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On the Cover

What's the diagnosis? This image reveals focal interstitial inflammatory infiltrate with several eosinophils pushing apart otherwise unremarkable tubules. When active interstitial inflammation is noted in non-atrophic parenchyma, a diagnosis of acute interstitial nephritis should be entertained. The differential diagnosis includes a number of causes and conditions; the biopsy findings are not specific and therefore only careful correlation with clinical data can lead to a correct diagnosis. In the developed and developing world, acute interstitial nephritis most commonly arises as a hypersensitivity reaction to drugs (NSAIDs, beta-lactam antibiotics, sulfonamides, diuretics, proton pump inhibitors, and a long list of other drugs). The presence of tissue eosinophils is not specific for drug-induced processes; furthermore, drug-related injury may present without eosinophils in the interstitial infiltrate. Other causes of acute interstitial nephritis include autoimmune diseases (lupus nephritis, Sjögren's syndrome, hypocomplementemic tubulointerstitial nephritis, IgG-related interstitial nephritis, ANCA-related renal disease), allograft rejection, tubulointerstitial nephritis and uveitis or TINU syndrome, infections (bacterial, viral, fungal), sarcoidosis, metabolic diseases with interstitial inflammation with or without associated crystal deposition (gout and hyperuricemic conditions, hyperoxaluric states), toxic processes (lithium, heavy metals, aristolochic acid), paraprotein-related diseases (systemic light chain or heavy chain deposition disease, cast nephropathy), physical causes (obstruction and radiation injury), and hereditary conditions (medullary cystic diseases and juvenile nephronophthisis). In summary, the biopsy findings are not very specific; correct diagnosis can be made by correlating the biopsy findings, laboratory data, and clinical history of substance use or exposure. *Image and text provided by Vanesa Bijol, MD, Brigham and Women's Hospital, Boston, MA.*