Nephroquiz 2: Differential Diagnoses of Mesangial Proliferative Glomerulonephritis

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CASE

A 38-year-old man was admitted to hospital for evaluation of kidney dysfunction. His serum creatinine on admission was 1.6 mg/dL. His past medical history was unremarkable and there was no family history of kidney dysfunction. His blood pressure was 130/80 mm Hg, and he had no history of hypertension. Physical examination revealed only mild pedal edema. On urinalysis, there were microscopic hematuria with dysmorphic erythrocytes and proteinuria. Twenty-four-hour urine collection revealed 1200-mg protein excretion per day. Studies of serum complements, antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, and hepatitis viral markers had unremarkable results. The size of the kidneys was normal on ultrasonography.

Biopsy of the kidney was performed, and light microscopic study of the tissue revealed 10 glomeruli all of which showing mesangial widening with hypercellularity. No obvious endocapillary proliferation or subendothelial deposits were identified (Figure 1). The immunofluorescence study revealed deposition of immunoglobulin A (IgA) and complement 3 (C3) in the mesangial regions (Figure 2). Based on pathologic findings, a diagnosis of mesangiopathic glomerulonephritis with IgA deposition, consistent with IgA nephropathy class III, was established.

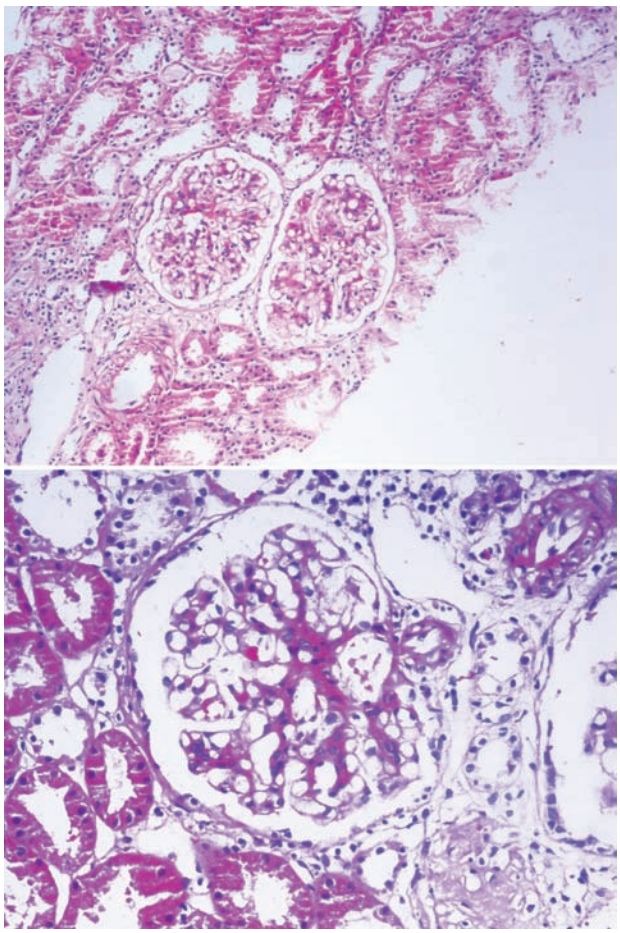

Figure 1. Glomeruli show mesangial widening with hypercellularity (hematoxylin-eosin).

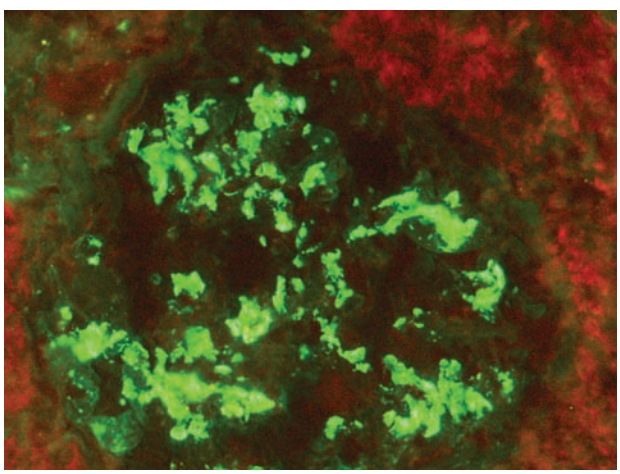

Figure 2. Immunofluorescent antibody technique study revealed deposition of immunoglobulin A and complement 3 in the mesangial regions.

QUIZ
What Are the Differential Diagnoses of Mesangial Proliferative Glomerulonephritis?

Mesangial proliferative glomerulonephritis is defined by the World Health Organization Committee on Classification of Renal Disease as an essentially uniform increase in mesangial cells (more than 3 mesangial cells per mesangial area) in more than 80% of the glomeruli. Included in this definition is the specification that capillary lumens are patent, which distinguishes mesangial proliferative glomerulonephritis from conditions with endocapillary proliferation. Mesangial proliferative glomerulonephritis represents a heterogeneous group of conditions rather than a single disease. Therefore, although a characteristic light microscopy appearance can be described, it is not possible to unify a typical manifestation or clinical course.[1]

Mesangial proliferative glomerulonephritis can be classified based on immune deposition. Deposition of IgA and C3 is characteristic of IgA nephropathy that can be associated with faint deposition of IgG.[2] Concomitant deposition of all antibodies (IgG, IgA, and IgM) along with C1q and C3 is diagnostic for mesangial lupus nephritis.[3] Deposition of IgM alone or along with faint staining of C3, C4, or C1q in a mesangial proliferative background can be in favor of IgM nephropathy.[4,5] Depositions of C1q predominantly but along with IgG and/or IgM in the mesangial area may remind us of the entity of C1q nephropathy.[6] Moreover, deposition of IgG and C3 can be found in a heterogeneous group of disorders including postinfectious glomerulonephritis-like infectious endocarditis or other rheumatologic disorders such as mixed connective tissue disease. Also, deposition of IgG, especially IgG-4 along with C3, in the mesangial area can be the pathologic manifestation of fibrillary glomerulonephritis.[7] On the other hand, lack of immune deposition in the presence of mesangial proliferation can be seen in patients with hematuria or proteinuria, even in nephritic ranges. The etiology of this latter condition is usually unclear, but it can be seen in focal segmental glomerulosclerosis, in Alport syndrome, or less possibly, in partially treated cases of lupus nephritis.[8,9]

In conclusion, the light microscopic entity of mesangial proliferative glomerulonephritis seems to be the common pathologic picture of a variety of disorders with quite different pathogenetic mechanisms. This emphasizes a deeper look and utilization of more sophisticated diagnostic tools in order to reach the accurate diagnosis.

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