Focal Segmental Membranoproliferative Glomerulonephritis

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Case scenario

These are representative images of a kidney biopsy from a 35-year-old female patient presenting with nephritic syndrome.

The biopsy was adequate with both cortex and medulla. Up to 15 glomeruli were included. The glomeruli showed a spectrum of morphologic lesions. Some of the representative glomeruli with pathologic lesions are shown in the following images.

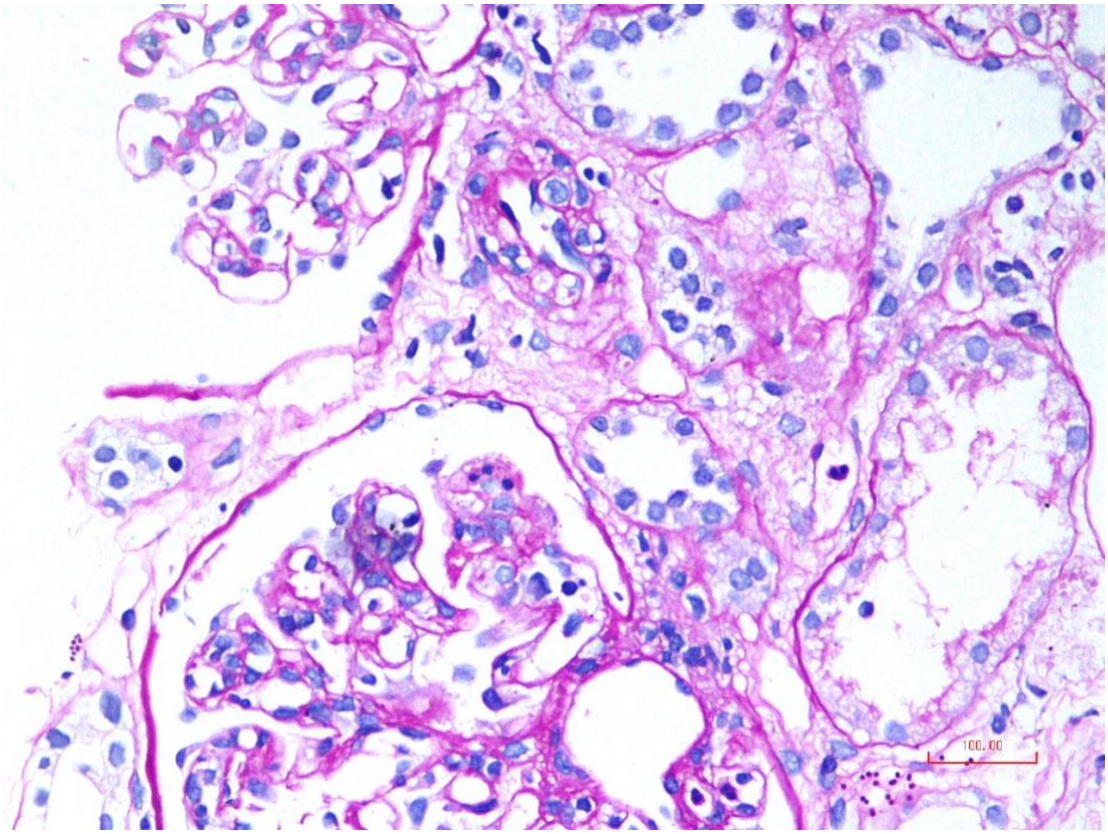

Figure 1. A high-power view of renal biopsy from the above case shows two glomeruli exhibiting different morphologic lesions. An arteriole and some tubules are seen in the background. (Periodic acid Schiff (PAS) stain, × 400).

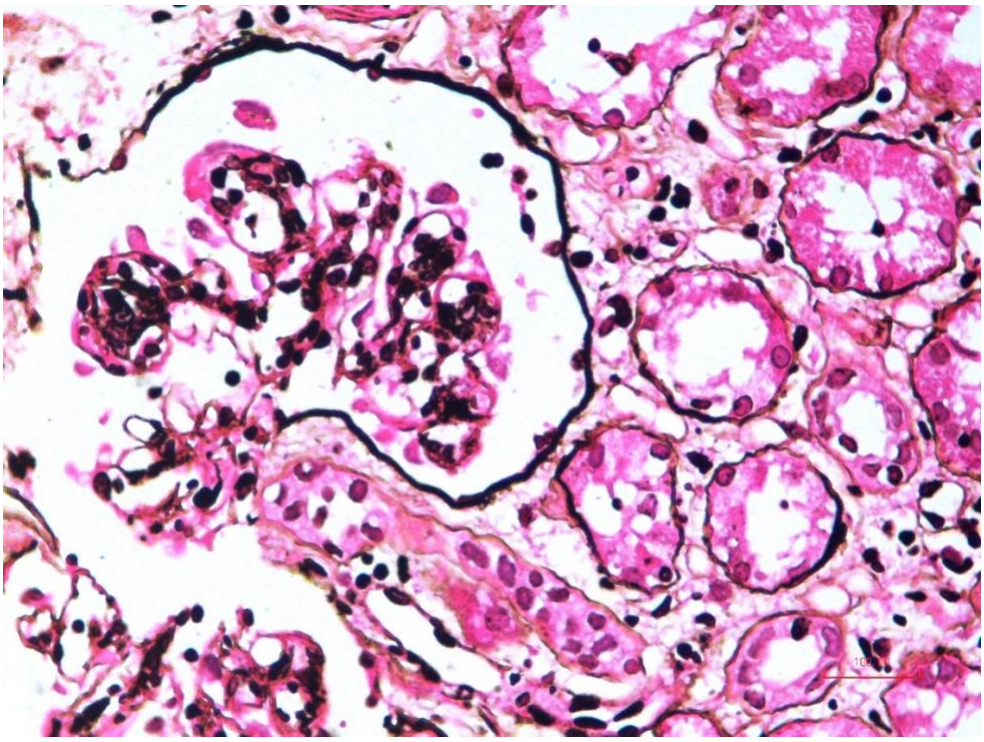

Figure 2. The high-power view of renal biopsy from the above case shows parts of two glomeruli exhibiting different morphologic lesions. An arteriole and some tubules are seen in the background. (Jones methenamine stain (JMS), × 400).

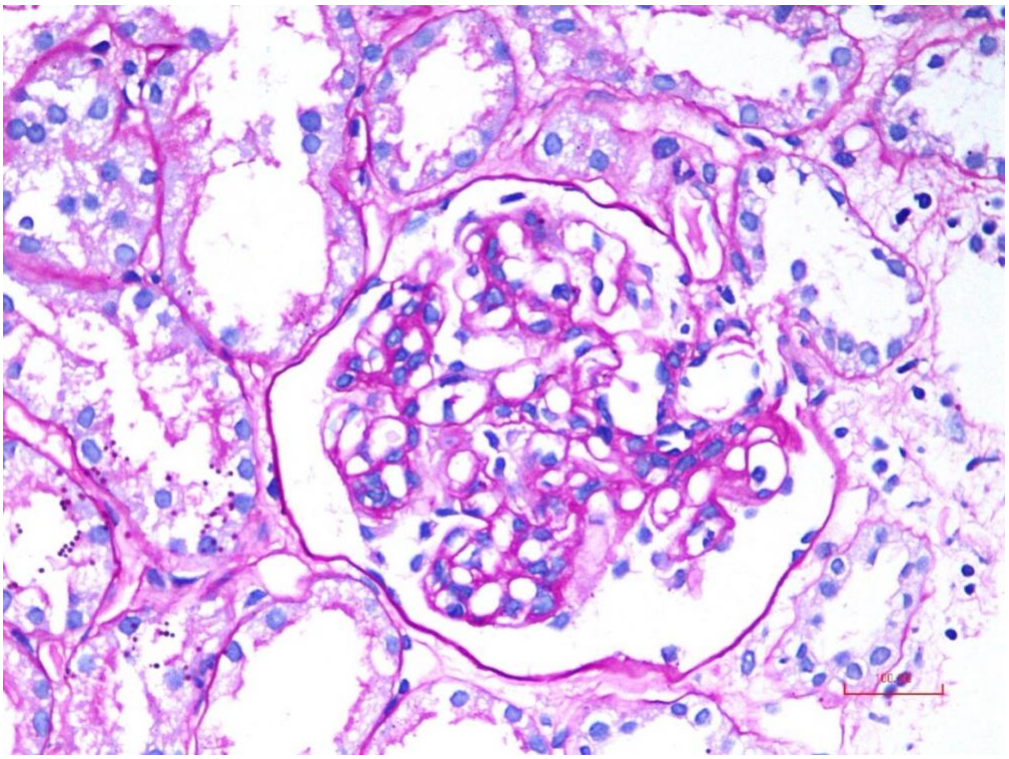

Figure 3. A high-power view of renal biopsy from the above case shows one glomerulus with different tufts exhibiting different morphologic lesions. (Periodic acid Schiff (PAS) stain, × 400).

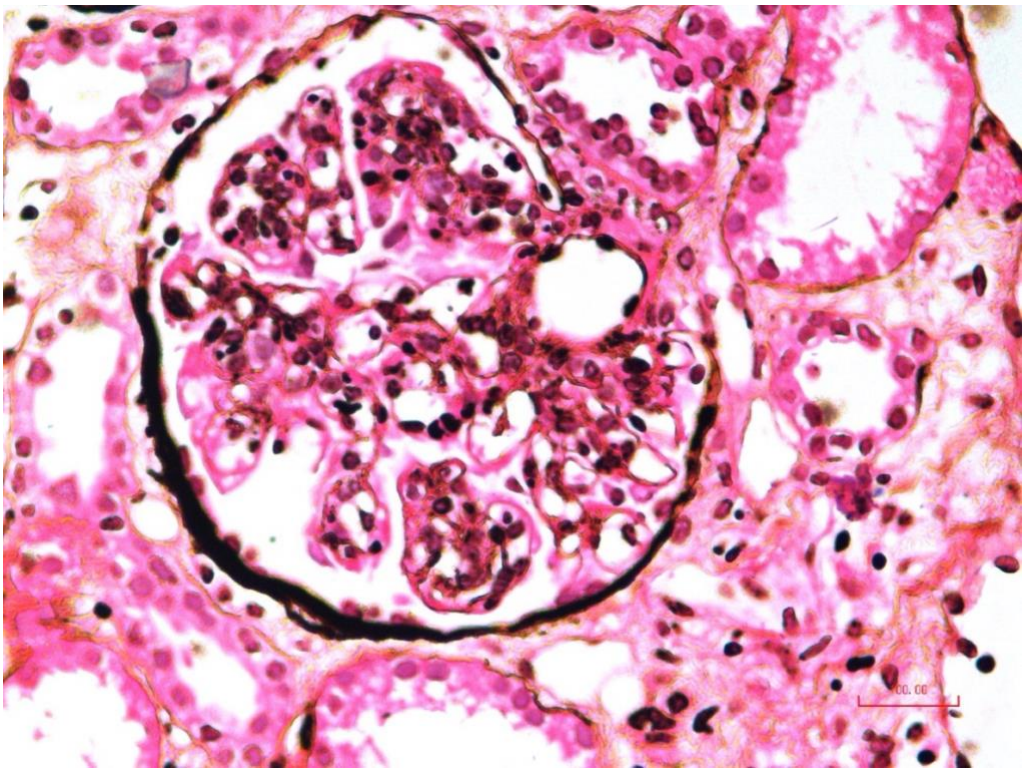

Figure 4. A high-power view of renal biopsy from the above case shows one glomerulus with different tufts exhibiting different morphologic lesions. (Jones methenamine stain (JMS), × 400).

Questions

Q1. What is the morphological pattern of glomerular injury in this biopsy?

Q2. What is the significance of this morphologic variant of glomerulonephritis (GN)?

Q3. What is the underlying disease in this case?

Answers:

Ans 1. The glomeruli in this biopsy show morphological pattern of focal segmental membranoproliferative glomerulonephritis (FSMPGN), a morphologic variant of membranoproliferative glomerulonephritis (MPGN). In this variant of MPGN, only some glomeruli exhibit lesions (eg. the lower glomerulus in Figure 1), while others appear unaffected (eg. the upper glomerulus in Figure 1). A characteristic feature of all MPGN lesions is thickening of the capillary walls along with mesangial proliferation, hence, the alternative term of mesangiocapillary GN, implying the involvement of both mesangium and capillary walls in this disease process.

Ans 2. This variant of MPGN is a transitional lesion that has the potential to evolve into typical MPGN, and conversely, typical MPGN may regress into its focal form. As a result, FSMPGN is often regarded as either an early manifestation of typical MPGN or a transitional stage during recovery.

Ans 3. All those diseases which give rise to MPGN pattern of injury can give rise to this lesion. Hence, its etiopathogenetic spectrum parallels that of the typical MPGN pattern of injury. It should be noted that both MPGN and FSMPGN are patterns of glomerular injury and not specific diseases. The latter can only be diagnosed by the correlation of all available clinical, serological, laboratory, immunofluorescence, and electron microscopy findings.

Discussion

D'Amico and Ferrario, in their extensive review of patients with membranoproliferative glomerulonephritis (MPGN) type I and dense deposit disease (DDD), identified six morphologic variants: classic, nodular, exudative, focal segmental, with massive subendothelial deposits, and crescentic. They proposed that these morphologic patterns reflect distinct etiologic and pathogenetic mechanisms and that clinical outcomes are influenced by the histopathologic subtype.[1]

Conversely, other researchers argue that these morphologic variants represent a continuum of MPGN's manifestations rather than distinct entities associated with specific etiologies, pathogenetic factors, or clinical outcomes. This perspective suggests that the varying patterns observed in MPGN biopsies may arise from different stages of disease progression rather than fundamentally separate processes. This nuanced approach underscores the complexity and variability of MPGN, emphasizing the need for comprehensive diagnostic evaluations that integrate morphologic, ultrastructural, and immunohistologic findings.

Focal segmental membranoproliferative glomerulonephritis (FSMPGN) is a morphologic variant of membranoproliferative glomerulonephritis (MPGN), in which only some glomeruli exhibit lesions, while others appear unaffected (Figures 1). In addition, within an individual glomerulus, some tufts are affected whereas others are not (Figures 2 - 4). However, it is still not clear whether glomeruli that appear normal under light microscopy harbor deposits detectable by electron microscopy or immunofluorescence techniques or not. Many researchers have reported this subtype of MPGN in their renal biopsy studies, mostly in pediatric patients.[2-5]

FSMPGN has the potential to evolve into typical MPGN, and conversely, typical MPGN may regress into its focal form. As a result, FSMPGN is often regarded as either an early manifestation of typical MPGN or a transitional stage during recovery. This transition was elegantly described by Kano et al. in a case report that described a girl with MPGN type- I, ultimately diagnosed through a third biopsy.[6] The initial biopsy revealed features of endocapillary proliferative glomerulonephritis, while the second biopsy was diagnosed as focal MPGN. This progression underscores the dynamic nature of MPGN, with varying presentations over time.

In summary, FSMPGN is just a transitional phase in the evolution or resolution of diffuse or typical MPGN and its etiopathogenesis and diagnostic approach are similar to those of typical MPGN.

References:

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