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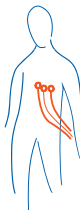
Major Nonglomerular Disorders of the Kidney



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INTRODUCTION

The tubulointerstitial compartment comprises 80% of renal parenchyma, with most of the volume accounted for by renal tubules, interstitial cells, and collagenous matrix. Tubulointerstitial disorders have two common clinical presentations: acute tubulointerstitial nephritis, characterized by sudden onset and a rapid decline in renal function, and chronic tubulointerstitial nephropathy, characterized by a more protracted clinical course. Although primary glomerular and vascular diseases are associated with significant tubulointerstitial changes, the clinical presentations are dominated primarily by injury (see Chapters 28 and 30). Acute tubular injuries are discussed in Chapter 31.

ACUTE INTERSTITIAL NEPHRITIS

Acute interstitial nephritis (AIN), also called *tubulointerstitial nephritis*, is characterized by inflammation and edema of the renal interstitium; glomeruli and vessels are distinctly normal. AIN is associated with an acute, rapid decline in renal function and is a common cause of acute kidney injury, accounting for 15% to 27% of acute kidney injury cases confirmed on biopsy.

On gross examination, the kidneys are pale and swollen. Histologically, the hallmarks of AIN include interstitial edema and infiltration of the interstitium with inflammatory cells comprising lymphocytes, monocytes, plasma cells, eosinophils, and macrophages (E-Figs. 29-1 and 29-2). This inflammation can result in fibrotic changes in 7 to 10 days. Immunofluorescence studies typically are unrevealing, except in cases in which linear or granular immunoglobulin G (IgG) or complement deposits along basement membrane are observed.

In most cases, AIN begins abruptly with a decrease in kidney function within days of exposure to the offending agent. However, AIN may ensue after several weeks of the exposure in some cases. Characteristic clinical manifestations include rash, fever, and eosinophilia. Modest proteinuria (usually <1g/day) or hematuria may be observed, and oliguria is uncommon. A high index of suspicion is required for diagnosis because these features may be absent.

The most common causes of AIN are shown Table 29-1. Frequently used therapeutic drugs merit particular emphasis. They include antibiotics, allopurinol, mesalamine, nonsteroidal anti-inflammatory drugs (NSAIDs), and proton pump inhibitors (PPIs). Other causes of AIN include infections, autoimmune disorders, tubulointerstitial nephritis and uveitis syndrome, snakebite, and herbal supplements.

When evaluating a patient with a recent decline in renal function, the diagnosis of AIN is suggested by a history of exposure to known offending agents coupled with typical clinical features. In addition to identifying elevated serum creatinine levels, a urinalysis can detect the characteristic findings of white blood cells, red blood cells, and white blood cell casts in urine. Identification of eosinophils in urine with Hansel or Wright stains is highly suggestive, but their absence does not rule out AIN. Moreover, eosinophils in urine can be observed in other diseases, including cholesterol embolism, urinary tract infections, parasitic disorders, and glomerulonephritis.

A definitive diagnosis of AIN requires a kidney biopsy, although it is not necessary for management when clinical features are highly suggestive. Treatment of the patients with AIN consists of removal of the offending drug and management of the underlying infection or autoimmune process. Kidney biopsy should be considered when the diagnosis is not obvious. The role of steroids in limiting the inflammatory process is controversial, but early use (within 7 to 14 days) may decrease the duration of

TABLE 29-1 CAUSES OF ACUTE INTERSTITIAL NEPHRITIS

CAUSE	EXAMPLES
Antibiotics	Penicillin Cephalosporin Sulfa drugs Ciprofloxacin Acyclovir
Nonsteroidal anti-inflammatory drugs	Naproxen Ibuprofen Diclofenac Celecoxib
Diuretics	Thiazides Furosemide Triamterene
Other drugs	Cimetidine Omeprazole Phenytoin Allopurinol
Systemic infections	Legionnaires disease Leptospirosis Streptococcal infection Cytomegalovirus infection
Primary kidney infections	Acute bacterial pyelonephritis
Autoimmune disorders	Sarcoidosis Sjögren syndrome