KIDNEY WEEK 2025

Renal Biopsy:
Clinical Correlations

Pre-Session Syllabus

Case 1 from Vanderlene L. Kung, MD, PhD, Oregon Health & Science University

A 40-year-old man with self-reported kidney dysfunction since his 20s, hyperlipidemia, hypertension, and gout presents to re-establish medical care. He has a 20-pack per year cigarette smoking history. No family history is initially obtained. Vitals on admission are all within normal limits. On physical exam, the patient is obese and without any peripheral edema. A comprehensive metabolic panel is notable for elevated serum creatinine of 3.9 mg/dL, hypocalcemia (8.3 mg/dL), and serum albumin within normal limits (3.9 g/dL). No erythrocytes or leukocytes are seen on urinalysis. Urine total protein-to-creatinine ratio is 2.0. Antinuclear antibody, ANCA, and Hepatitis B and C serologies are negative. Serum C3 and C4 complement levels are within normal limits. A retroperitoneal ultrasound shows bilateral small kidneys with cortical thinning, increased echogenicity, and bilaterial cortical cysts. A kidney biopsy is performed for CKD with subnephrotic proteinuria.

Biopsy Images

Figure 1. Light microscopy, Jones silver-stained sections:

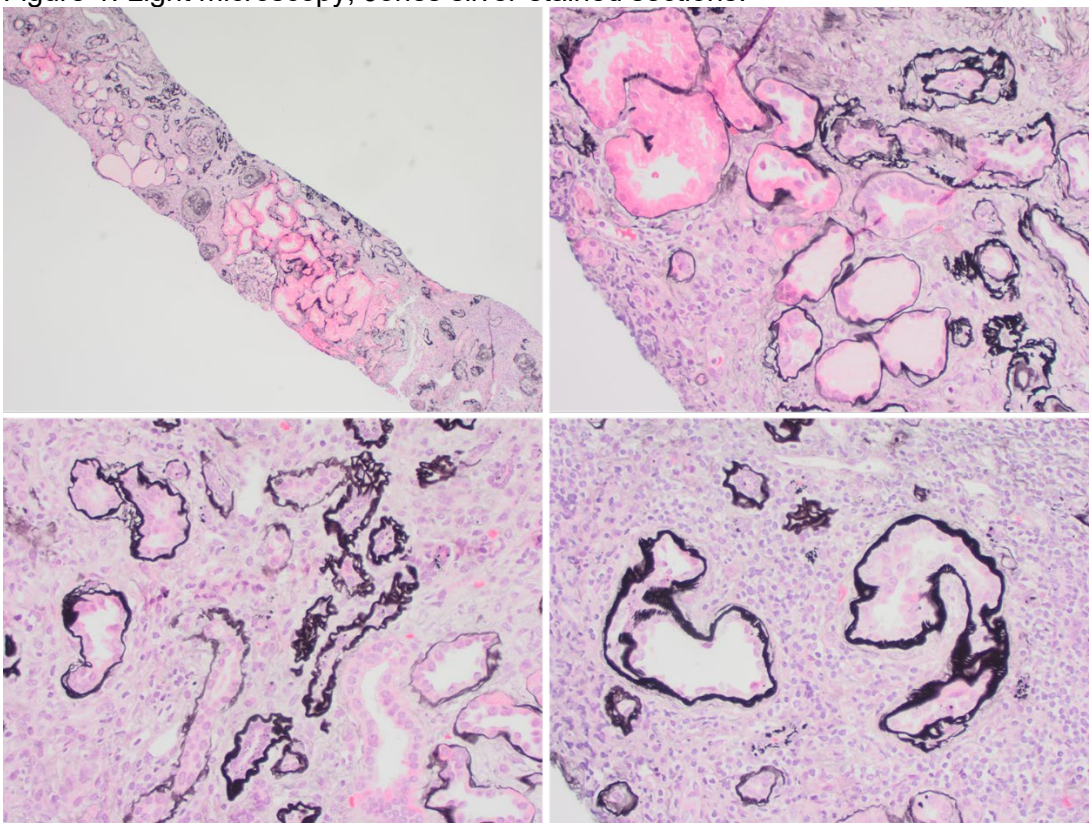
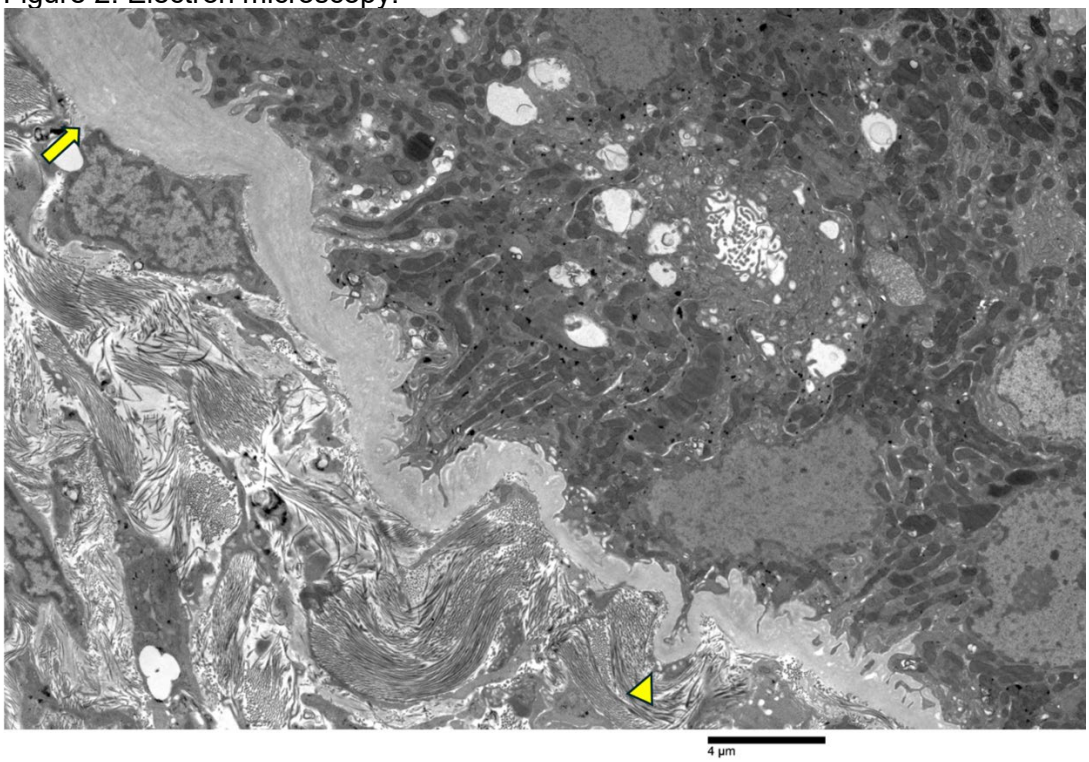


Figure 2. Electron microscopy:



Questions for Case 1

1. The light microscopy in this case shows chronic interstitial nephritis (dense, lymphoplasmacytic inflammation associated with interstitial fibrosis and tubular atrophy, sparing the preserved tubulointerstitium).

All but which scenario can be associated with chronic interstitial nephritis, similar to this case?

A. 5-aminosalicylic acid use
B. History of ifosfamide exposure
C. Vesicoureteral reflux
D. Acute pyelonephritis

2. The immunofluorescence microscopy is negative for any tubulointerstitial immune complex deposits in this case.

What tubulointerstitial diseases are associated with tubular basement membrane immune deposits? Select all that apply.

A. IgG4-related kidney disease
B. Antibrush border antibody disease
C. ADTKD-*UMOD*
D. Sjogren syndrome

3. What ultrastructural alterations in tubular basement membranes can be seen in ADTKD?

A. Duplication, lamellation, irregular thickness, and disruption
B. Collagen bundles
C. Electron-dense immune complex-type deposits
D. Amorphous powdery deposits

Case 2 from Mercury Y. Lin, MD, Cedars-Sinai Medical Center

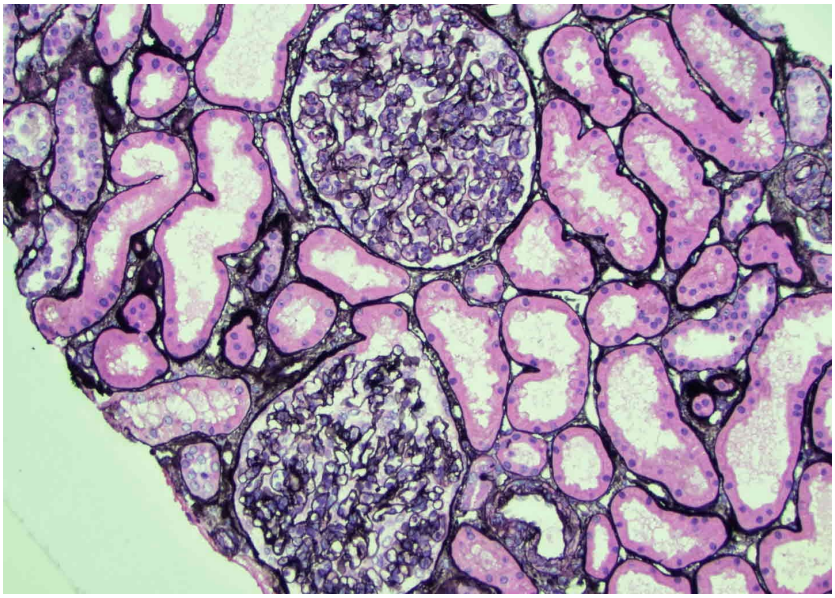
A 60-year-old woman presents to urgent care with a history of hypertension and a baseline serum creatinine level of 0.8 mg/dL. She was reportedly in her usual state of health until five days ago, at which time she began experiencing fatigue, nausea, chills, and sore throat. She became febrile (temperature of 103° F at home) and has had episodes of vomiting. She denies abdominal pain and dysuria. The patient did not receive COVID-19 vaccination but denies loss of taste or smell. Her vital signs are temperature of 104° F, BP of 103/70, BMI 28, pulse of 104/min, respiratory rate of 20, and oxygen saturation of 96%. Her outpatient medication consists of metoprolol 50 mg twice daily.

On physical exam, she is well-developed, well-nourished, and alert and awake. There is no skin rash and no palpable lymphadenopathy. There is no report of hepatosplenomegaly. Lung and heart sounds are unremarkable. There is no lower extremity edema.

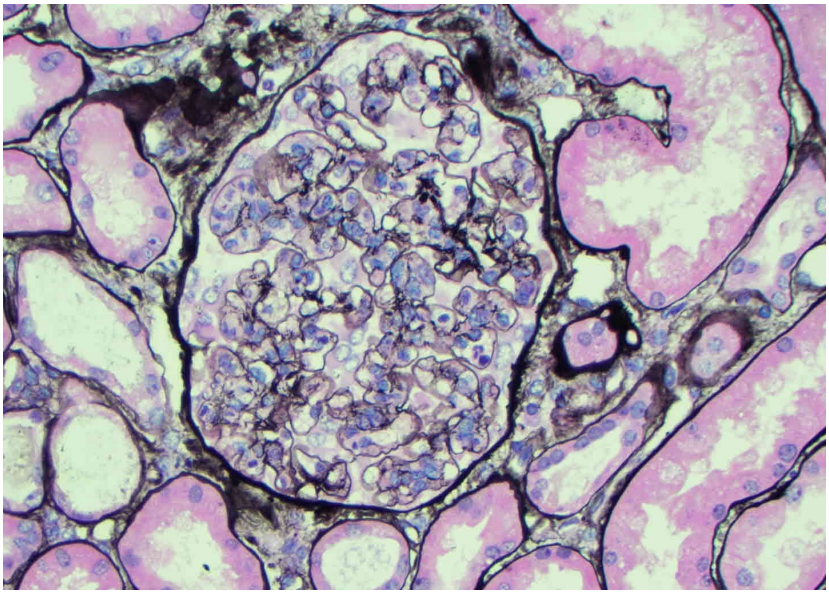
A portable chest radiograph is obtained and shows normal cardiomediastinal silhouette and no infiltrate. Clinical laboratory evaluation reveals serum creatinine of 3.7 mg/dL (eGFR 15 mL/min/173 m^2), blood urea nitrogen of 38 mg/dL, glucose of 171 mg/dL, and albumin of 2.9 g/dL. Aspartate aminotransferase and alanine aminotransferase are within normal limits. Her complete blood count is within normal limits (white blood cells 8.2 K/uL, hemoglobin 11.8 g/dL, hematocrit 35.6%, and platelets 365 K/uL). Urinalysis reveals 1+ proteinuria, 3–10 red blood cells (RBCs) per high power field, negative urine nitrite, and negative urine leukocyte esterase. COVID-19 and rapid Streptococcus A tests are negative. She is diagnosed with acute kidney failure and is admitted to a community hospital. Additional inpatient laboratory studies reveal positive ANA, negative ANCA, negative cryoglobulin test, low serum complement levels, and a kappa:lambda light chain ratio of 1.5 (ref range: 0.26 to 1.65). She is started on empiric antibiotic therapy. Nephrology consultation is obtained, and a kidney biopsy is performed.

Biopsy Images

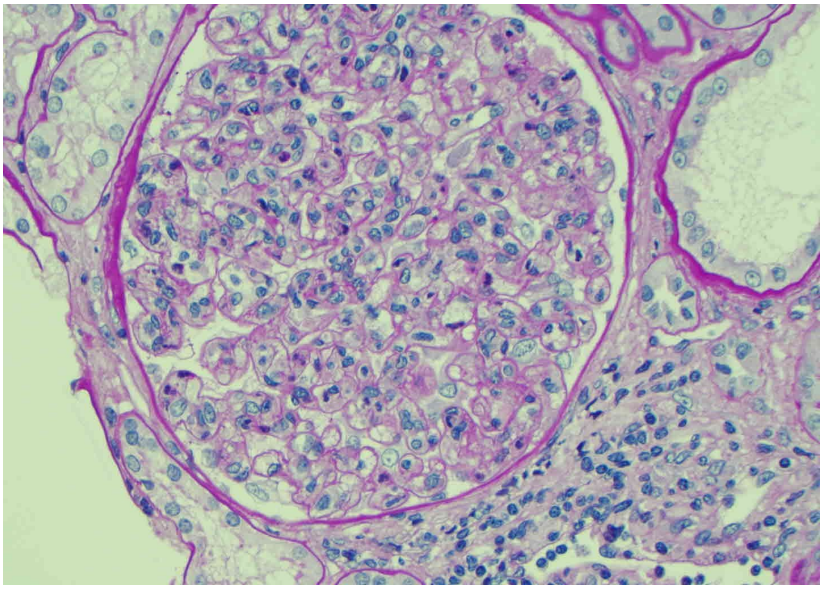
Light Microscopy:
Jones silver stain:



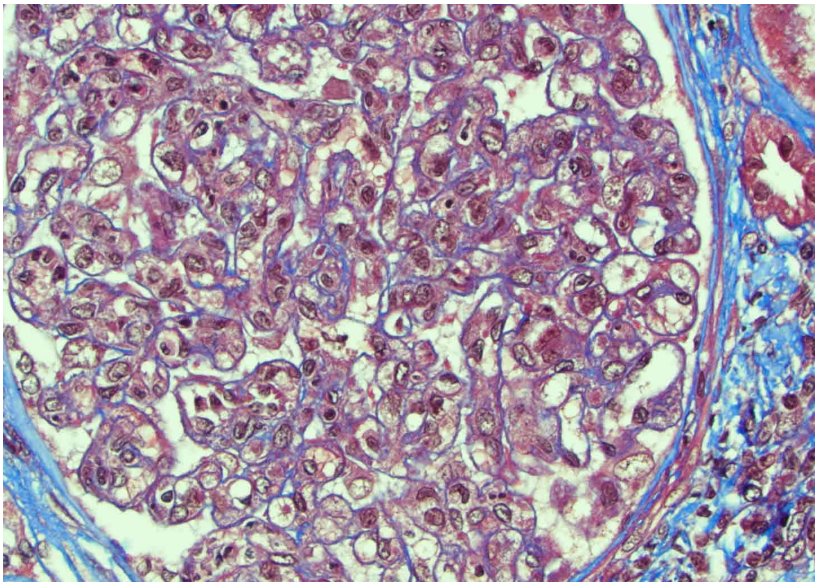
Jones silver stain:



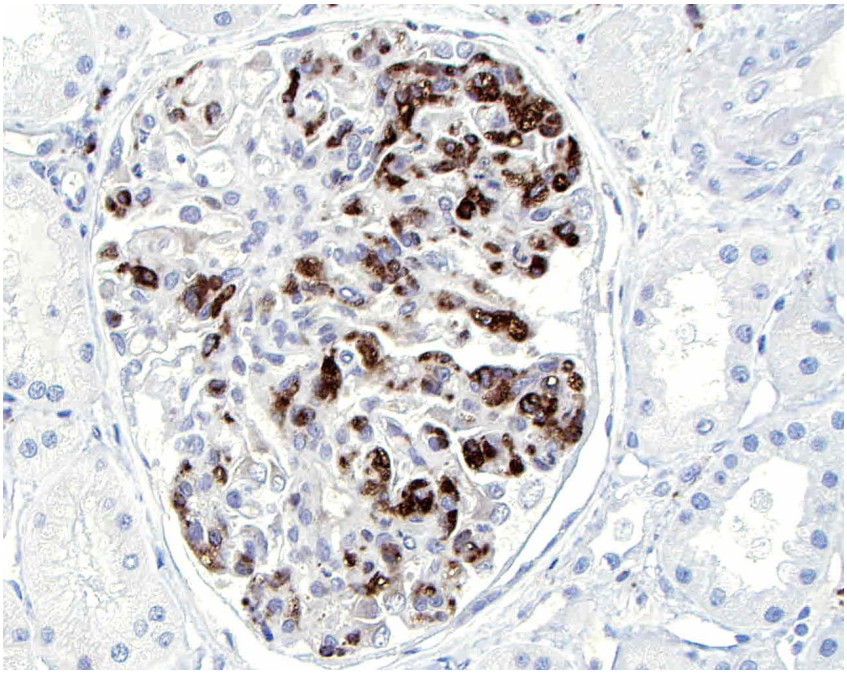
PAS stain:



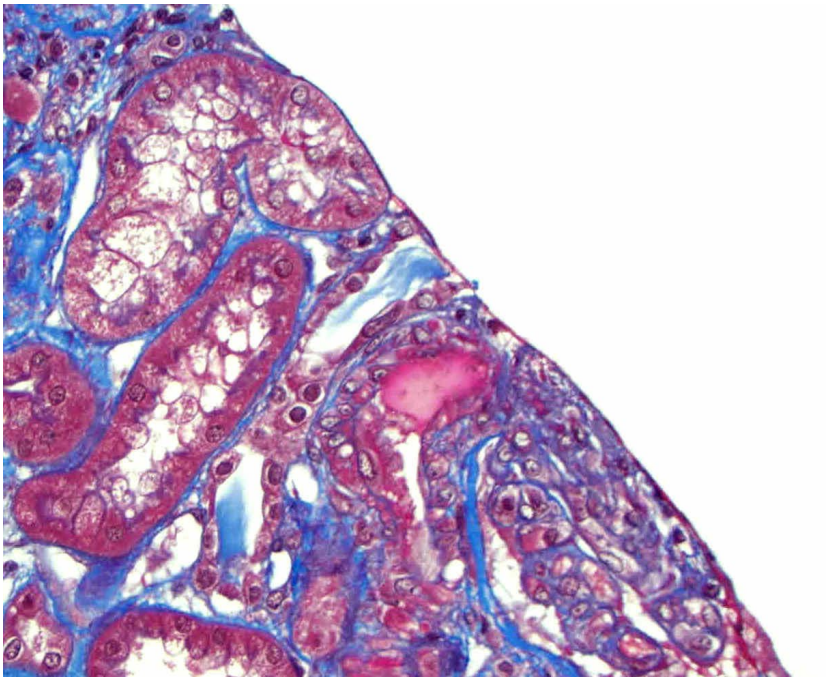
Masson trichrome:



CD68:

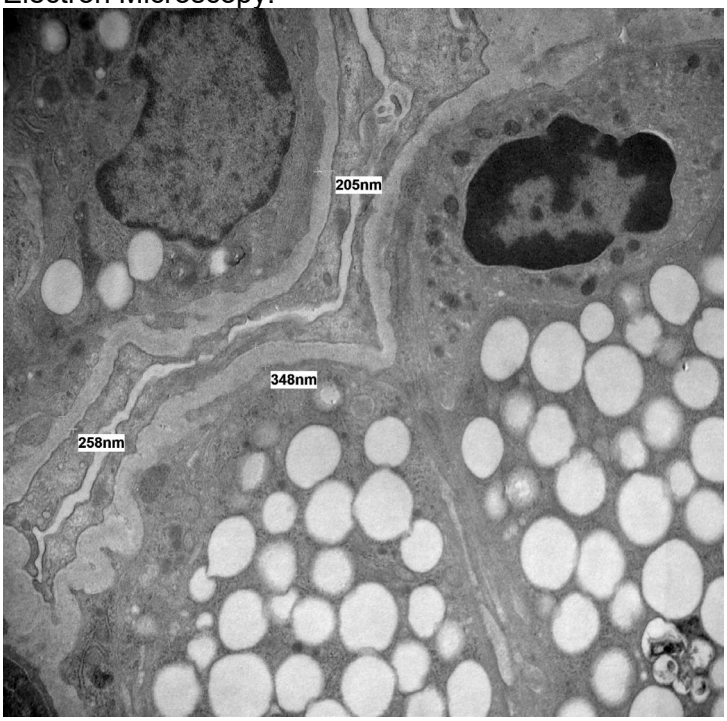


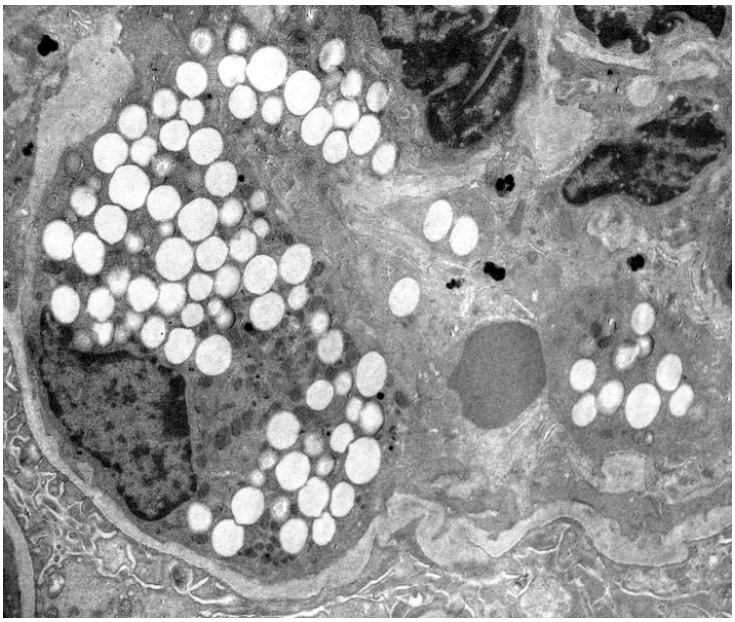
Masson trichrome:



Immunofluorescence Microscopy: Noncontributory.

Electron Microscopy:





Questions for Case 2

1. **To highlight intracapillary histiocytes in histiocytic glomerulopathy, what is the most appropriate immunohistochemical stain?**

    A. CD1a
    B. CD3
    C. CD20
    D. CD31
    E. CD68

2. A 75-year-old man presents with multiple myeloma and glomerulopathy characterized by many intracapillary CD68+ histiocytes showing bright lambda light chain staining, no kappa light chain staining, and numerous crystalline deposits detected by electron microscopy.

    What is the most accurate diagnosis?

    A. Histiocytic glomerulopathy
    B. Crystal-storing histiocytosis, lambda light chain
    C. Glomerular thrombotic microangiopathy (TMA)
    D. Cryoglobulinemic glomerulonephritis
    E. Lipoprotein glomerulopathy

3. **Under electron microscopy, which ultrastructural finding is commonly observed in histiocytic glomerulopathy?**

    A. Mesangial immune complex deposits
    B. Mesangial lipid debris
    C. Endothelial tubuloreticular inclusions
    D. Focal glomerular endothelial swelling and loss of fenestrations
    E. Lamellated podocyte lipid inclusions

Case 3 from Cathryn J. Lapedis, MD, MPH, MSc, University of Michigan

A 68-year-old white man with a history of smoking (unknown amount, quit 35 years ago), hypertension, stroke, type 2 diabetes, gout, and arthritis presents to nephrology due to increasing creatinine up to 2.8 mg/dL (up from 2.2 mg/dL 5 months prior). Per a clinical note, a potential diagnosis of lupus nephritis is under consideration due to a positive dsDNA of 39 IU/mL in January 2025, and ANA has been negative. Prior rheumatology evaluation in 2016 showed ANA-negative, normal complements, and a confirmed diagnosis of arthritis and gout with no evidence of lupus. Additional labs provided at the time of biopsy include: Creatinine of 2.83 mg/dL (eGFR 23), glucose high at 168 mg/dL, ANA-negative. Urinalysis shows: Negative leukocyte esterase; negative for white and red blood cells; no squamous epithelial cells, no bacteria, and no hyaline casts; albumin-to-creatinine ratio of 2141 mg/g creatinine; and HbA1c 6.7%. Recent testing for complements, lactate dehydrogenase, and haptoglobin were not completed. Medications include spironolactone, vitamin C, zinc, turmeric root extract, dulaglutide, multivitamin, amlodipine/benazepril, duloxetine, doxazosin, coenzyme Q10, colchicine, vitamin D3, carvedilol, aspirin, canagliflozin, hydralazine, and chlorthalidone. The patient has a history of fentanyl use for severe pain but has been weaned off opioids after a long withdrawal period. This biopsy is to determine the etiology of his proteinuria and CKD.

Biopsy Images

Stained sections of representative glomeruli:

Figure 1: Light microscopy, Jones silver stain 4x, cortex:

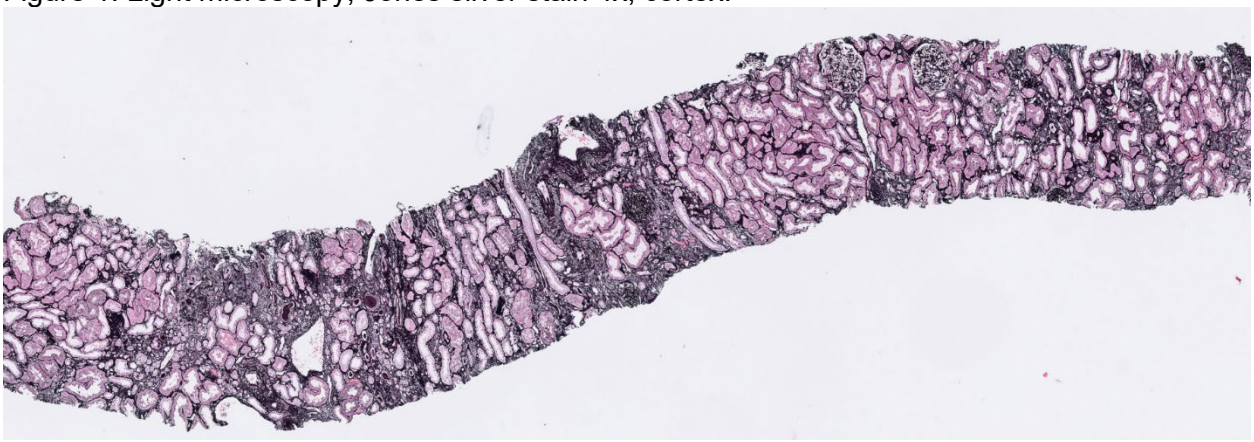


Figure 2: Light microscopy, PAS 20x:

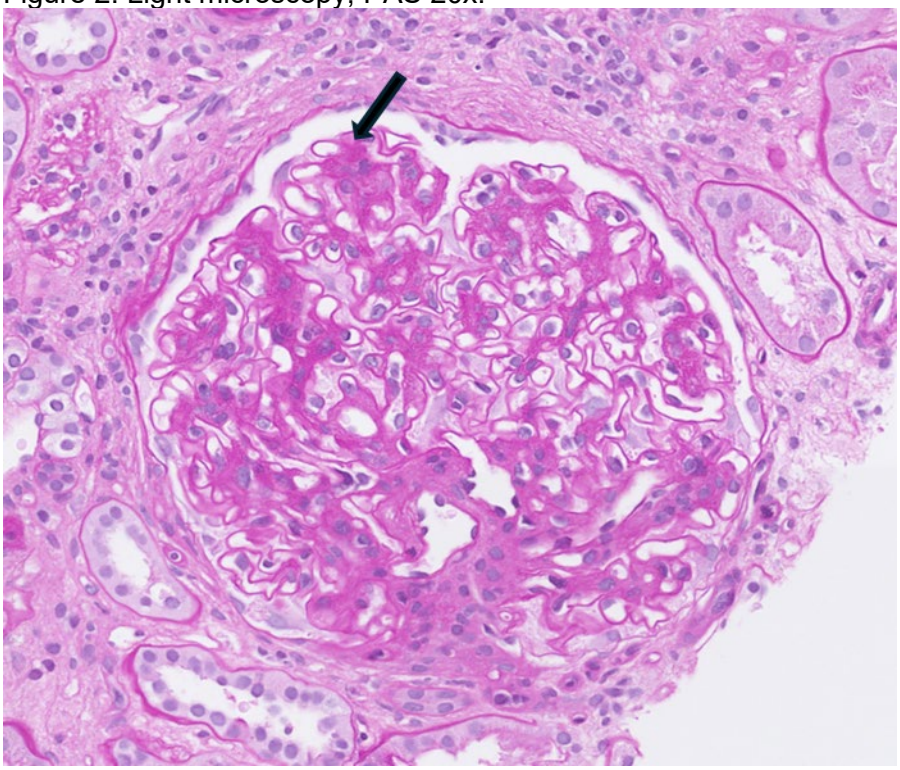


Figure 3: Light microscopy, PAS stain 20x:

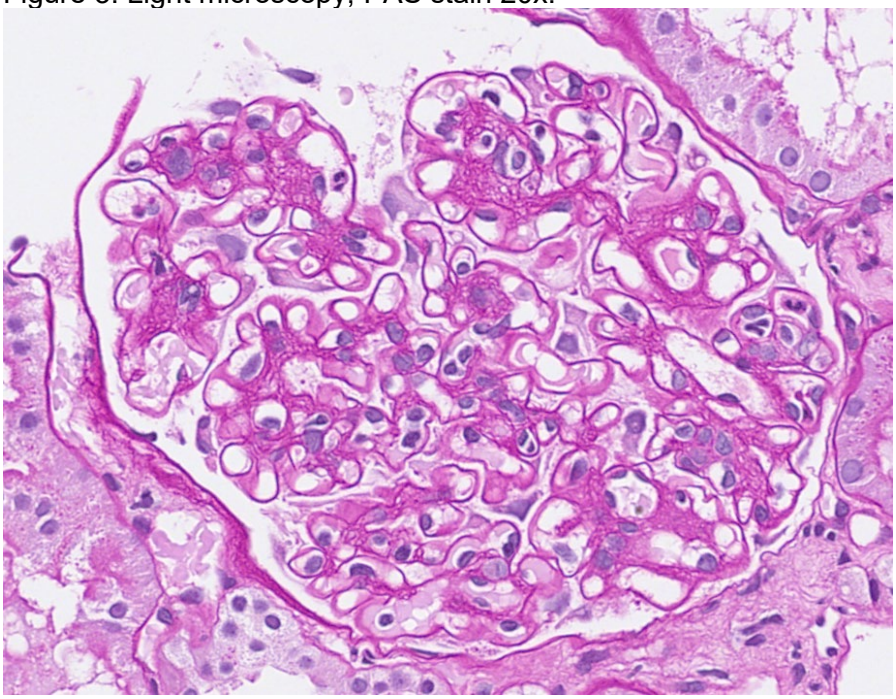


Figure 4: Light microscopy, Jones silver stain, 30x (same glomerulus as Figure 3):

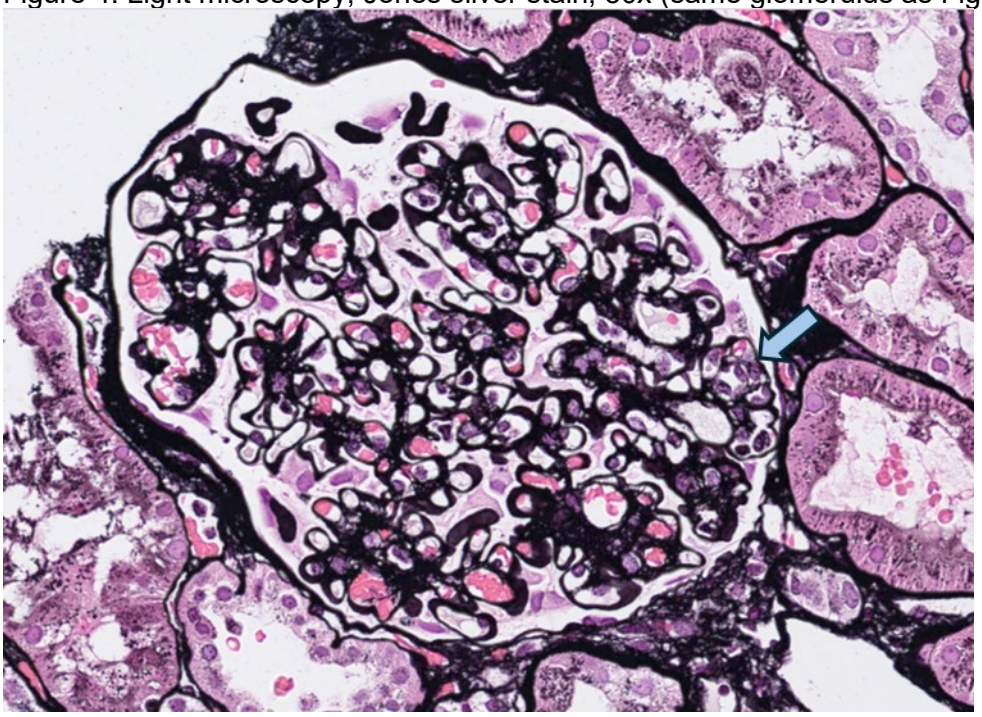


Figure 5: Light microscopy, Jones silver stain, 30x:

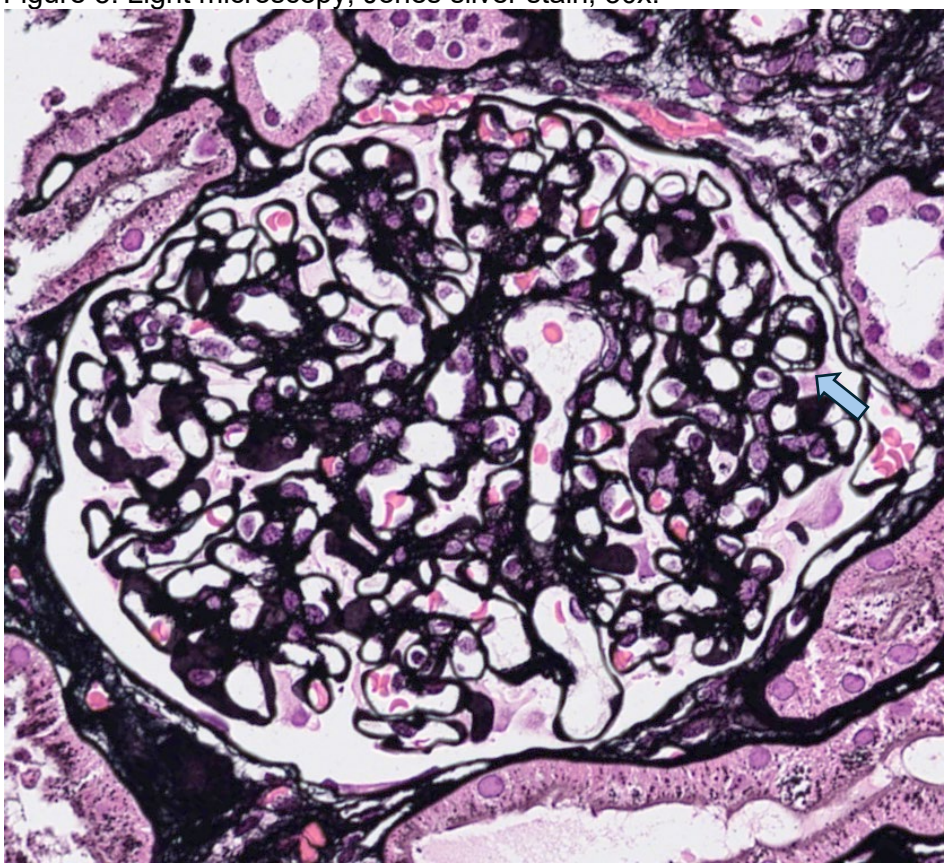


Figure 6. Immunofluorescence, IgA:

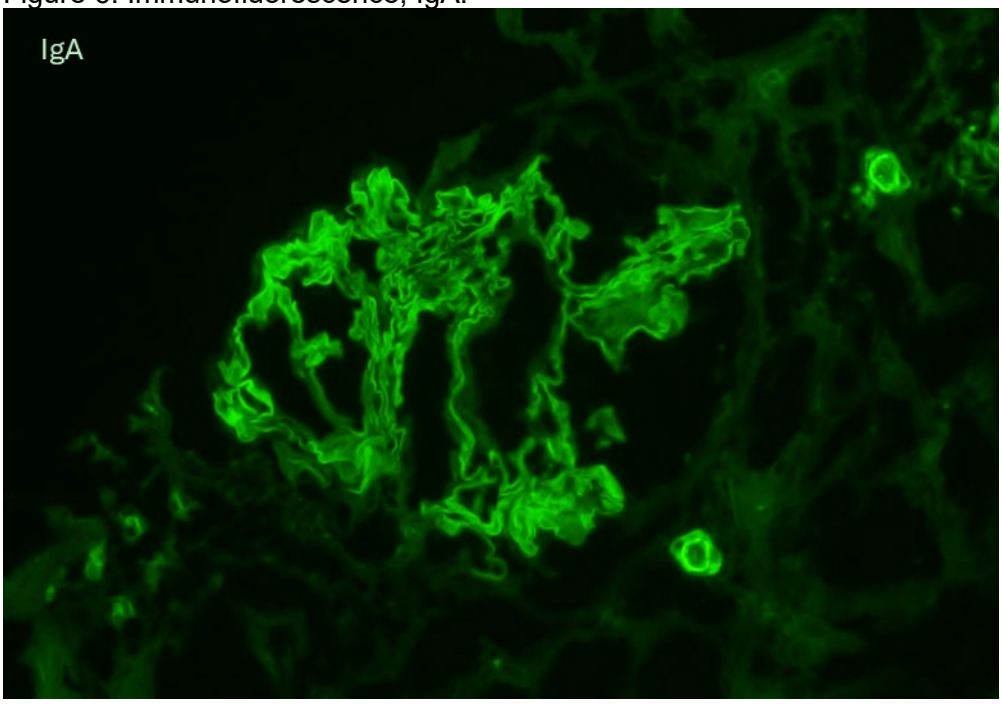


Figure 7. Immunofluorescence, lambda:

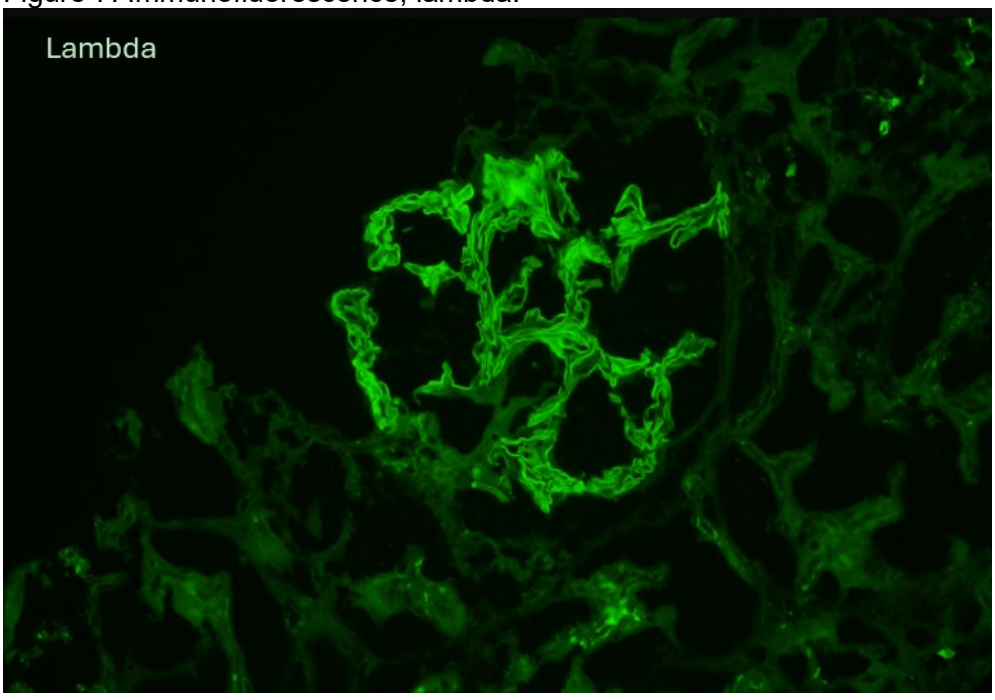


Figure 8. Immunofluorescence, kappa:

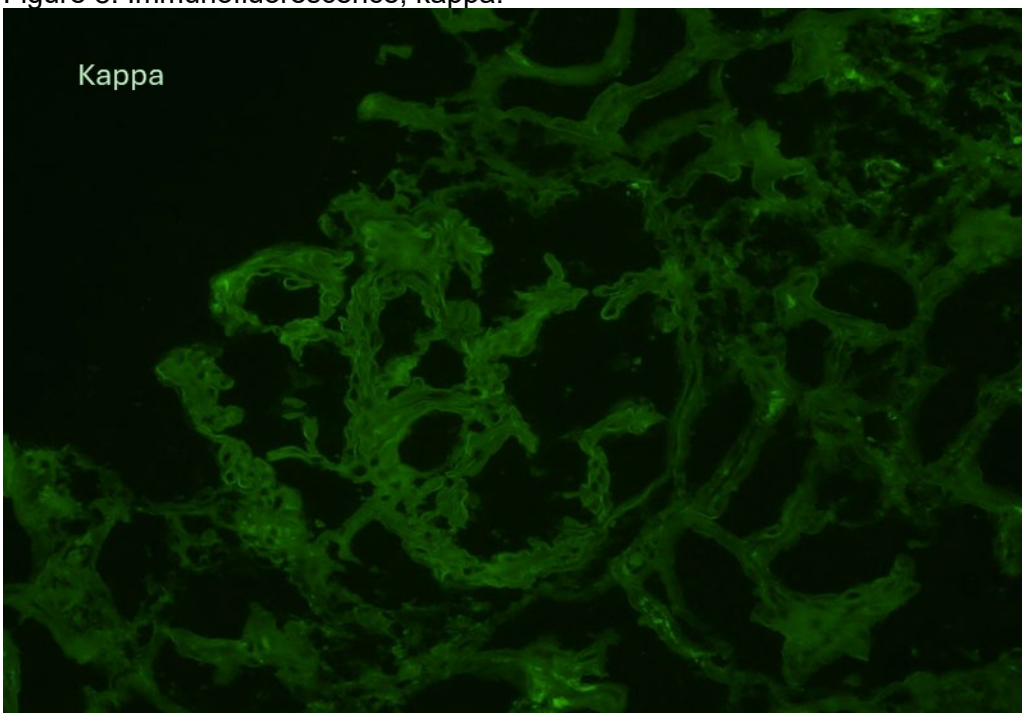


Figure 9. Electron microscopy:

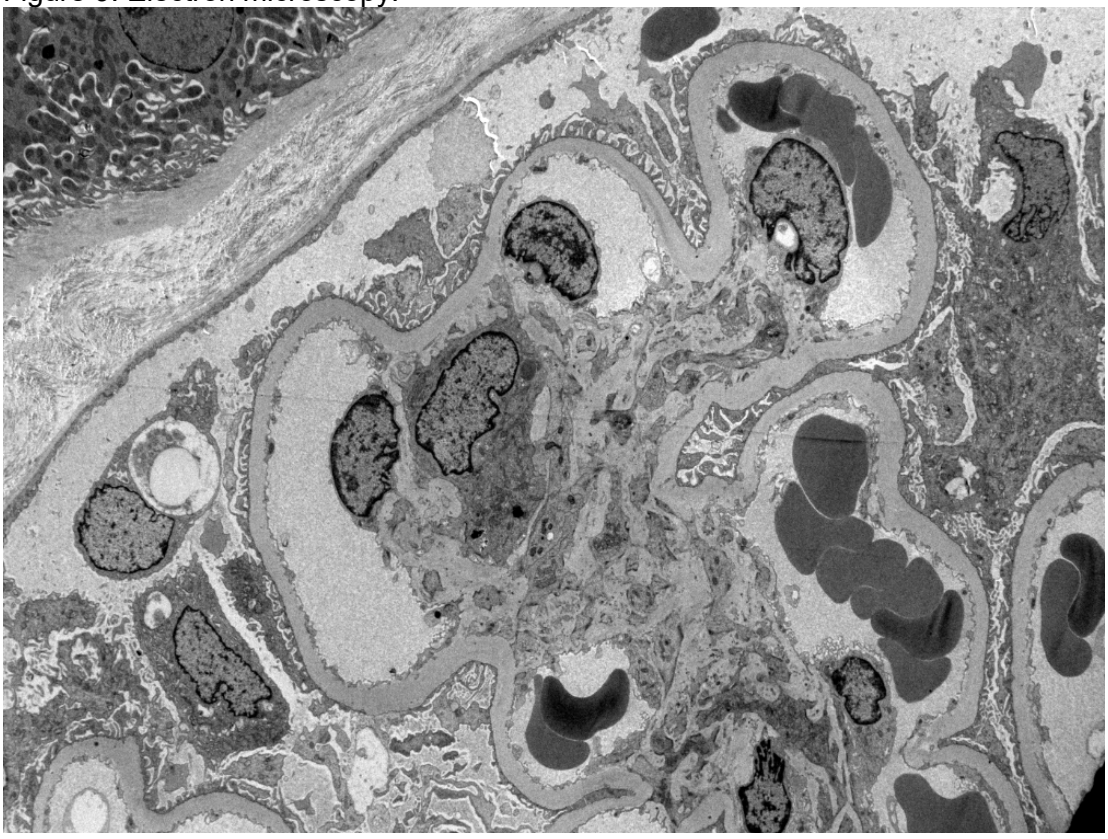


Figure 10. Electron microscopy:

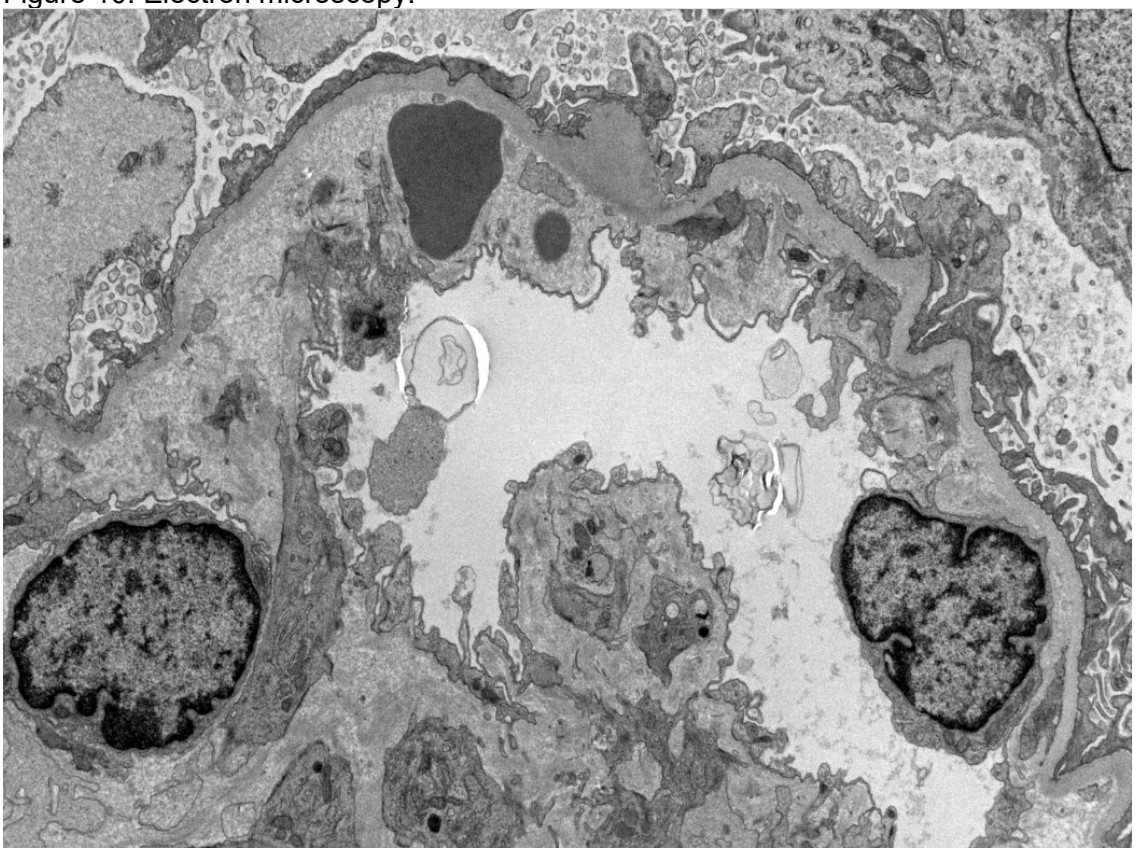
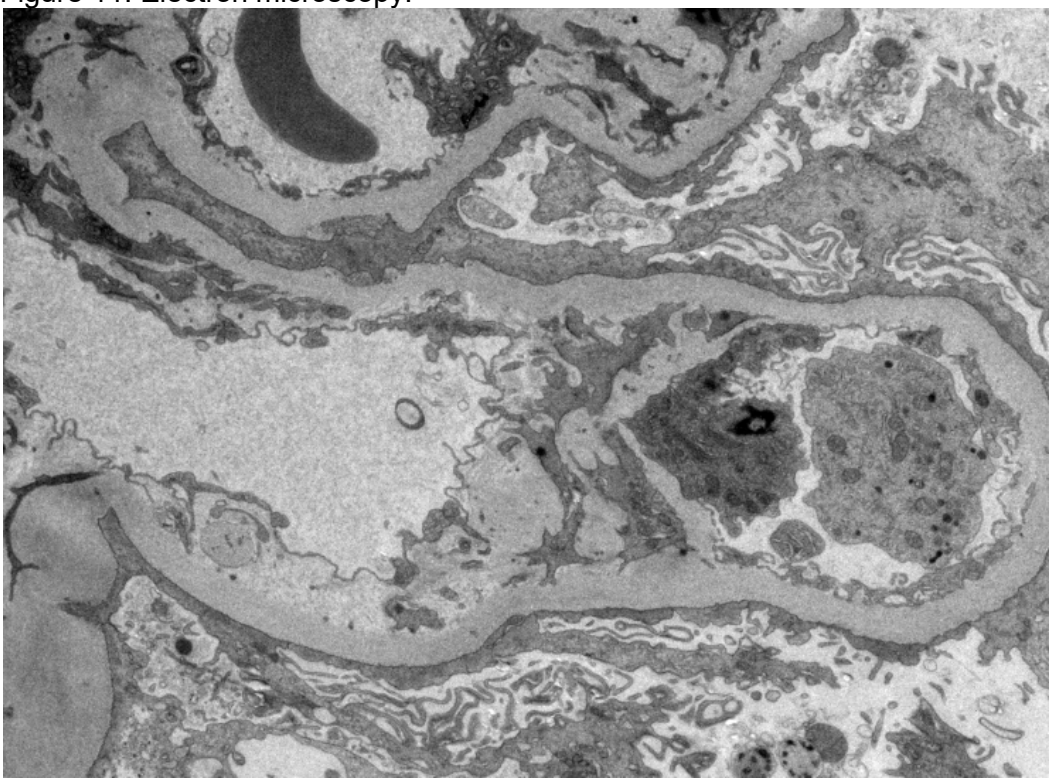


Figure 11. Electron microscopy:



Questions for Case 3

1. **In Figures 3 and 4 (PAS and Jones silver stain), what glomerular pattern of injury is depicted?**

    A. Crescentic glomerulonephritis
    B. Endocapillary hypercellularity
    C. Normal glomerulus
    D. Membranous glomerulonephritis

2. **How do you interpret the immunofluorescence microscopy findings (Figures 6, 7, and 8) from the biopsy?**

    A. Nonspecific linear staining, nondiagnostic
    B. Linear capillary wall staining for IgA and lambda
    C. Mesangial staining for IgA and lambda
    D. Granular capillary wall staining for IgA and lambda

3. **What is the pattern of injury seen in the electron microscopy image in Figure 10?**

    A. Mesangiolysis
    B. Subendothelial deposits
    C. Double contour
    D. Normal capillary loop

Case 4 from Sujal Shah, MD, Brigham and Women's Hospital

A 41-year-old man with schizophrenia on paliperidone and a history of smoking, stopped years ago, is admitted to the hospital with several weeks of fluid retention/generalized anasarca and weight gain (up to 230 pounds from baseline around 160 pounds). He first noticed this as swelling in his legs, corresponding to a new exercise regimen; the swelling then extended into his testicles and then his abdomen. More recently, he has noticed difficulty breathing. He does not report any changes in urine habits or appetite. The only new medication he is on is a diuretic, which was started for the swelling but has not been effective in decreasing it. There is no remarkable family history.

On admission, he has a BP reading of 143/95, but his vitals are otherwise unremarkable. On physical exam, the abdomen is distended with fluid, and the extremities reveal edema. A comprehensive metabolic panel is notable for elevated serum creatinine of 2.70 mg/dL (reported baseline ~1mg/dL), hypocalcemia (8.0 mg/dL), and markedly low serum albumin (1.4 g/dL). Urinalysis reveals 4+ protein, and a 24-hour urine study reveals proteinuria of 22.34g. Serologies are not ordered by the clinical team, as the feeling is that they would not preclude the need for biopsy.

The patient is started on furosemide and has a "great response". He is not initially started on steroids due to mental health history and the good response to furosemide. He is discharged home with a plan for outpatient kidney biopsy, which is performed three weeks later.

Biopsy Images

Figure 1. Light microscopy, Jones silver stain 4x, cortex:

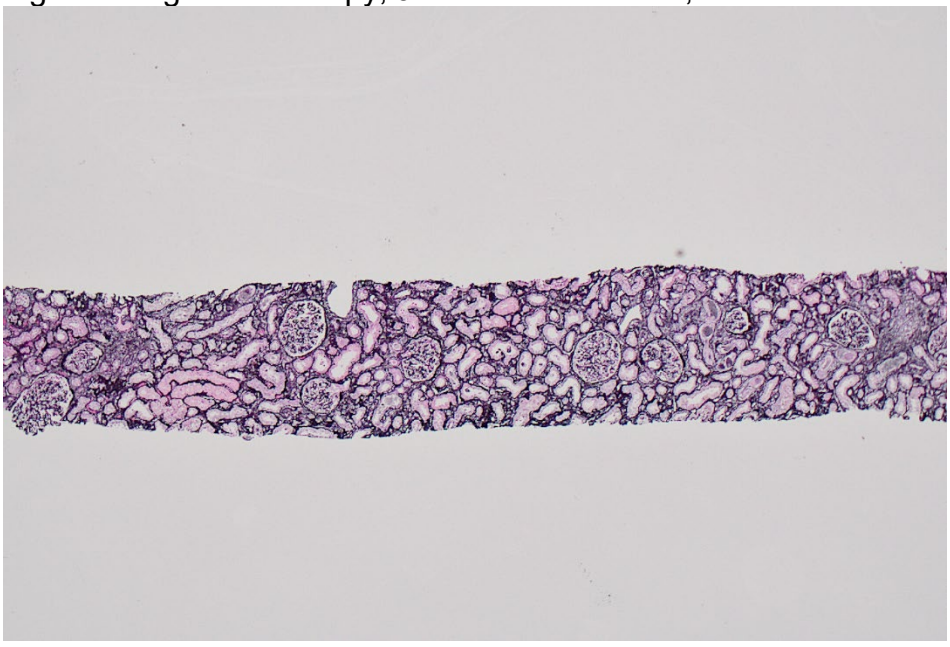


Figure 2. Light microscopy, PAS 10x, cortex:

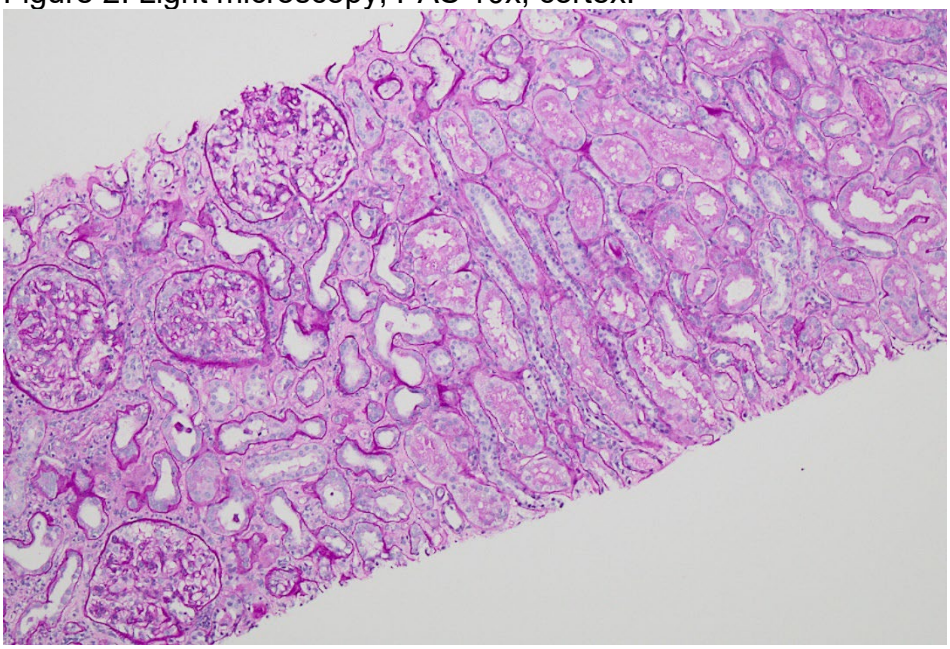


Figure 3. Light microscopy, hematoxylin and eosin (H&E) 40x, representative glomeruli:

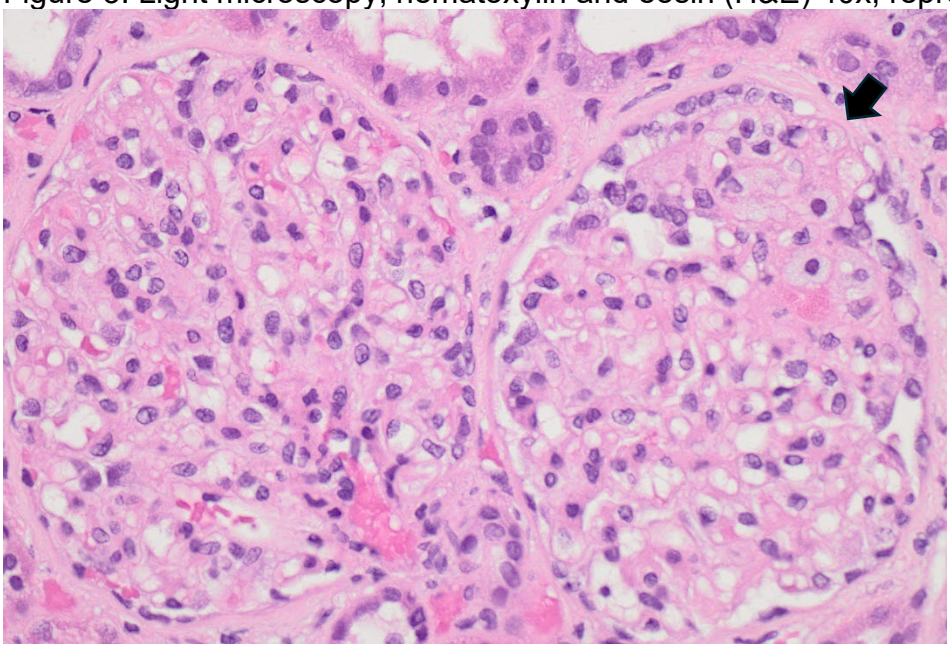
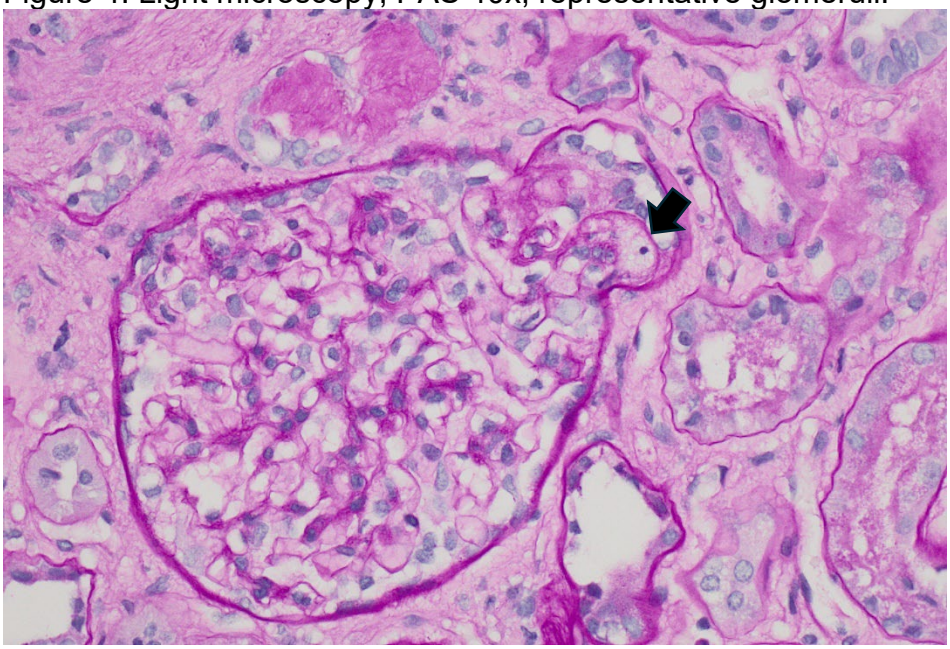
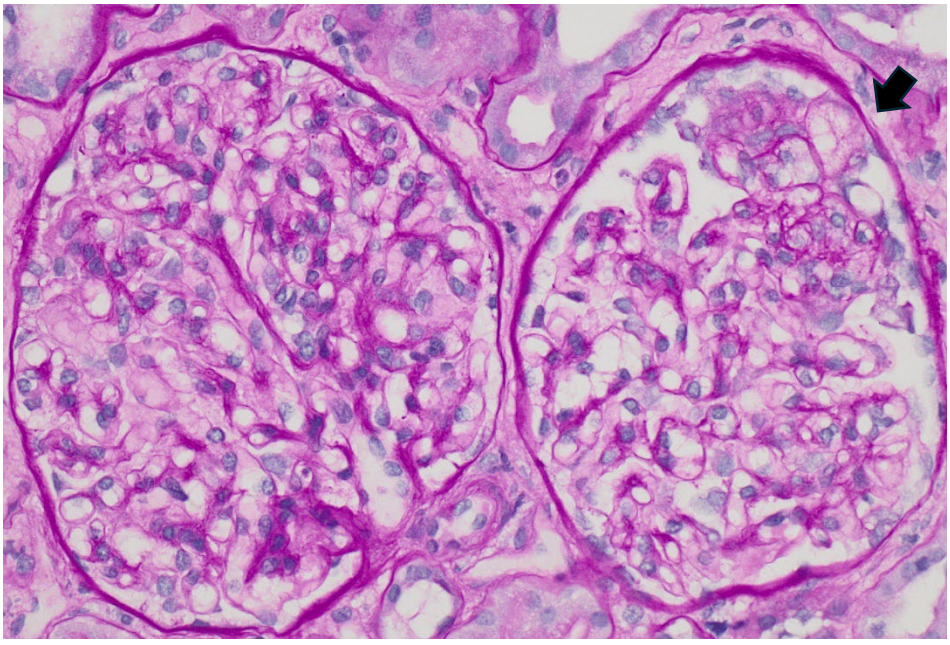


Figure 4. Light microscopy, PAS 40x, representative glomeruli:





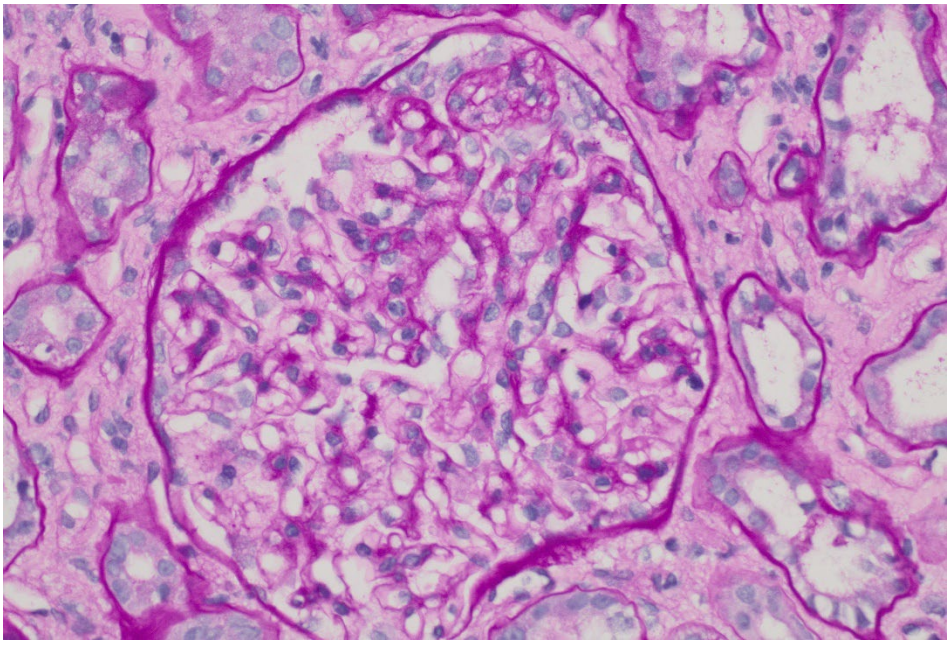


Figure 5. Light microscopy, Jones silver stain 40x, representative glomeruli:

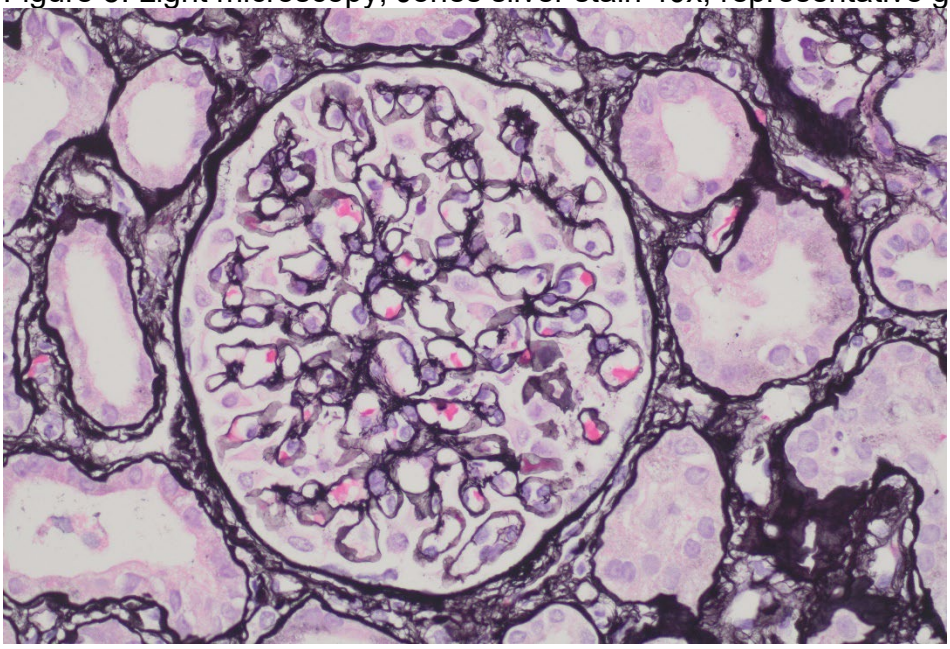
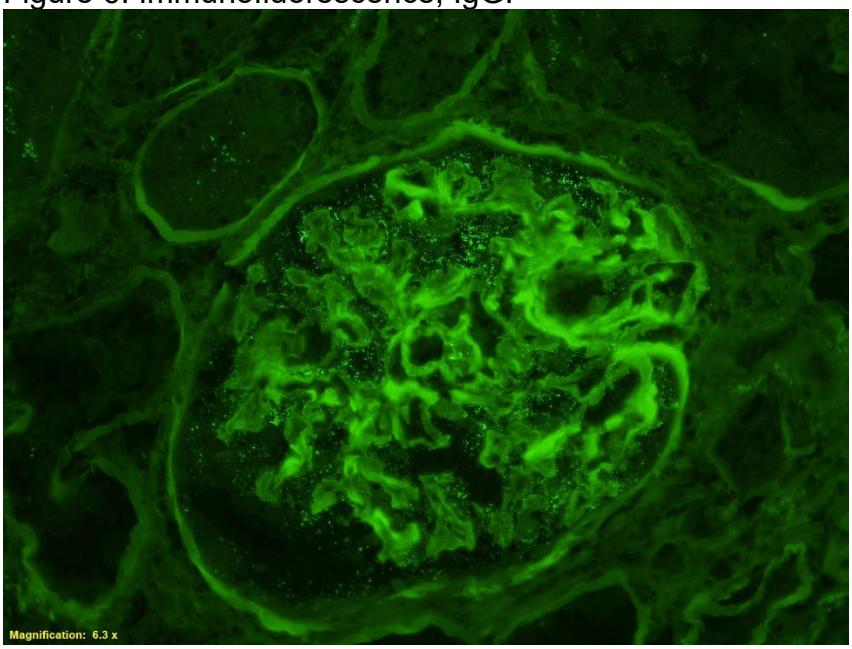
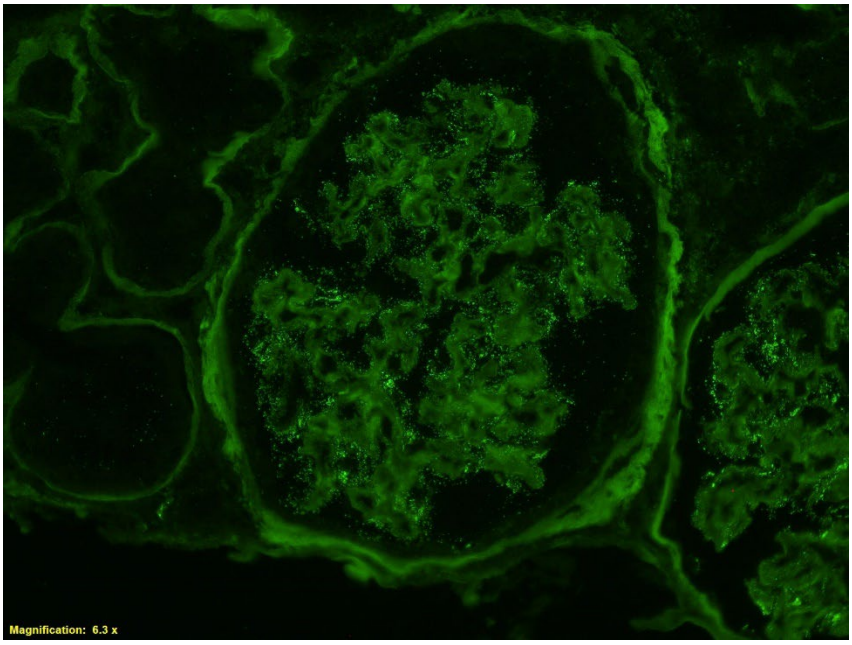


Figure 6. Immunofluorescence, IgG:





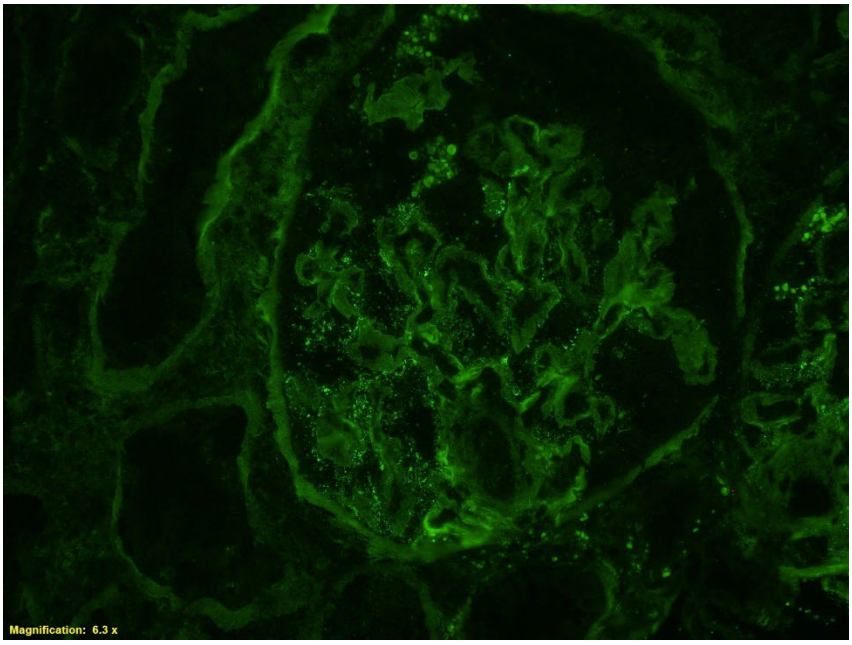
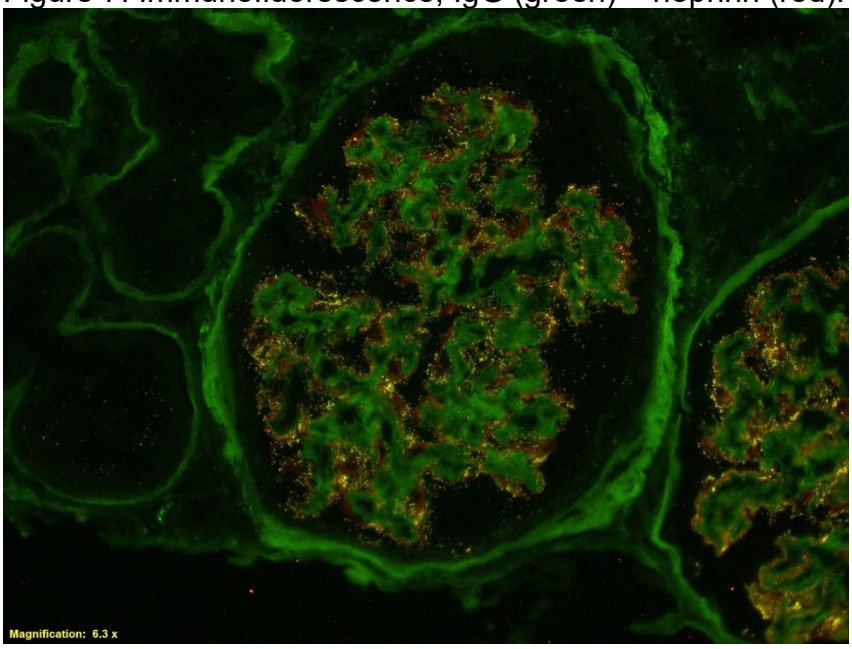


Figure 7. Immunofluorescence, IgG (green) + nephrin (red):



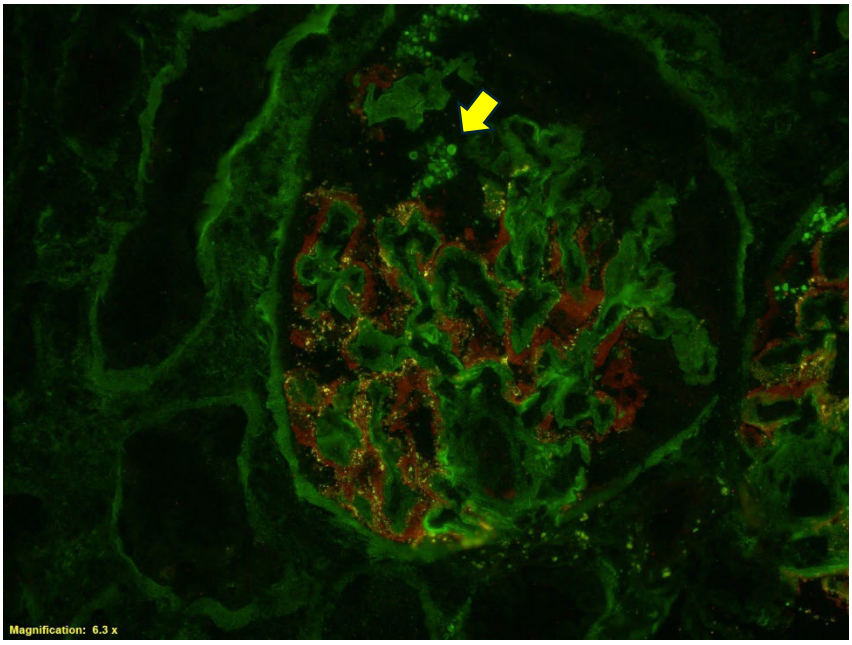
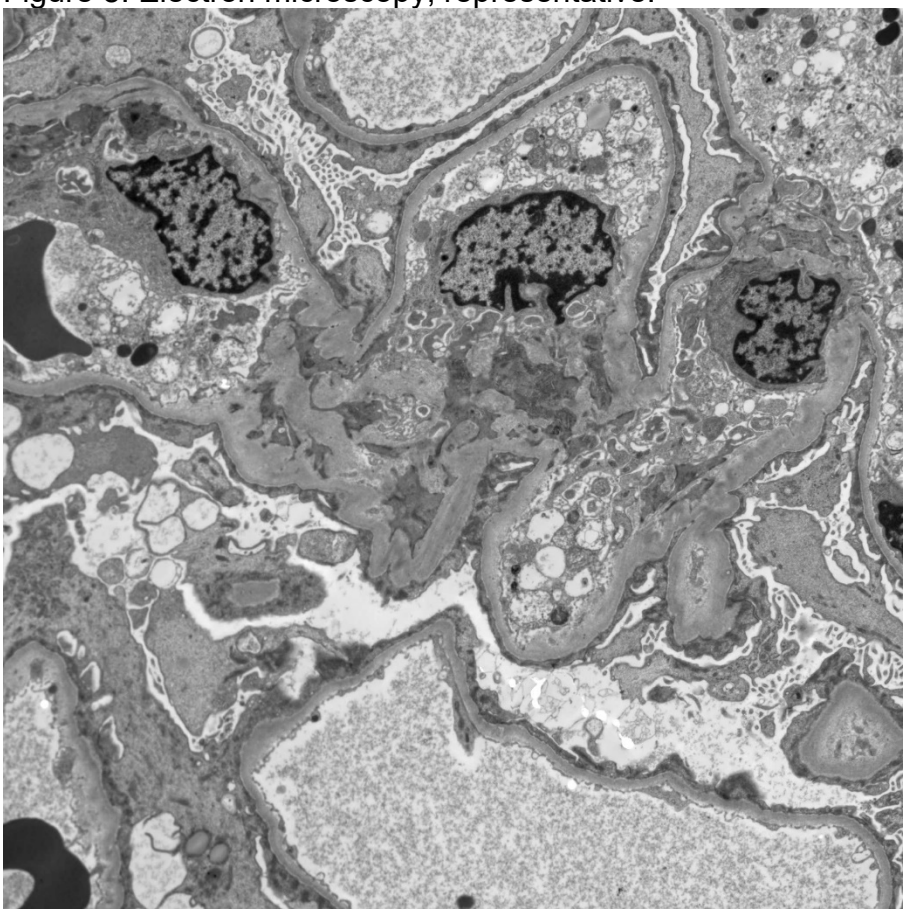
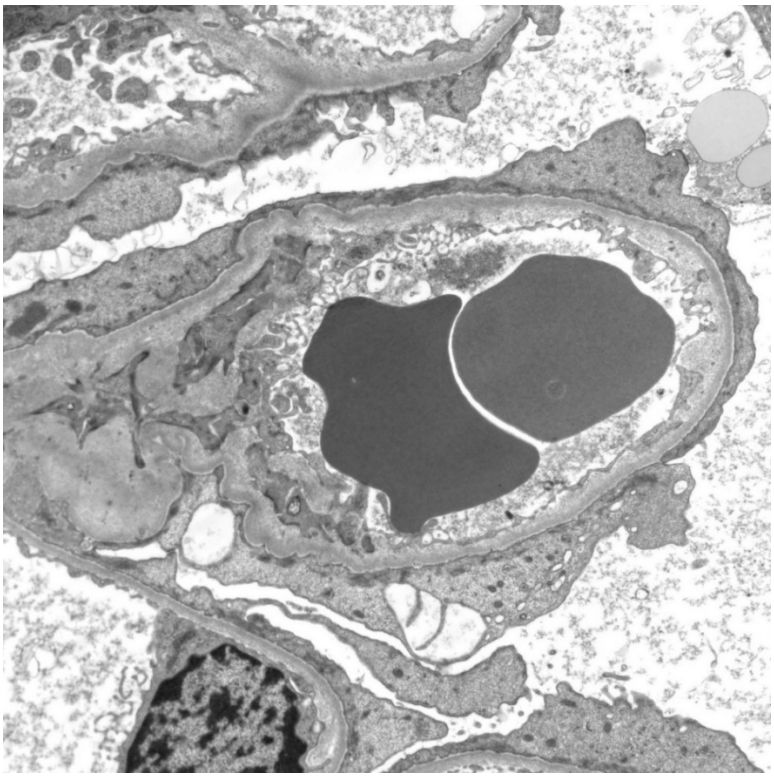


Figure 8. Electron microscopy, representative:





Questions for Case 4

1. **What is the glomerular pattern of injury seen on the light microscopy samples?**

    A. Crescentic
    B. Membranoproliferative
    C. Mesangial hypercellularity
    D. Membranous
    E. Tip lesions/segmental glomerulosclerosis

2. **How do you interpret the immunofluorescence findings from Figure 5?**

    A. Linear glomerular capillary wall staining for IgG
    B. Fine granular capillary wall staining for IgG
    C. Fine granular staining for IgG over the podocytes (“dusting”)
    D. Mesangial staining for IgG

3. **What is the pattern of injury seen on electron microscopy?**

    A. Subepithelial capillary deposits
    B. Diffuse foot process effacement without associated capillary loop deposits
    C. Subendothelial capillary loop deposits
    D. Mesangial deposits and hypercellularity
    E. Normal glomerular capillary loops