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Acute Interstitial Nephritis

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Introduction/Clinical Setting

Acute interstitial nephritis (AIN) may be the result of indirect injury by drugs, reaction to systemic infections, direct renal infection (viral and selected bacteria), humoral immune responses (anti–tubular basement membrane disease), hereditary and metabolic disorders, and obstruction and reflux in the acute stages. Similar changes can also be observed in the kidney in systemic diseases such as lupus erythematosus and in transplant rejection. Acute tubulointerstitial nephritis also occurs to varying degrees in association with glomerulonephritides. This section is largely confined to the drug-induced, reactive, idiopathic and immunologic disorders inducing AIN. Acute interstitial nephritis usually presents with acute renal failure, often oliguric; it is sometimes associated with systemic manifestations such as arthralgia fever, eosinophilia and rash, typically as a consequence of drug hypersensitivity (1–3).

Pathologic Findings

On gross examination, kidneys with AIN are enlarged with a pale cortex and a distinct corticomedullary junction. Histologically there is diffuse interstitial edema with an interstitial infiltrate of lymphocytes, monocyte-macrophages, and plasma cells to varying degrees (Fig. 13.1). Eosinophils may comprise from 0% to 10% of the infiltrate, depending on the etiology of the AIN. When there are many eosinophils, they may be focally concentrated. The inflammatory cells are often prominent at the corticomedullary junction, and are generally confined to the cortex. Neutrophils and basophils are infrequent; large numbers of neutrophils suggest a diagnosis of acute infectious interstitial nephritis. In some cases granulomas may be found in the interstitium or around ruptured tubules. Glomeruli and vessels are usually uninvolved. The inflammation extends into the walls and lumina of tubules (tubulitis), with distal tubules more often affected than
proximal tubules. There are varying numbers of degenerating and regenerating tubular epithelial cells; occasionally desquamated cells may be observed in tubular lumina. Proximal tubules often have focal loss of brush border staining. Immunofluorescent studies are usually negative but infrequently reveal granular deposits of complement in the tubular basement membranes (TBM) and rarely fibrin in the interstitium. In cases of anti-TBM antibody formation, there is linear staining of TBM for immunoglobulin G (IgG).

Etiology/Pathogenesis

Acute interstitial nephritis is a morphologic entity with many pathogenetic etiologies. These include cell-mediated immunity of the delayed hypersensitivity type and possibly direct cytotoxicity, humoral immunity such as anti-TBM antibody formation, and others possibly including complement activation and enhanced expression of major histocompatibility complex (MHC) class I or class II antigens. Some studies have reported drug-induced acute interstitial nephritis to represent approximately 6.5% of nontransplant biopsies. Delayed hypersensitivity is the likely mechanism for AIN induced by drugs, particularly antibiotics and nonsteroidal antiinflammatory drugs (NSAIDs). T cells carrying both CD4 and CD8 antigens in varying proportions have been identified in kidneys with drug-induced AIN. This variability may be related to the offending agent or the time course of the biopsy. The T cells have been shown to carry activation markers and therefore are presumed to be effector cells in the hypersensitivity process. B cells are also present to some extent, more so with NSAID-induced AIN. This allergic form of AIN may be associated