

When the Kidney Meets the Eye: Tubulointerstitial Nephritis and Uveitis Syndrome – A Case Series of 8 Patients from a Moroccan Tertiary Center

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DOI: <https://doi.org/10.36347/sjmcr.2026.v14i04.010>

Received: 17.02.2026 | Accepted: 30.03.2026 | Published: 08.04.2026

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Abstract

Case Report

Introduction: Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare clinicopathological entity characterized by the association of acute tubulointerstitial nephritis and uveitis in the absence of other systemic diseases. Because renal and ocular manifestations may occur at different times and symptoms are often non specific, the diagnosis may be delayed or overlooked. The aim of this study was to describe the clinical, biological, histological, and therapeutic characteristics of patients diagnosed with TINU syndrome in a tertiary care center. **Materials and Methods:** We conducted a retrospective monocentric study in the Department of Nephrology, Dialysis and Renal Transplantation at Ibn Sina University Hospital in Rabat, Morocco. Medical records of patients diagnosed with TINU syndrome were reviewed. The diagnosis of TINU syndrome was established based on the association of acute tubulointerstitial nephritis and uveitis after exclusion of other systemic diseases. Demographic, clinical, biological, ophthalmological, histological, therapeutic, and outcome data were collected. **Results:** Eight patients with TINU syndrome were included, with a mean age of 27.8 ± 8.1 years and a female predominance. Ocular involvement preceded renal manifestations in five patients, with a median delay of 2 months, and was concomitant in the remaining cases. All patients presented with acute kidney injury, with a mean serum creatinine level of 808.2 ± 528.4 $\mu\text{mol/L}$. All patients received oral corticosteroid therapy combined with adjunctive measures. Complete renal recovery was achieved in six patients (75%), while one patient progressed to chronic kidney disease and one to end-stage renal disease. No renal relapse was observed. Uveitis relapse occurred in three patients (37.5%), with a mean delay of approximately 6 months. **Discussion:** The pathogenesis of TINU syndrome remains incompletely understood but is thought to involve immune-mediated mechanisms targeting shared antigens between renal tubular cells and the uveal tract. Early recognition and timely corticosteroid therapy are associated with favorable outcomes in most cases. Our findings are consistent with previous reports describing a predominance in young females and generally favorable renal outcomes with corticosteroid therapy. **Conclusion:** TINU syndrome should be considered in patients presenting with unexplained acute kidney injury associated with uveitis. Early diagnosis and close collaboration between nephrologists and ophthalmologists are essential to improve renal and visual outcomes.

Keywords: Tubulointerstitial nephritis and uveitis syndrome, kidney biopsy, acute kidney injury, uveitis ; corticosteroid therapy.

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INTRODUCTION

TINU syndrome is a rare inflammatory disorder combining renal and ocular involvement. It predominantly affects adolescents and young adults and typically presents as bilateral non-granulomatous anterior uveitis [1-2].

Renal involvement usually manifests as acute kidney injury with sterile leukocyturia, hematuria, or mild proteinuria, with histological confirmation on kidney biopsy [3]. Although its pathophysiology is not fully understood, immune-mediated mechanisms and

potential triggers such as infections or medications have been suggested [4].

The aim of this study was to describe the demographic, clinical, biological, histological, and therapeutic characteristics, as well as the outcomes, of patients diagnosed with TINU syndrome in a Moroccan tertiary care center.

MATERIALS AND METHODS

We conducted a retrospective monocentric study in the Department of Nephrology, Dialysis, and Renal Transplantation at Ibn Sina University Hospital in Rabat, Morocco. Medical records of patients with TINU syndrome were retrospectively reviewed. The diagnosis was established based on the association of acute tubulointerstitial nephritis and uveitis after exclusion of other systemic diseases.

Data collected included demographic, clinical, biological, ophthalmological, histological, therapeutic, and outcome variables. Patients were excluded if another systemic condition could explain the association of uveitis and interstitial nephritis. These conditions were classified as follows:

➤ Autoimmune and systemic diseases:

- Systemic lupus erythematosus
- Sjögren syndrome
- Behçet disease
- Sarcoidosis
- IgG4-related disease
- ANCA-associated vasculitis

➤ Infectious diseases:

- Tuberculosis
- Syphilis
- Herpes virus infection
- Toxoplasmosis

These conditions were systematically ruled out based on clinical, biological, and immunological assessments.

Complete remission was defined as normalization of renal function (return of serum creatinine to normal or near-baseline levels), along with resolution of urinary abnormalities and ocular inflammation. Renal relapse was defined as a recurrence of kidney dysfunction, characterized by an increase in serum creatinine and/or reappearance of urinary abnormalities after initial improvement. Ophthalmological relapse was defined as the recurrence of uveitis after a period of remission.

Quantitative variables were expressed as mean \pm standard deviation. Qualitative variables were expressed as counts and percentages.

RESULTS

A total of eight patients with TINU syndrome were included. The mean age at diagnosis was 27.8 ± 8.1 years (range: 17–40), with a female predominance (male-to-female ratio = 0.33). Ocular involvement preceded renal manifestations in five patients, with a median delay of 2 months, and occurred concomitantly in the remaining cases. Red eye was the most common presenting symptom. Decreased visual acuity was observed in seven patients (87.5%), while ocular pain was reported in four patients (50%). Photophobia was less frequent, occurring in one patient (12.5%). Ocular involvement was bilateral in four cases (50%) and unilateral in four cases (50%) (Figure 1). At presentation, impaired renal function was observed in all patients. The mean initial serum creatinine level was 808.2 ± 528.4 $\mu\text{mol/L}$. Urinary abnormalities included leukocyturia in six patients (75%) and microscopic hematuria in four patients (50%), often associated with mild to moderate proteinuria.

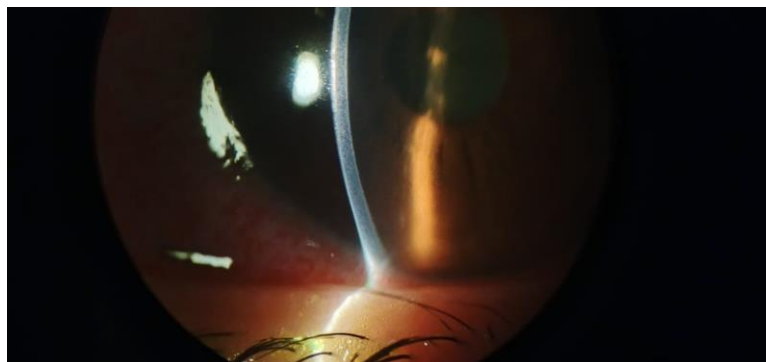


Figure 1: Slit-lamp examination showing a positive Tyndall effect with keratic precipitates, consistent with active anterior uveitis

Kidney biopsy was performed in all patients and confirmed acute tubulointerstitial nephritis, characterized by interstitial edema and a predominantly

mononuclear inflammatory infiltrate, as illustrated in figure 2 and 3

All patients received oral corticosteroid therapy at an initial dose of 1 mg/kg/day with a maximum of 80mg/day and gradual tapering over 6 to 12 months. This treatment was combined with adjunctive measures, including a low-sodium diet, gastric protection, and calcium and vitamin D supplementation, as well as topical ophthalmologic therapy (corticosteroids and mydriatic agents).

Clinical outcomes were favorable in most cases. Complete remission was achieved in six patients (75%), while one patient progressed to chronic kidney disease (CKD) and one to end-stage renal disease (ESRD). No renal relapse was observed. Ophthalmological relapse occurred in three patients (37.5%), with a mean delay of approximately 6 months after initial diagnosis. The mean follow-up duration was 9.4 ± 3.0 months. The main demographic, clinical, ocular, and renal characteristics of the patients are summarized in table 1.

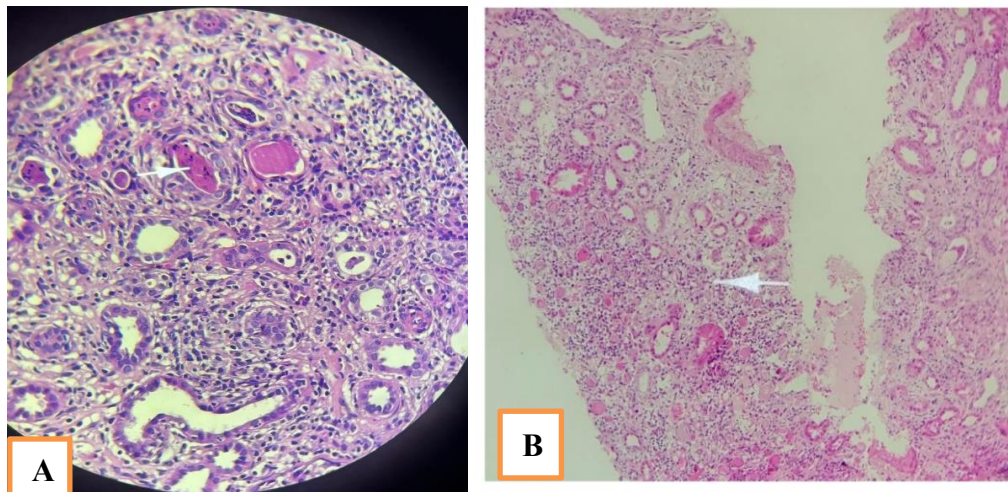


Figure 1: Renal biopsy (hematoxylin–eosin stain). (A) High magnification (×200) showing interstitial inflammatory infiltrate with tubular injury and tubulitis. (B) Low magnification (×20) showing diffuse interstitial involvement of the renal parenchyma. Overall findings are consistent with acute tubulointerstitial nephritis in TINU syndrome

Table 1: Demographic, ocular and renal characteristics of patients with TINU syndrome (n = 8)

Variable	P1	P2	P3	P4	P5	P6	P7	P8
Demographics								
Age (years)	31	17	25	18	29	26	36	40
Sex	F	M	F	F	M	F	F	F
Drug exposure history	Azithromycin	None	None	Omeprazole	NSAIDs	None	None	None
Recent infection	COVID	None	HP	HP	None	None	None	None
Ocular findings								
Red eye	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pain	Yes	Yes	No	Yes	No	No	No	Yes
Photophobia	No	No	No	No	No	Yes	No	No
Decreased visual acuity	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Laterality	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Unilateral	Bilateral	Bilateral
Renal findings								
Creatinine ($\mu\text{mol/L}$)	1131.5	145	353.6	1511.6	327	1043	1564	380
Proteinuria (g/day)	1.5	0.5	0.8	0.9	0.28	0.76	0.6	1.08
Hematuria	Yes	No	Yes	No	No	Yes	No	Yes
Leukocyturia	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Renal outcome	Complete remission	Complete remission	Complete remission	Complete remission	ESRD	Complete remission	CKD	Complete remission

P = Patient; *F* = Female; *M* = Male; *ESRD* = End-stage renal disease; *CKD* = Chronic kidney disease; *HP* = *Helicobacter pylori*; *NSAIDs* = Non-steroidal anti-inflammatory drugs

DISCUSSION

TINU syndrome is a rare inflammatory disorder combining renal and ocular involvement. It predominantly affects adolescents and young adults and typically presents as bilateral non-granulomatous anterior uveitis [2–5]. In our series, the mean age at diagnosis was 27.8 ± 8.1 years, with a female predominance. These findings are consistent with previous studies indicating that TINU syndrome mainly affects young individuals. While earlier reports described a marked female predominance, more recent data suggest a more balanced sex distribution [2].

Ocular involvement was a prominent clinical manifestation in our cohort. In five patients, ocular symptoms preceded renal manifestations, with a median delay of 2 months, highlighting the variable temporal relationship between ocular and renal involvement in TINU syndrome. Red eye was observed in all cases, frequently associated with decreased visual acuity and ocular pain. This is consistent with previous reports identifying anterior non-granulomatous uveitis as the most common presentation. Bilateral involvement was observed in half of the cases, which is slightly lower than the 70–80% reported in other series [6].

Renal involvement was characterized by impaired kidney function associated with urinary abnormalities, including leukocyturia and microscopic hematuria, consistent with tubulointerstitial inflammation. Systemic symptoms such as weight loss were also observed, reflecting the inflammatory nature of the disease [7].

The pathophysiology of TINU syndrome remains incompletely understood. Current evidence supports an immune-mediated mechanism involving shared antigens between renal tubular epithelial cells and ocular tissues. Antibodies directed against modified C-reactive protein (mCRP) have been proposed as a potential pathogenic factor. Additionally, environmental

triggers such as infections or drug exposure may contribute to disease onset in genetically susceptible individuals [4]. The diagnosis of TINU syndrome remains one of exclusion, requiring thorough evaluation to rule out systemic autoimmune and infectious conditions.

Systemic corticosteroid therapy remains the cornerstone of treatment and is generally associated with rapid improvement in renal function and control of ocular inflammation. In our study, all patients received systemic corticosteroids combined with topical ophthalmologic therapy, resulting in favorable outcomes in most cases. The use of prolonged corticosteroid therapy with gradual tapering may have contributed to the favorable renal outcomes observed in our cohort. However, additional immunosuppressive therapy may be required in recurrent or refractory cases. The prognosis is generally favorable when treatment is initiated early [7,8].

In our cohort, complete renal remission was achieved in 75% of patients, while one patient progressed to chronic kidney disease and one to ESRD. No renal relapse was observed, whereas ophthalmological relapse occurred in 37.5% of cases, typically within the first 6 months after diagnosis. This highlights the recurrent nature of ocular involvement in TINU syndrome and underscores the need for prolonged ophthalmologic follow-up. These findings are consistent with previous studies reporting that most patients recover renal function, although a minority may develop persistent renal impairment (Table 2).

This study has several limitations, including its retrospective design and small sample size. Nevertheless, given the rarity of TINU syndrome, our case series provides valuable insight into its clinical presentation and outcomes. It also highlights the importance of close collaboration between nephrologists and ophthalmologists to ensure early diagnosis and optimal management.

Table 2: Comparison of the present study with major published case series of TINU Syndrome

Study	Country	Patients (n)	Mean age (years)	Female (%)	Bilateral uveitis (%)	Renal recovery (%)
Mandeville <i>et al.</i> , 2001 [9]	USA	133	15(median)	74	80	80
Mackensen <i>et al.</i> , 2009 [10]	Germany	33	26	70	73	75
Amaro <i>et al.</i> , 2020 [11]	Portugal	48	29	67	71	79
S. Haddad <i>et al.</i> , 2019 [12]	Tunisia	13	34	84	69	90
Present study	Morocco	8	27	75	50	75

CONCLUSION

TINU syndrome is a rare but important cause of combined renal and ocular inflammation. It should be

considered in patients presenting with unexplained acute kidney injury associated with uveitis. Early recognition and prompt corticosteroid therapy are essential to improve renal and visual outcomes. Multidisciplinary

collaboration between nephrologists and ophthalmologists remains crucial for optimal diagnosis and management.

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