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Acute Renal Failure Unmasking Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome in A Young Male: A Case Report and Literature Review

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Abstract **Case Report**

Background: Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare and underdiagnosed cause of acute kidney injury (AKI) in young patients. It combines acute interstitial nephritis with uveitis and is frequently overlooked because renal and ocular manifestations may occur asynchronously. ***Case Presentation:*** We report the case of a previously healthy 25-year-old military man admitted for unexplained AKI, with a peak serum creatinine of 5.2 mg/dL and urea 0.64 g/L. Laboratory evaluation revealed a tubular profile with low-grade proteinuria (320 mg/day), sterile urine, and normal electrolytes. Inflammatory markers were mildly elevated (CRP 15 mg/L), while immunology and infectious serologies were negative. Renal ultrasound showed normal-sized kidneys without obstruction. A history of sporadic NSAID intake for back pain was noted. Ophthalmological consultation, prompted by suspicion of TINU, revealed bilateral non-granulomatous anterior uveitis. Renal biopsy was deferred because of progressive recovery under therapy. ***Management and Outcome:*** The patient received intravenous rehydration and oral prednisone (1 mg/kg/day) for nephritis and topical corticosteroids for uveitis. Dialysis was not required. Renal function improved within three weeks, with serum creatinine returning to 1.5 mg/dL. Ocular inflammation resolved completely. At early follow-up, no relapses were observed. ***Conclusion:*** This case illustrates a typical presentation of TINU syndrome in a young adult with AKI. The asynchrony between renal and ocular findings emphasizes the need for multidisciplinary collaboration. NSAID exposure may have contributed as a potential trigger. Early recognition and corticosteroid therapy led to full recovery.

Keywords: TINU syndrome, acute kidney injury, interstitial nephritis, uveitis, NSAIDs, corticosteroids.

INTRODUCTION

Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare and frequently underdiagnosed entity, first described by Dobrin and colleagues in 1975. It is characterized by the association of acute tubulointerstitial nephritis (TIN) with uveitis, typically anterior and non-granulomatous, after exclusion of systemic diseases that can produce a similar clinical picture. Although uncommon, TINU is increasingly recognized as an important cause of acute kidney injury (AKI) in adolescents and young adults, with ophthalmology series suggesting that it may account for up to 1–2% of all uveitis cases. Despite this, awareness among clinicians remains limited, and diagnosis is often delayed because renal and ocular manifestations may occur asynchronously.

The pathogenesis of TINU is not yet fully understood, but current evidence points toward an immune-mediated mechanism. Proposed triggers include preceding infections (such as Epstein–Barr virus, Chlamydia, or streptococcal infection), drug exposures (especially nonsteroidal anti-inflammatory drugs and certain antibiotics), and genetic susceptibility with reported associations to HLA class II alleles. Autoimmune reactions targeting common renal and ocular antigens have also been described. The result is a tubulointerstitial inflammatory process leading to AKI and a bilateral anterior uveitis that may relapse independently of the renal disease.

Clinically, patients usually present with nonspecific systemic symptoms such as fatigue, malaise, or weight loss, accompanied by laboratory evidence of tubular dysfunction and elevated creatinine. Uveitis may appear before, during, or after the nephritis, sometimes separated by weeks to months, which makes the syndrome difficult to recognize. Prognosis is generally favorable, with most patients recovering renal function

under supportive care and corticosteroid therapy, but uveitis is more prone to relapse and requires long-term ophthalmologic follow-up. Here, we describe the case of a 25-year-old man who presented with acute kidney injury and was subsequently diagnosed with TINU syndrome, and we provide a brief review of the literature.

CASE REPORT

Patient Information

A 25-year-old previously healthy male military worker, engaged in physical outdoor activity, presented with unexplained fatigue. He had no significant medical history, no family history of autoimmune disease, and reported only sporadic use of NSAIDs for back pain. He was not taking other medications.

Clinical Presentation & Timeline

On admission, blood tests revealed acute kidney injury with a peak serum creatinine of 5.2 mg/dL and blood urea nitrogen of 0.64 g/L. The patient reported no fever, rash, weight loss, arthralgia, or urinary symptoms. He did describe a sensation of dry eyes. Because the biochemical profile suggested a tubulointerstitial process, nephrology suspected tubulointerstitial nephritis with uveitis (TINU) syndrome and referred the patient for ophthalmological evaluation. This revealed bilateral, non-granulomatous anterior uveitis.

Diagnostic Assessment

- **Laboratory tests** showed normal serum electrolytes, mildly elevated CRP (15 mg/L), and a tubular profile with low-grade proteinuria (320 mg/day). There was no hematuria or glucosuria, and urine was sterile.
- **Immunological and infectious work-up** (ANA, ANCA, viral serologies including EBV, CMV, hepatitis, HIV, and TB screen) was negative.
- **Renal ultrasound** demonstrated normal-sized kidneys (~12 cm), with no obstruction or structural abnormalities.
- **Renal biopsy** was postponed due to early clinical improvement and ultimately not performed.

Therapeutic Interventions

The patient was initially managed with intravenous rehydration and oral prednisone at 1 mg/kg/day, started at the time of diagnosis for the interstitial nephritis. Topical corticosteroid eye drops were administered concurrently for bilateral anterior uveitis. After maintaining full-dose prednisone for approximately one month, a gradual taper was initiated over the subsequent weeks, according to clinical response and in coordination with both nephrology and ophthalmology. At the time of discharge, a tapering schedule was planned to continue under outpatient follow-up. Dialysis was not required at any point.

Follow-up and Outcomes

Renal function progressively improved, with serum creatinine normalizing to 1.5 mg/dL (15 mg/L) within three weeks. The uveitis also resolved completely with treatment. At early follow-up, no relapses were reported.

Patient Perspective

The patient expressed relief at regaining normal kidney function and vision, and satisfaction with the collaborative care he received.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

Table 1. Key Laboratory Findings and Medications

Parameter	Admission	Follow-up (3 weeks)	Reference Range	Notes
Serum Creatinine	5.2 mg/dL (52 mg/L)	1.5 mg/dL (15 mg/L)	0.6–1.2 mg/dL	AKI → recovery
Urea (BUN)	0.64 g/L	0.25 g/L	0.15–0.45 g/L	Mild elevation
Proteinuria	320 mg/day	150 mg/day	<150 mg/day	Low-grade, tubular
Hematuria	Absent	Absent	–	Sterile urine
Glucosuria	Absent	Absent	–	No glycosuria
CRP	15 mg/L	5 mg/L	<5 mg/L	Mild inflammation
Electrolytes (Na, K, Ca, P)	Normal	Normal	–	–
ANA/ANCA/viral serologies	Negative	–	–	Exclusion of systemic causes

Medications during hospitalization and follow-up:

- **Oral prednisone** 1 mg/kg/day for 1 month, followed by gradual taper over several weeks.
- **Topical corticosteroid eye drops** for bilateral anterior uveitis.
- **Intravenous fluids** (rehydration).

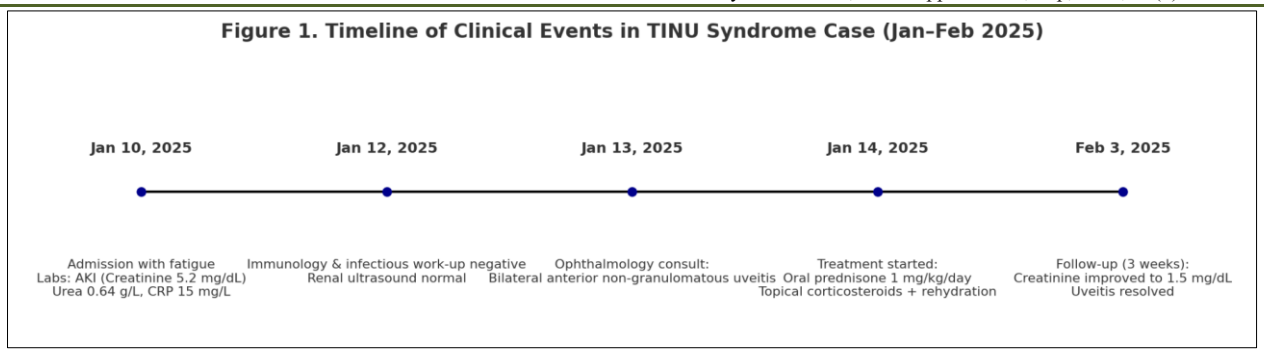

Figure 1. Timeline of Clinical Events

Day 0: Admission with fatigue; labs show AKI (creatinine 5.2 mg/dL). NSAID history noted.
Day 1–2: Work-up excludes systemic autoimmune/infectious causes. Renal ultrasound normal.
Day 3: Ophthalmology consult → bilateral anterior non-granulomatous uveitis diagnosed.
Day 3: Initiation of oral prednisone (1 mg/kg/day) and topical corticosteroids; supportive IV fluids.
Week 2–3: Renal function progressively improves; creatinine returns to 1.5 mg/dL. Uveitis resolves.
Early follow-up: No relapse observed; long-term monitoring planned.

DISCUSSION

1) Background & Epidemiology

Tubulointerstitial nephritis and uveitis (TINU) syndrome is an uncommon disorder first described by Dobrin et al. in 1975 [1]. It is defined by the coexistence of acute tubulointerstitial nephritis (TIN) and uveitis, after excluding systemic diseases that can mimic this association. Although considered rare, its true prevalence is likely underestimated due to asynchronous presentation of renal and ocular symptoms and limited awareness among clinicians [2]. In ophthalmology cohorts, TINU has been estimated to account for 1–2% of all uveitis cases, with higher proportions reported in tertiary centers [3]. Among nephrology series, TINU represents a small fraction of acute interstitial nephritis diagnoses but should be considered in unexplained AKI in young patients [4].

Epidemiologically, TINU predominantly affects adolescents and young adults, with a median age between 15 and 30 years [5]. A slight female predominance has been observed in several cohorts, though cases in young men are well documented [6,7]. The condition has been described worldwide, with cases reported in Europe, Asia, and North America, suggesting no ethnic restriction. Early recognition is important because prognosis is generally favorable with appropriate therapy, but delays in diagnosis can lead to chronic kidney disease or ocular complications such as recurrent uveitis [8].

2) Pathogenesis

The exact mechanism underlying TINU syndrome remains incompletely understood, but most evidence supports an immune-mediated process involving both the kidney and the eye [9]. Several environmental triggers have been implicated, including infectious agents such as Epstein–Barr virus, Chlamydia, tuberculosis, and varicella-zoster virus, as well as drugs, especially nonsteroidal anti-inflammatory drugs (NSAIDs) and certain antibiotics [10,11]. These exposures may initiate an abnormal immune response against renal tubular and ocular antigens. In our patient, the history of sporadic NSAID intake may have contributed as a possible trigger.

Genetic susceptibility also plays a role. Associations with HLA-DQA1*01, HLA-DQB1*05*, and HLA-DRB1*0102 have been described in several cohorts [12,13]. More recently, autoantibodies against modified C-reactive protein (mCRP)—expressed in renal tubular basement membranes and ocular tissues—have been proposed as mediators of the shared renal and ocular inflammation [14]. This dual autoimmune response may explain the hallmark of the syndrome: simultaneous or sequential nephritis and uveitis. These findings reinforce the concept of TINU as an organ-specific autoimmune disease in genetically predisposed individuals exposed to environmental triggers.

3) Clinical Features

The clinical presentation of TINU is heterogeneous and often non-specific, leading to underdiagnosis. Renal involvement usually presents as acute interstitial nephritis, with symptoms such as fatigue, malaise, or weight loss, although some patients remain asymptomatic until laboratory abnormalities are identified [15]. Laboratory evaluation typically reveals acute kidney injury with elevated creatinine and urea, along with tubular abnormalities such as low-grade proteinuria, sterile pyuria, glycosuria, or elevated urinary β2-microglobulin [16]. Unlike glomerular disease, nephrotic-range proteinuria or heavy hematuria are rarely seen. Imaging usually shows normal kidney size and echogenicity, ruling out obstruction [17].

Ocular manifestations most often present as acute, bilateral, non-granulomatous anterior uveitis, though intermediate and posterior uveitis or panuveitis have been described in a minority of cases [18,19]. Importantly, uveitis may precede, coincide with, or follow nephritis, sometimes with a delay of several months [20]. The ocular course tends to be relapsing, even when renal disease has resolved, necessitating prolonged ophthalmologic surveillance. Complications such as posterior synechiae, cataract, and glaucoma can occur if inflammation is not adequately controlled [21].

4) Differential Diagnosis

The diagnosis of TINU is one of exclusion, as many systemic diseases can present with both interstitial nephritis and uveitis. Sarcoidosis is an important differential diagnosis, since it may cause granulomatous interstitial nephritis and uveitis, often with pulmonary or systemic features [22]. Autoimmune diseases such as Sjögren's syndrome and systemic lupus erythematosus (SLE) are also potential mimics, though serological testing usually identifies them [23]. Infectious causes—including tuberculosis, syphilis, and Lyme disease—should be excluded, particularly in endemic regions [24].

Other considerations include drug-induced interstitial nephritis without ocular involvement, particularly with antibiotics or NSAIDs [25]. Rarely, conditions such as IgG4-related disease or systemic vasculitides (e.g., granulomatosis with polyangiitis) can cause combined renal and ocular inflammation, but these are typically distinguishable by systemic features, histopathology, or serology [26]. A thorough immunologic and infectious evaluation, as performed in our patient, is essential before confirming TINU.

5) Management

The management of TINU syndrome depends on the severity of renal and ocular involvement. For the nephritis, supportive care with hydration and avoidance of nephrotoxic drugs is recommended. In patients with significant renal impairment, systemic corticosteroids are the standard of care, usually initiated as prednisone 1 mg/kg/day with tapering over several weeks to months [27]. Early corticosteroid therapy has been associated with faster renal recovery and reduced risk of progression to chronic kidney disease, though mild cases may recover spontaneously [28].

For ocular disease, topical corticosteroids and cycloplegic agents are indicated for anterior uveitis, while systemic corticosteroids may be required in severe or recurrent cases [29]. In refractory or relapsing uveitis, steroid-sparing immunosuppressive agents such as methotrexate, azathioprine, or mycophenolate mofetil have been used effectively [30]. Biologic therapies (anti-TNF agents) have been employed in rare resistant cases [31]. Close collaboration between nephrology and ophthalmology is critical to ensure both renal and ocular disease are appropriately monitored and treated.

6) Prognosis

The renal prognosis in TINU is generally favorable, with most patients recovering near-baseline renal function within weeks to months under appropriate therapy [32]. Progression to chronic kidney disease is uncommon and usually associated with delayed diagnosis, inadequate treatment, or severe interstitial fibrosis on biopsy [33]. Relapses of nephritis are rare compared to other causes of interstitial nephritis.

The ocular prognosis is less predictable, as uveitis frequently relapses independently of renal recovery. Some series report recurrence rates up to 50%, often requiring long-term topical or systemic therapy [34]. Recurrent inflammation increases the risk of ocular complications, including posterior synechiae, cataract, and glaucoma, which can threaten vision if inadequately treated [35]. Consequently, long-term ophthalmologic follow-up is recommended for all patients, even after complete renal recovery. Multidisciplinary management ensures early detection of recurrences and optimization of long-term outcomes.

CONCLUSION

TINU syndrome is a rare but important differential diagnosis in young patients presenting with acute kidney injury of tubular origin, particularly when accompanied by ocular symptoms or risk factors such as drug exposure. The case highlights the need for early multidisciplinary collaboration between nephrologists and ophthalmologists, since the renal and ocular manifestations often occur asynchronously. While renal outcomes are usually favorable with supportive care and corticosteroid therapy, uveitis is prone to recurrence, underscoring the importance of long-term ophthalmologic surveillance. Prompt recognition and treatment not only ensure recovery of renal function but also reduce the risk of irreversible ocular complications.

Key Messages

- **TINU syndrome** is a rare but underdiagnosed cause of acute interstitial nephritis with uveitis, especially in adolescents and young adults.
- **Renal and ocular involvement may be asynchronous**, so nephrologists should consider ophthalmology referral in unexplained acute kidney injury with tubular features.
- **NSAIDs and infections** are recognized potential triggers, but genetic predisposition (HLA associations) likely contributes.
- **Systemic corticosteroids** accelerate renal recovery, while
- **topical corticosteroids** are first-line for anterior uveitis.

- **Renal prognosis is generally favorable**, but **uveitis frequently relapses**, requiring long-term ophthalmologic follow-up.

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