Variants in which other genes produce GBM abnormalities that can be visualized under an electron microscope?
 - A. *COL4A3*, *COL4A4*, *COL4A5*
 - B. *MYO1E*, *MYH9*, *CD151*
 - C. *PAX2*, *WT1*, *CUBN*, *LMX1B*
 - D. *COL4A4*, *COL4A5*, *MYO1E*
 - E. All of the above

3. A kidney biopsy from our patient shows a focus of heterotopic cartilage within an area of interstitial fibrosis and tubular atrophy (Figure 2B).

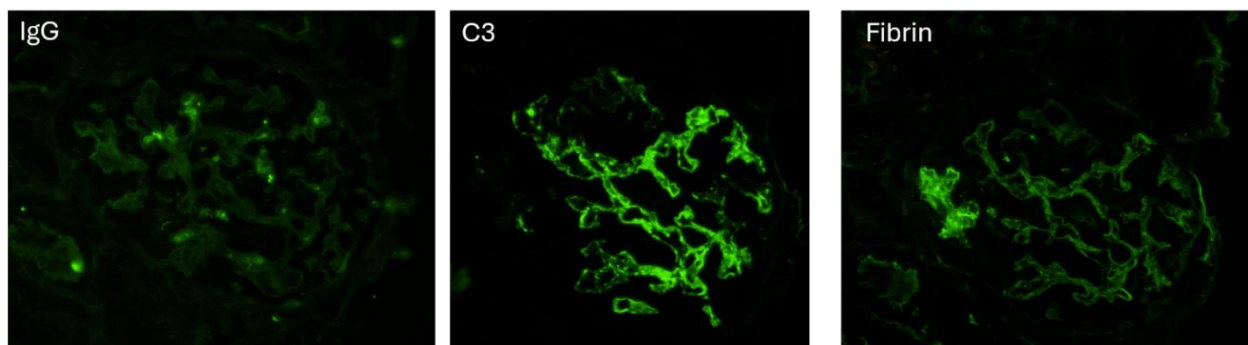
What is the most appropriate interpretation of this finding?

- A. It is nonspecific chondro-osseous metaplasia arising in chronically scarred parenchyma, incidental to the *LAMB2* diagnosis.
- B. It is a characteristic feature of *LAMB2*-associated (Pierson) disease that supports the genetic diagnosis.
- C. It is diagnostic of renal dysplasia, indicating a developmental malformation underlying the proteinuria.
- D. It is evidence of a coexisting *WT1* or *PAX2* disorder that should replace the *LAMB2* diagnosis.
- E. It is a metaplastic response specific to laminin $\beta 2$ deficiency in the GBM.

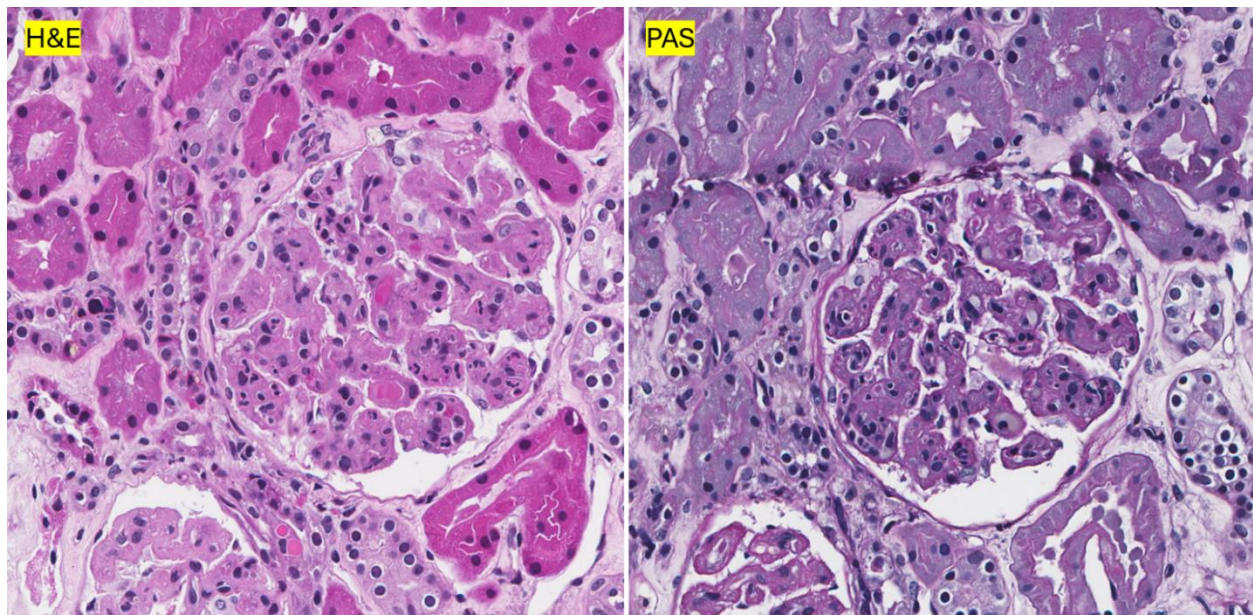
Case 4 from Dao-Fu Dai, MD, PhD, Johns Hopkins University

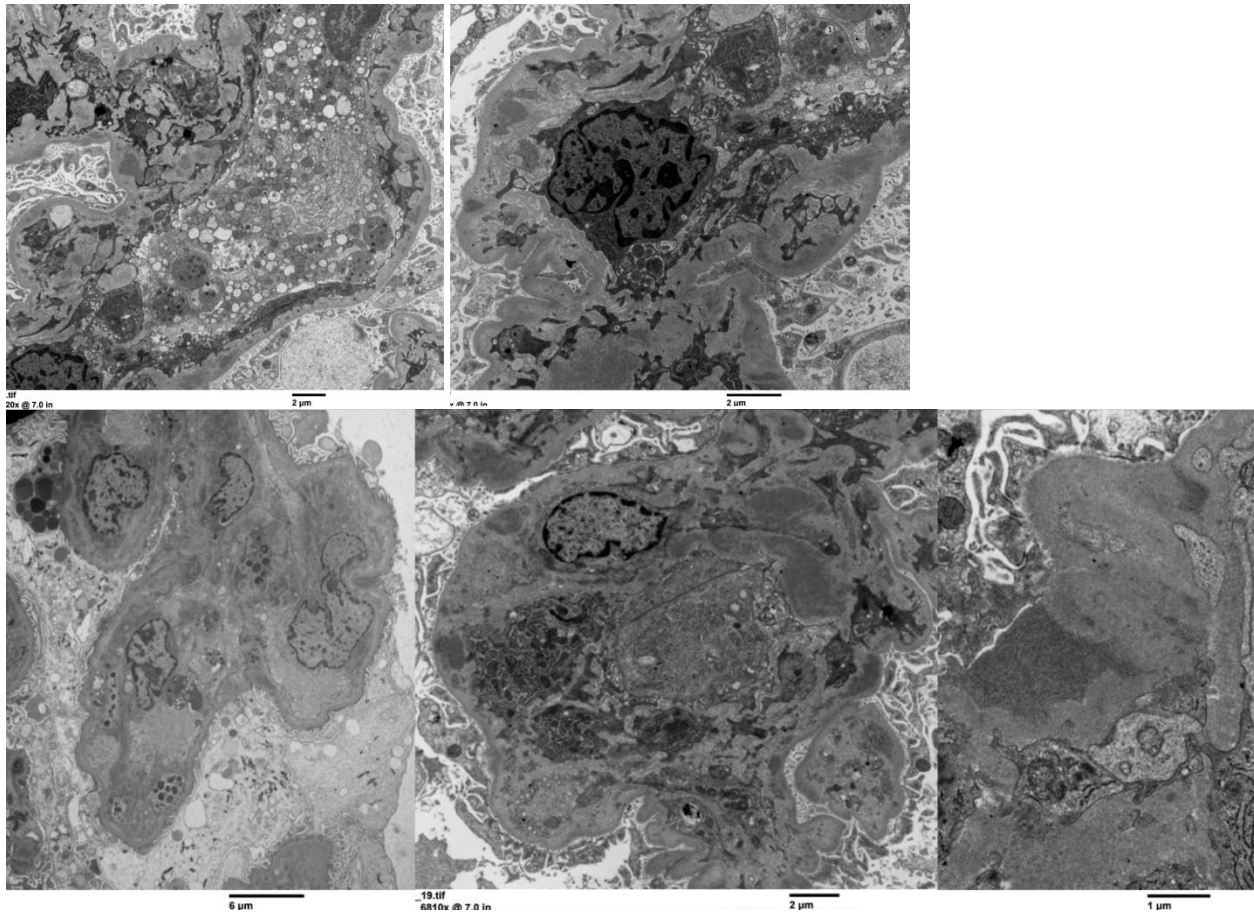
A Caucasian man in his mid-50s is admitted for foot gangrene, osteomyelitis, and *Clostridioides difficile* infection, and is clinically suspicious for vasculitis. His laboratory data show serum creatinine of 2 mg/dL, C3 of 33.6 (low), and normal C4. Urinalysis showed 22 red blood cells per high-power field (RBC/HPF), 3 white blood cells (WBCs), 3+ protein. He also had prior elevated haptoglobin, lactate dehydrogenase (LDH): 326 (reference range: 105-233 U/L), and elevated PR3 antibody (343 U/mL). All other serologic testing are unremarkable, including negative myeloperoxidase (MPO), negative antinuclear antibody (ANA), negative cryoglobulinemia, negative rheumatoid factors, and negative immunofixation (without evidence of monoclonal gammopathy). Serum protein electrophoresis showed acute chronic inflammatory patterns.

Biopsy #1 Images

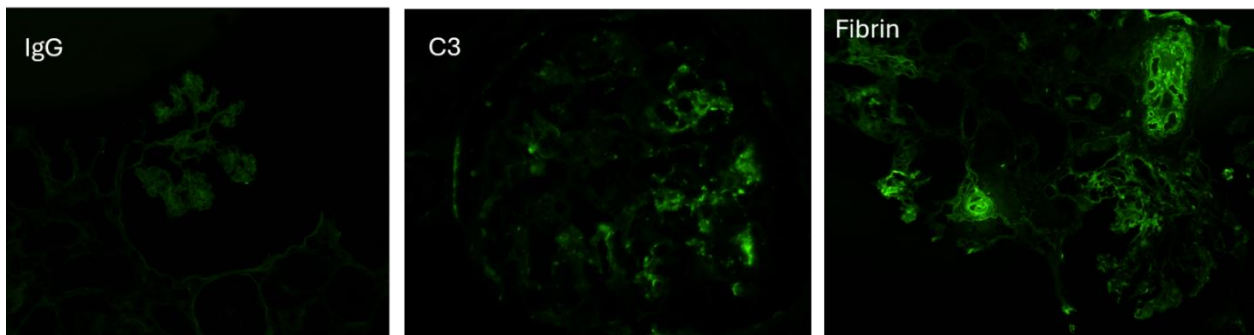


Similar pattern for IgG, kappa, and lambda (all 1+). Other immunostaining is unremarkable.

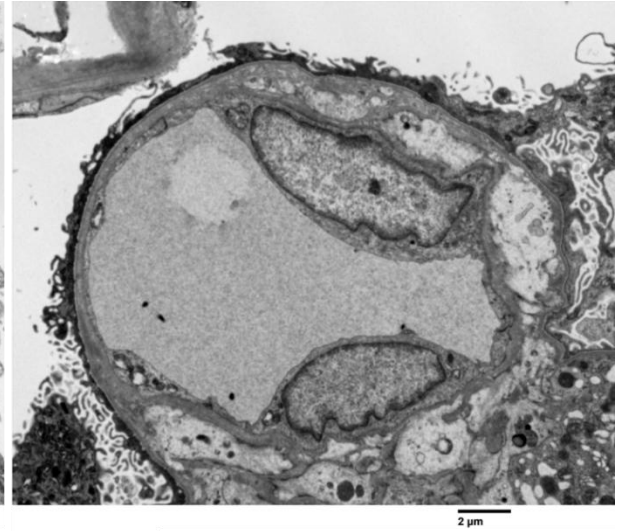
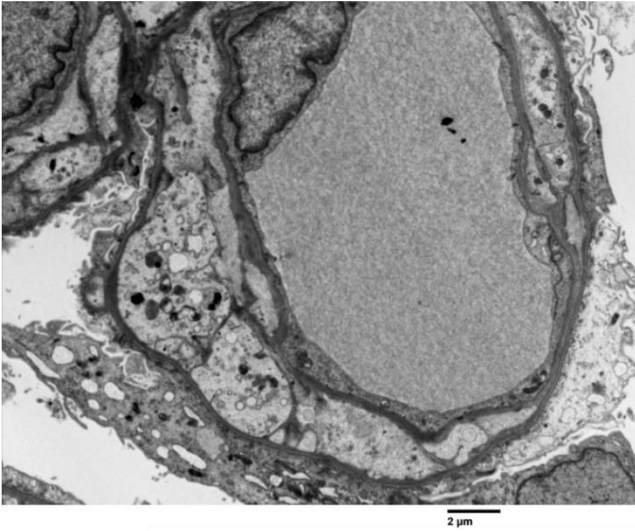
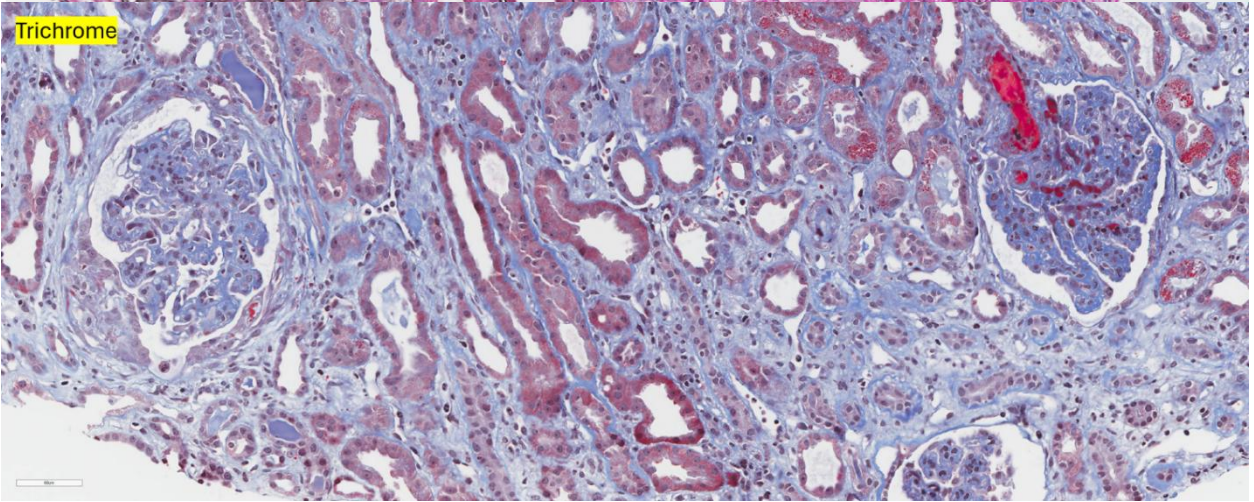
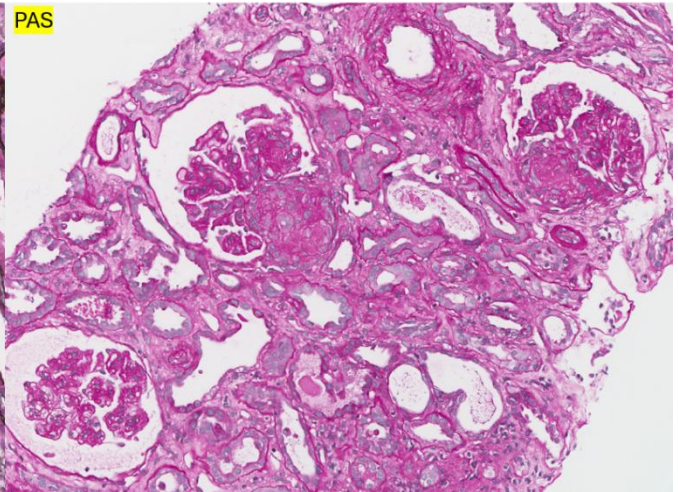
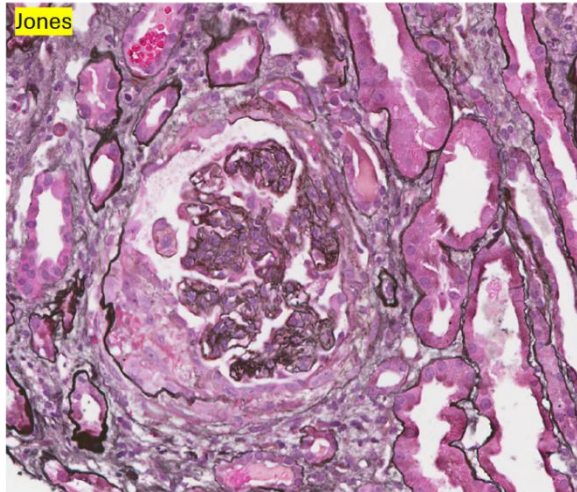




[Biopsy #2 Images](#)



Other immunofluorescence staining was unremarkable.



Questions for Case 4

1. Based on the findings in the first biopsy, which diagnosis is least likely?

- A. IgG-dominant infection-associated GN (IAGN)
- B. Immune complex-mediated membranoproliferative GN (MPGN)
- C. Dysregulated alternative complement pathways, such as C3 glomerulopathy (C3G)
- D. Thrombotic microangiopathy (TMA)
- E. Fibrillary glomerulonephritis

2. Based on the findings in both biopsies, which is the most likely diagnosis of the second biopsy? Select all that apply.

- A. IAGN
- B. Immune complex-mediated MPGN
- C. Dysregulated alternative complement pathways, such as C3G
- D. TMA
- E. Fibrillary glomerulonephritis

3. Which test would be least helpful in confirming the diagnosis?

- A. C3 and C5 nephritic factors
- B. Genetic testing
- C. ADAMTS13
- D. Anti-GBM antibodies
- E. Autoantibodies against factor H and B