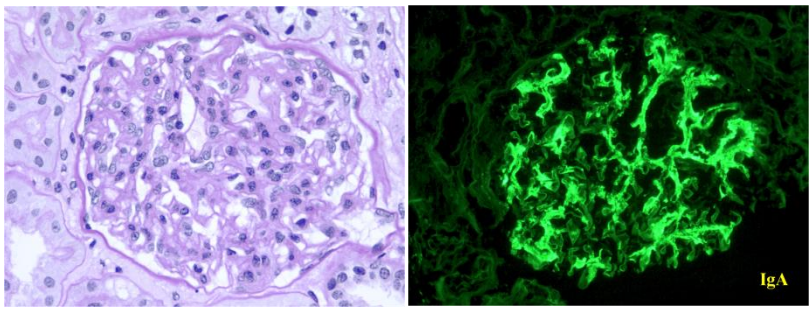
**Solutions to *e*AJKD's Test Your Knowledge: Proliferative Glomerulonephritis**

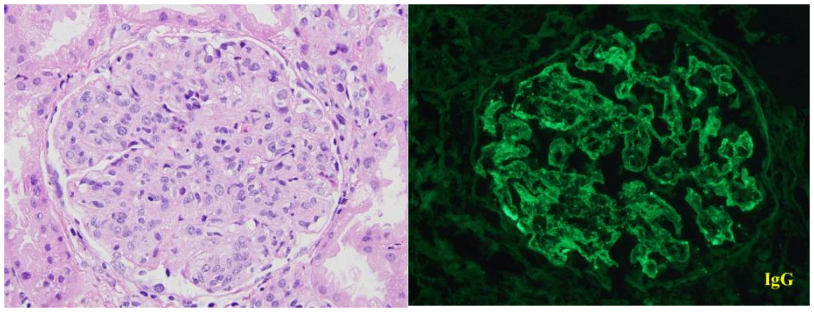
*All images courtesy of Dr. Isaac E. Stillman*

**Image 1: Mesangial Proliferative GN – Image D**




IgA nephropathy is a GN defined by the IF finding of mesangial IgA that is dominant (stronger staining) over IgG (or occasionally co-dominant with IgG). The LM patterns associated with IgA nephropathy are variable. The most common, as seen here, is mesangial proliferation (capillary lumens are open) where the PAS reaction highlights the mild increase in mesangial matrix and cells. Other common patterns include segmental sclerosis (associated with proteinuria), endocapillary proliferative GN, and crescentic GN. IgA nephropathy may be normal by LM. The IF pattern shows strong staining restricted to the mesangium. In contrast, IgA dominant post-infectious GN (seen usually in diabetics) shows deposits primarily along the capillary wall (subepithelial humps).

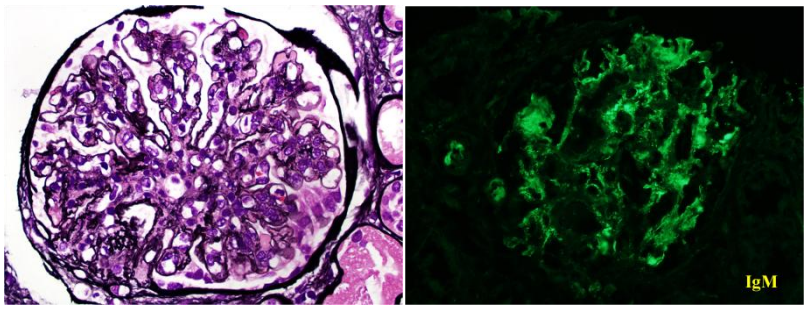
**Image 2: Exudative Endocapillary Proliferative GN – Image E**




This H&E stain shows global endocapillary proliferation, with associated occlusion of the capillary lumens. Much of the hypercellularity is due to the influx of inflammatory cells that are difficult to recognize by LM. Neutrophils are the distinctive exception, hence the designation "exudative" when they are present. This LM pattern while non-specific is

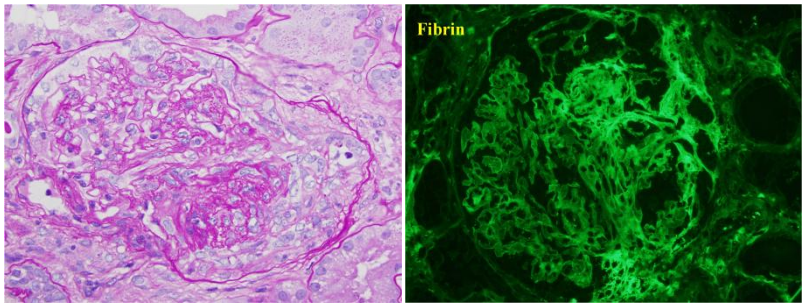
usually associated with IC deposition on IF. The associated pattern of IgG deposition seen here is predominantly that of “starry sky,” ie, finely granular mesangial and endocapillary deposits, with occasional “humps” seen along the capillary walls. This pattern is typical of post-infectious GN and usually seen early in the course of the disease. An alternate early pattern is the “garland,” which may have a worse prognosis. With time, these patterns often evolve into deposition limited to the mesangium.

**Image 3: Membranoproliferative GN – Image C**



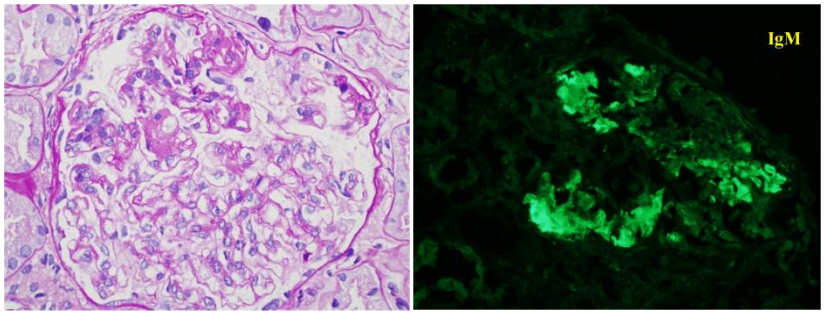

The Jones stain shows mesangial and segmental endocapillary proliferation and especially highlights duplicated glomerular basement membranes (“tram tracking”). Also seen are silver negative deposits between the membranes, as well as occasionally within capillary lumens. These pseudothrombi (as opposed to true fibrin thrombi) are typical of lupus nephritis as well as cryoglobulinemic GN. The monoclonal component of type II mixed cryoglobulinemia (associated with hepatitis C infection) is almost always IgM kappa. The strong polyclonal IgM dominant staining seen here in the mesangium and also along capillary walls (with only minimal accompanying IgG) suggests chronic viral infections such as hepatitis C, sometimes with associated cryoglobulins, as seen in this patient.

**Image 4: Crescentic (Extracapillary Proliferative) GN – Image A**



While this PAS section does not stain the cytoplasm of the cells present in the urinary space, it does highlight the presence of a crescent by delineating its boundaries - staining the tuft, as well as the membrane of Bowman capsule. Segmental necrosis, accompanied by fibrin in the urinary space, incites crescent development as illustrated by the strong staining for fibrin within a segment of the glomerulus and in the urinary space. These findings are common to all crescentic GN, regardless of etiology. Crescentic GN are classified on the basis of their IF findings, a model for the classification system proposed by Sethi. This patient showed no significant Ig or C3 deposition ("pauci-immune"), a finding strongly associated with ANCA vasculitis (in this case due to high titer anti-MPO).

**Image 5: Segmental Sclerosis - Image B**




Sclerosis, the glomerular scaring process defined by architectural obliteration due to increased matrix, can be the end result of proliferative GN. Segmental necrosis, for example, can "heal" as segmental sclerosis, as seen here. While the lower half of the tuft appears normal, the upper side shows areas of increased PAS positive matrix with loss of normal structure. Some of these foci show strongly PAS positive refractile hyaline droplets, reflecting plasma proteins that have "exudated" into the areas of chronic injury. The corresponding IF pattern reveals the non-specific deposition (or entrapment) of IgM and C3 from the circulation within areas of sclerosis. These coarse and chunky deposits are not present in uninvolved areas, and thus do not suggest a complement-mediated GN.