Acute and Chronic Tubulointerstitial Nephritis of Rheumatic Causes

Nestor Oliva-Damaso, MD[a,*], Elena Oliva-Damaso, MD, PhD[b], Juan Payan, MD[a]

KEYWORDS

• Tubulointerstitial nephritis • Acute interstitial nephritis • Chronic interstitial nephritis • Systemic lupus erythematous • Sjögren syndrome • Sarcoidosis • Scleroderma • TINU syndrome

KEY POINTS

- Rheumatic diseases represent 10% to 20% of all cases of tubulointerstitial nephritis (TIN), and the rest are drug-induced or infectious-related forms.
- TIN may be a complication of sarcoidosis, Sjögren syndrome, TIN with uveitis syndrome, immunoglobulin G4–related disease, systemic lupus erythematous, scleroderma, and vasculitis.
- TIN should be suspected in the decline of kidney function with tubular proteinuria (usually less than 1 g/d), leukocyturia, and extrarenal symptoms.
- Kidney biopsy is generally required to make a definitive diagnosis.
- Corticosteroids represent the first therapeutic approach whereby relapses are frequent in systemic diseases.

INTRODUCTION

Tubulointerstitial nephritis (TIN) is a renal histologic lesion characterized by the presence of inflammatory infiltrates and edema within the tubulo-interstitial compartment, usually not affecting the glomerular and vascular compartments (**Fig. 1**).[1,2] This lesion was first described by Biermer[3] in 1860 and defined as an entity in 1898 by Councilman.[4] Depending on the clinical course, TIN is divided into acute interstitial nephritis (AIN) or chronic interstitial nephritis (CIN). AIN is a frequent cause of acute kidney injury

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[a] Department of Medicine, Division of Nephrology, Hospital Costa del Sol, A-7, Km 187, 29305 Marbella, Malaga, Spain; [b] Department of Medicine, Division of Nephrology, Hospital Doctor Negrin, Barranco de la Ballena, 35010 Las Palmas de Gran Canaria, Spain
* Corresponding author. Division of Nephrology, Department of Medicine, Hospital Costa del Sol, A-7, Km 187, 29305, Marbella, Malaga, Spain.
E-mail address: nestorod@hotmail.com

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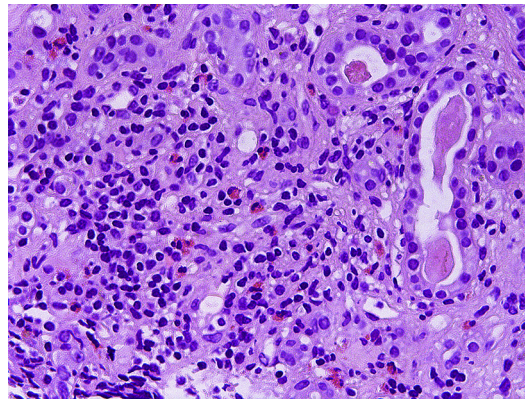

Fig. 1. Kidney biopsy specimen. Light microscopy (hematoxylin-eosin stain, original magnification ×400) demonstrates acute interstitial nephritis with an interstitial lymphoplasmacytic infiltrate with eosinophils and associated interstitial edema.

(AKI) that can lead to chronic kidney disease (CKD).[5] Although AIN is reversible (particularly if an offending medication is discontinued), the disease may progress and cause fibrosis and CIN. The likelihood of chronicity increases with systemic inflammatory or rheumatologic diseases and delayed removal of the causative medication in drug-induced TIN.[6] AIN is divided by cause into the following categories: allergic/drug-induced (antibiotics, nonsteroidal antiinflammatory drugs [NSAIDs], proton pump inhibitors, others); infection-related (including bacteria, fungi, and viruses); autoimmune/systemic; and idiopathic forms of disease.[6] Drug-induced AIN accounts for most cases (71%), of which antibiotics represent the most common responsible class of drug followed by proton-pump inhibitors and NSAIDs.[7] Rheumatic/autoimmune diseases are the second most frequent cause of TIN, accounting for approximately 10% to 20% of all cases; of these, sarcoidosis is the most common cause.[7] The other rheumatic diseases that can cause TIN include systemic lupus erythematous (SLE), Sjögren syndrome, scleroderma, TIN with uveitis (TINU) syndrome, immunoglobulin G4 (IgG4)–related disease, and vasculitis.

The prevalence of biopsy-proven AIN seems to be between 0.5% and 2.6% of all renal biopsies.[8] However, in patients with AKI, AIN represents 18% to 27% of biopsied cases.[8–10] Altogether AIN represents the second leading cause of intrinsic AKI after acute tubular necrosis.[11] The true incidence and prevalence of TIN might be underestimated, as a significant number of patients do not undergo renal biopsy and are treated empirically or because the vagueness of clinical symptoms can be attributed to other causes of renal injury.[11] In recent years, the prevalence of AIN has increased (from 3.6% to 10.5% of total kidney biopsies), which is more marked among elderly patients[12] possibly because of an increased use of certain medications[8] or an increased detection.[13] In adults with TIN the median percentage of interstitial kidney fibrosis was 30% and median glomerulosclerosis was 8% indicating chronic changes.[14] In children, TIN (both acute and chronic) accounts for 1% to 7% of the histologic diagnoses in renal biopsies.[15,16]

Autoimmune and systemic diseases causing AIN are rare in the elderly (65 years of age and older) whereby most cases are drug-related AIN; rheumatic causes are mostly seen in younger patients.[17] AIN is associated with an immune-mediated infiltration of the kidney interstitium by inflammatory cells that can progress to interstitial fibrosis and, therefore, transform into chronic interstitial nephritis.[5] Rheumatic disease