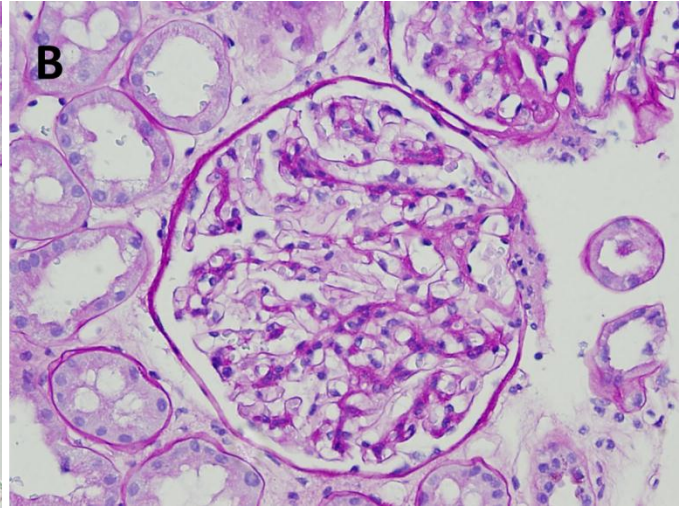
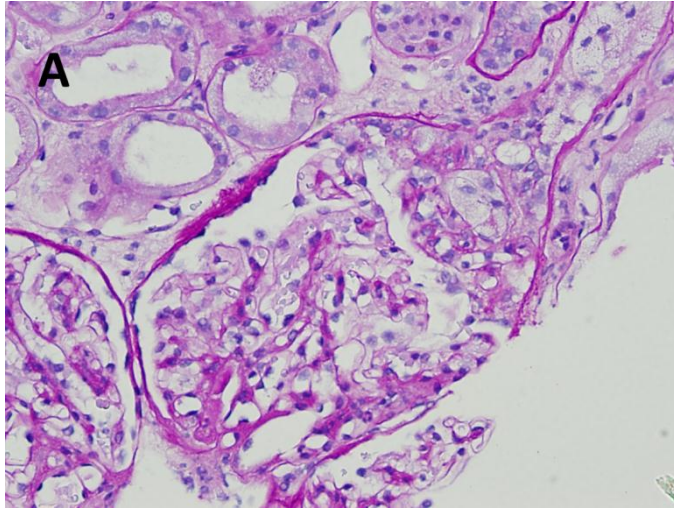


Atlas: Clinical Quiz 1

A 52-year-old white man with a history of mild hypertension and tobacco use presents with several months of worsening lower extremity swelling. Evaluation confirmed nephrotic syndrome with 12 g of proteinuria in a 24-hr collection, generalized edema, and a serum albumin of 1.8 g/dL. His serum creatinine was 1.33 mg/dL with an eGFR of 56 mL/min. Serum complement levels were normal, ANA negative, and hepatitis B and C serologies negative. He was slightly anemic. WBC count was 6200 and platelet count was 270,000/ μ L. Urine sediment showed 6-10 RBCs/HPF. A kidney biopsy was performed. What is the most likely diagnosis?

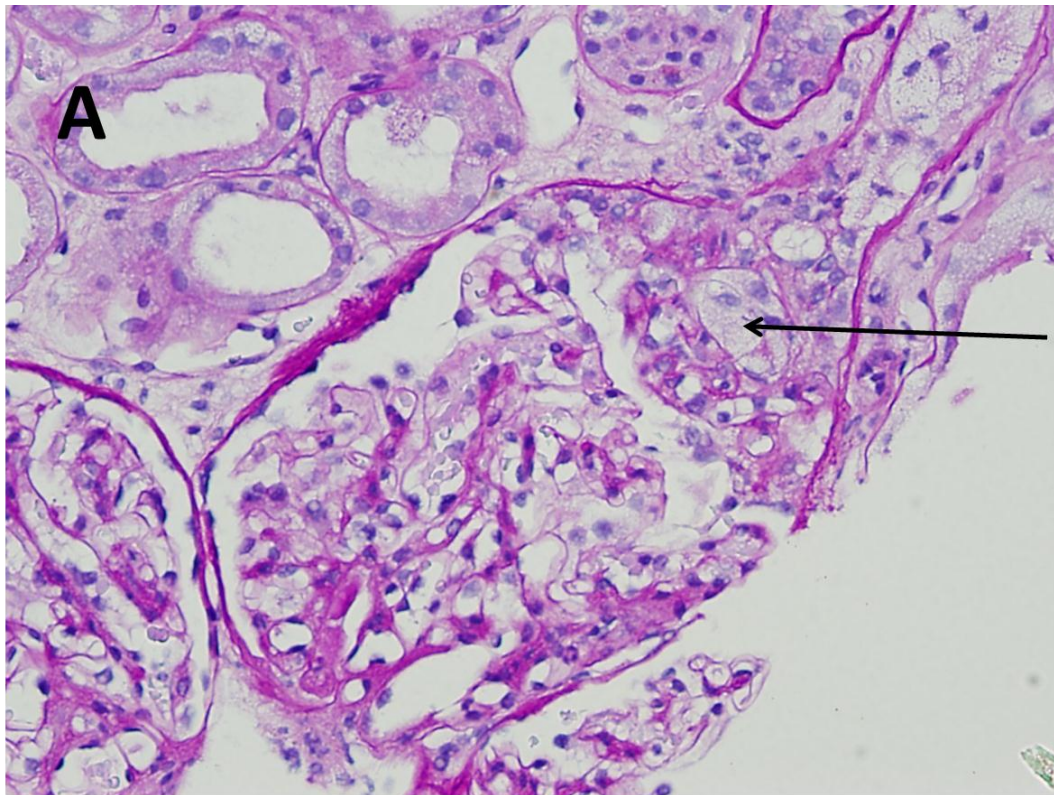


- A. Crescentic glomerulonephritis
- B. Minimal change disease
- C. Focal segmental glomerular sclerosis (FSGS), tip lesion variant
- D. IgA nephropathy with secondary FSGS

Solution to AJKD Blog's [Atlas: Clinical Quiz 1](#)

C: Focal segmental glomerular sclerosis with glomerular tip lesions

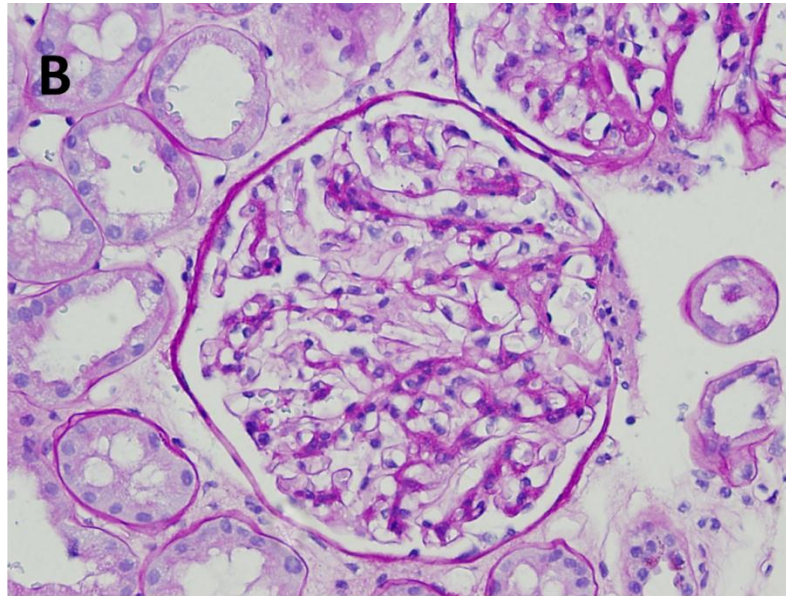
Paraffin sections contained well-preserved renal cortex with up to 48 glomeruli per section. Up to 10 glomeruli per section had areas of segmental sclerosis localized to the glomerular tip, the area of Bowman capsule where the proximal tubule originates (see arrow on Image A).



“Tip lesion” with foam cells [arrow], PAS.

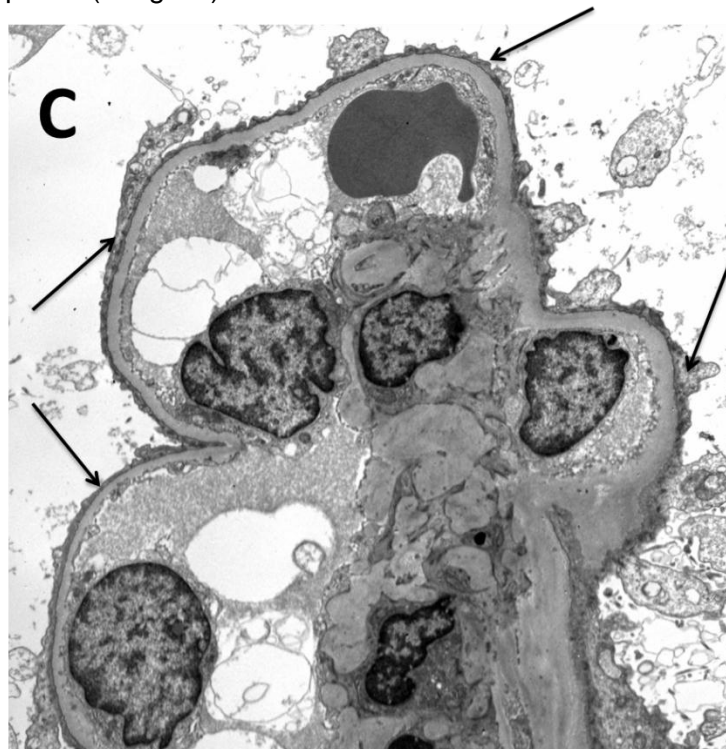
Some of these tip lesions contained foam cells (see at the tip of the arrow).

Most glomeruli were enlarged but otherwise unremarkable under the light microscope (see Image B).



Unremarkable glomerulus, PAS.

Immunofluorescence did not reveal immune complex deposits. Electron microscopy indicated diffuse foot process effacement, normal glomerular basement membranes, and no electron-dense immune-type deposits (Image C).



No deposits, total foot process effacement. (arrows)

Glomerular tip lesion, although classified as a variant of FSGS in the Columbia Classification, is clinically more similar to minimal change disease; patients with isolated glomerular tip lesions (no other light microscopic abnormality, absence of immune complex deposition) frequently present with nephrotic syndrome responsive to steroid treatment. Other forms of FSGS (perihilar, collapsing, cellular, and not otherwise specified [NOS] variants) are more commonly steroid resistant and have a worse outcome. Glomerular tip lesion is classified as a form of FSGS because, unlike minimal change disease, not all glomeruli are normal on light microscopy; some of them show segmental sclerosis/adhesion at the origin of the proximal tubule (the glomerular tip). Immune complex deposits are absent and there is widespread foot process effacement. The definition of the tip lesion vary between investigators; according to the Columbia classification of FSGS, up to 25% of the glomerular tuft can be obliterated by sclerosis at or close to the vascular pole. Others consider less extensive segmental lesions as true tip lesions. We believe that the glomerular tip lesion is a nonspecific reaction of the glomerulus that can be seen in a variety of glomerular diseases with heavy proteinuria, including minimal change disease and FSGS, but also membranous glomerulopathy and diabetic nephropathy. The pathogenesis of the tip lesion is unclear, but it is possible that it is related to herniation of the glomerular capillary tufts into the origin of the proximal tubules, podocyte injury, and subsequent adhesions of the glomerular capillaries to the glomerular tip. As pointed out above, most patients with isolated glomerular tip lesions and heavy proteinuria will respond to steroids just like minimal change disease. Steroid-resistant patients frequently develop progressive FSGS. Unfortunately, there are no consistent markers to predict which patient with glomerular tip lesion will behave like minimal change disease and which will have progressive FSGS.

Post prepared by and all images courtesy of Tibor Nadasdy, MD, AJKD Blog Contributor and AJKD Kidney Biopsy Teaching Case Advisory Board member.

To view the related installment on [Tip Lesion Variant of FSGS](#) (freely available), please visit the [Atlas of Renal Pathology II](#) at AJKD.org.