Renal Histopathology, Urine Cytology, and Cytopathology of Acute Renal Failure

Lorraine C. Racusen
Cynthia C. Nast

Causes of acute renal failure can be divided into three categories: 1) prerenal, due to inadequate perfusion; 2) postrenal, due to obstruction of outflow; and 3) intrinsic, due to injury to renal parenchyma. Among the latter, diseases of, or injury to, glomeruli, vessels, interstitium, or tubules may lead to a decrease in glomerular filtration rate (GFR).

Glomerular diseases that lead to acute renal failure are the proliferative glomerulonephritides, including postinfectious and membranoproliferative glomerulonephritis secondary to glomerular deposition of immune complexes. If glomerular injury is severe enough to damage the glomerular basement membrane, leakage of fibrin and other plasma proteins stimulates formation of cellular extracapillary "crescents" composed of epithelial cells and monocytes and macrophages. Crescents may form as a result of an inflammatory reaction to immune complexes formed to nonglomerular antigens; antibody reaction to intrinsic glomerular antigens, as in anti–glomerular basement membrane disease; and, in the absence of immune complexes, the pauci-immune processes, which include the small vessel vasculitides, including Wegener's granulomatosis and microscopic polyarteritis. Immunohistologic examination and electron microscopy play important roles in the diagnosis of these processes. Extensive crescent formation is accompanied by rapidly progressive acute renal failure. The urine sediment in these diseases often contains red blood cells and red cell casts.

Vascular diseases (involving veins, arteries, or arterioles and capillaries) can lead to hypoperfusion and acute renal failure. Venous thrombosis, most often due to trauma or a nephrotic state, and arterial thrombosis due to trauma or vasculitis, cause parenchymal ischemia and

CHAPTER 9

infarction. Small vessel vasculitides involve small arteries, arterioles, and glomerular capillaries, causing injury and necrosis in the glomerular tuft, which may result in crescent formation. Thrombotic microangiopathies result from endothelial injury damage in small arteries and arterioles, producing thrombosis, obstruction to blood flow, and glomerular hypoperfusion. Urine sediment in these diseases often shows hematuria or cellular casts, reflecting ischemia.

Interstitial inflammatory processes lead to acute renal failure via compression of peritubular capillaries or injury to tubules. Causes of acute interstitial nephritis include infection, and immune-mediated reactions. With infection, polymorphonuclear leukocytes may be seen in tubules as well as in interstitium. Inflammatory infiltrates in hypersensitivity reactions, often due to drug exposure, feature eosinophils. Immunohistologic studies may reveal the presence of immune complexes; immune complex deposition around tubules occurs as a primary process or associated with immune glomerular injury. Tubulitis is seen when the inflammatory reaction extends into the tubular epithelium. Epithelial cell injury is often produced by such inflammatory processes. The urine sediment reveals white blood cells and white cell casts, which may include numerous polymorphonuclear leukocytes or eosinophils.

The most common cause of acute renal failure is injury to tubule epithelium. Primary tubule cell injury typically results from ischemia, toxic injury, or both. Cell injury results in disruption of the epithelium and its normal reabsorptive functions, and may lead to obstruction of tubule lumens. Cell exfoliation often occurs, and intact cells and cell fragments and debris can be seen in the urine sediment; these may be in the form of casts. Necrotic cells may be seen in situ along the tubule epithelium or in the tubule lumen, but often overt cell necrosis is not prominent. Apoptosis of tubule cells is seen after injury as well.

Glomerular Diseases

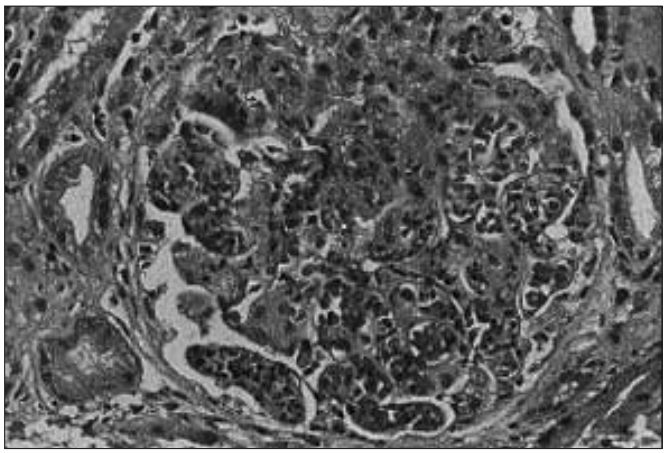

FIGURE 9-1 (see Color Plate)
Early postinfectious glomerulonephritis. Numerous polymorphonuclear leukocytes in glomerular capillary loops contribute to the hypercellular appearance of the glomerulus. There is also a segmental increase in mesangial cells (hematoxylin and eosin, original magnification × 400). This reactive inflammatory process occurs in response to glomerular deposition of immune complexes, including the large subepithelial "hump-like" deposits which are typical of post-infectious glomerulonephritis. The glomerulonephritis is usually self-limited and reversible, and especially with appropriate treatment of the underlying infection, long-term prognosis is excellent [1].

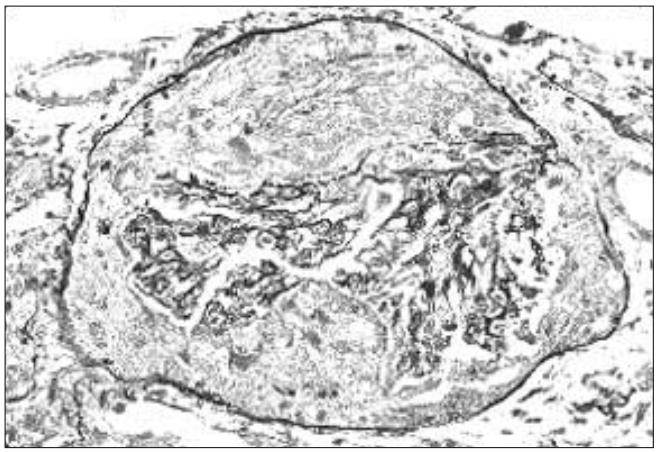

FIGURE 9-2 (see Color Plate)
A large epithelial crescent fills Bowman's space and compresses the capillary loops in the glomerular tuft. This silver stain highlights the glomerular mesangium and the basement membrane of the glomerular capillaries (silver stain, original magnification × 400). The patient presented with hematuria and acute renal failure. Immunostains were negative in this case, a finding consistent with a pauci-immune process. The differential diagnosis includes small vessel vasculitis, and anti-neutrophil cytoplasmic antibody may be positive. Crescentic glomerulonephritis may also occur with anti-glomerular basement membrane antibody disease, or as a complication of immune complex glomerulonephritis [2].

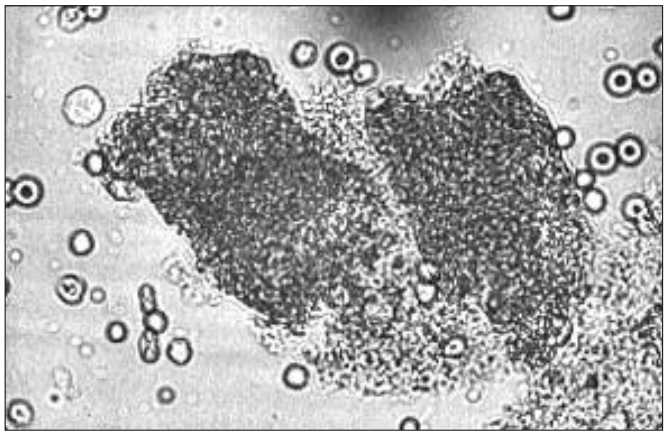

FIGURE 9-3 (see Color Plate)
Urine sediment of a patient with acute renal failure revealing red blood cells and some red blood cell casts (original magnification × 600). Biopsy in this case revealed crescentic glomerulonephritis. However, hematuria may be seen in any proliferative glomerulonephritis or with parenchymal infarcts. The "casts" assume the cylindrical shape of the renal tubules, and confirm an intrarenal source of the blood in the urine. Fragmented or dysmorphic red blood cells may be seen when the red cells have traversed through damaged glomerular capillaries.

Vascular Diseases

FIGURE 9-4 (see Color Plate)
An early thrombus is seen in a small renal artery in a patient with patchy cortical infarction (original magnification × 250). The patient presented with acute renal failure. The thrombosis may be due to a hypercoaggulable state (*eg*, disseminated intravascular coaggulation) or endothelial injury (*eg*, hemolytic uremic syndrome). If the cortical necrosis is patchy, recovery of adequate renal function may occur [3].

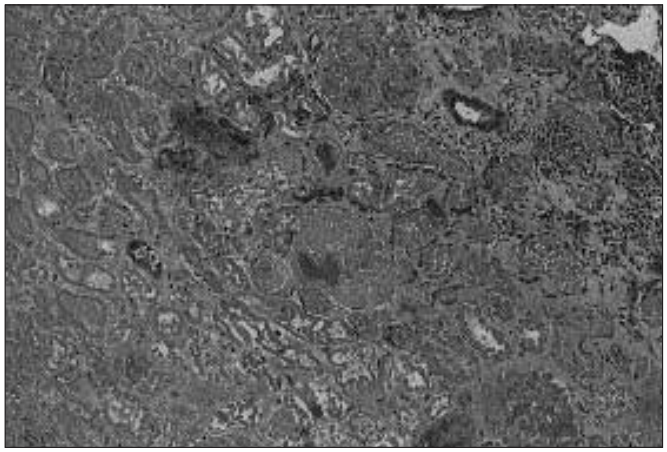

FIGURE 9-5 (see Color Plate)
A parenchymal infarct in a patient with renal vein thrombosis (hematoxylin and eosin, original magnification × 200). A few surviving tubules and a rim of inflammatory cells are seen at the periphery of the infarct. Infarcts may also be seen with arterial thromboses, and with severe injury to the microvasculature, as occurs in thrombotic microangiopathies [3]. If the process is extensive, acute cortical necrosis may occur, often leading to irreversible renal failure.