Glomerular Lesions Associated with Systemic Diseases

Many immunologically mediated, metabolic, or hereditary systemic disorders are associated with glomerular injury; in some (e.g., SLE and diabetes mellitus), the glomerular involvement is a major clinical manifestation. Most of these diseases are discussed elsewhere in this book. Here we briefly recall some of the lesions and discuss only those not considered in other sections.

Lupus Nephritis

The various types of lupus nephritis were described in Chapter 6. As discussed, SLE gives rise to a wide variety of renal lesions and clinical presentations. The clinical manifestations can include recurrent microscopic or gross hematuria, the nephritic syndrome, rapidly progressive glomerulonephritis, the nephrotic syndrome, acute and chronic renal failure, and hypertension.

Henoch-Schönlein Purpura

This childhood syndrome consists of purpuric skin lesions, abdominal pain and intestinal bleeding, and arthralgias along with renal abnormalities. Skin lesions characteristically involve the extensor surfaces of arms and legs as well as buttocks; abdominal manifestations include pain, vomiting, and intestinal bleeding. The renal manifestations occur in one third of patients and include gross or microscopic hematuria, nephritic syndrome, nephrotic syndrome, or some combination of these. A small number of patients, mostly adults, develop a rapidly progressive form of glomerulonephritis with many crescents. Not all components of the syndrome need to be present for the diagnosis, and individual patients may have purpura, abdominal pain, or urinary abnormalities as the dominant feature. The disease is most common in children 3 to 8 years old, but it also occurs in adults, in whom the renal manifestations are usually more severe. There is a strong background of atopy in about one third of patients, and onset often follows an upper respiratory infection. IgA is deposited in the glomerular mesangium in a distribution similar to that of IgA nephropathy. This has led to the concept that *IgA nephropathy and Henoch-Schönlein purpura are manifestations of the same disease.* The finding of Ig and C3 deposits in glomeruli suggests that immune complexes are involved in the disease.

MORPHOLOGY

On histologic examination, the renal lesions vary from mild focal mesangial proliferation to diffuse mesangial proliferation and/or endocapillary proliferation to crescentic glomerulonephritis. Whatever the histologic lesions, the pathognomonic feature by fluorescence microscopy is the **deposition of IgA, sometimes with IgG and C3, in the mesangial region**, sometimes with deposits extending to the capillary loops. The skin lesions consist of subepidermal hemorrhages and a necrotizing vasculitis involving the small vessels of the dermis. Deposits of IgA, along with IgG and C3, are also present in such vessels. Vasculitis also occurs in other organs, such as the gastrointestinal tract, but is rare in the kidney.

The course of the disease is variable, but recurrences of hematuria may persist for many years after onset. Most children have an excellent prognosis. Patients with the more diffuse lesions, crescents, or the nephrotic syndrome have a somewhat poorer prognosis.

Glomerulonephritis Associated with Bacterial Endocarditis and Other Systemic Infections

Glomerular lesions occurring in the course of bacterial endocarditis or other systemic infections, such as infected atrioventricular shunts, represent a type of immune complex nephritis initiated by complexes of bacterial antigen and antibody. Hematuria and proteinuria of various degrees characterize this entity clinically, but an acute nephritic presentation is not uncommon, and even RPGN may occur in rare instances. The histologic lesions, when present, generally reflect these clinical manifestations. The histologic features may vary from a focal and segmental necrotizing glomerulonephritis to a diffuse and more global exudative and proliferative glomerulonephritis, which may have a MPGN pattern. More severe forms show a diffuse proliferative glomerulonephritis. The lesions may be acute (influx of neutrophils) or chronic (fully developed MPGN pattern with basement membrane changes); the rapidly progressive forms show large numbers of crescents. Immunofluorescence and electron microscopy show the presence of glomerular immune deposits.

Diabetic Nephropathy

Diabetes mellitus is a major cause of renal morbidity and mortality, and diabetic nephropathy is the leading cause of chronic kidney failure in the United States. Advanced or end-stage kidney disease occurs in as many as 40% of both insulin-dependent 1 diabetics and type 2 diabetics. The pathology and pathogenesis of this disorder is discussed in Chapter 24.

Fibrillary Glomerulonephritis

Fibrillary glomerulonephritis is a morphologic variant of glomerulonephritis associated with characteristic fibrillar deposits in the mesangium and glomerular capillary walls that resemble amyloid fibrils superficially but differ ultrastructurally and do not stain with Congo red. The glomerular lesions usually show membranoproliferative or mesangioproliferative patterns by light microscopy. By immunofluorescence microscopy, there is selective deposition of polyclonal IgG, often of the IgG4 subclass, complement C3, and Igκ and Igλ light chains. Clinically, patients develop nephrotic syndrome, hematuria, and progressive renal insufficiency. The disease recurs in kidney transplants. The pathogenesis of this entity is unknown.

Other Systemic Disorders

Goodpasture syndrome (Chapter 15), *microscopic polyangiitis*, and *granulomatosis with polyangiitis (formally called Wegener granulomatosis)* (Chapter 11) are commonly associated with glomerular lesions, as described in the discussion of these diseases. Suffice it to say here that the glomerular lesions in these three conditions can be histologically similar and are principally characterized by foci of glomerular necrosis and crescent formation. In the early or mild forms of renal