# Tubulointerstitial Nephritis and Uveitis
## Report of a Rare Syndrome

Shokoufeh Savaj, Mojgan Asgari

Tehran University of Medical Sciences, Tehran, Iran

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Tubulointerstitial nephritis and uveitis (TINU) is a rare syndrome with unknown pathogenesis. Data have shown a higher prevalence in female gender. We present a man with tubulointerstitial nephritis and uveitis syndrome and antitubular antibody. A 23-year-old man presented with a history of weight loss, nausea, and vomiting, and uveitis. His serum creatinine was 2.1mg/d with pyuria and proteinuria in urinalysis. Other laboratory and imaging studies were unremarkable. Kidney biopsy showed granulomatous interstitial nephritis. Normal renal tissue specimen treated with patient's serum showed focal cytoplasmic staining in cortical tubular cells. The patient received prednisolone for 1 month. Interstitial nephritis and uveitis were well controlled. There was no recurrence in 1-year follow-up. We suggest that tubulointerstitial nephritis and uveitis syndrome should be considered in differential diagnosis of patients with interstitial nephritis and uveitis. Antitubular antibody may be used as a diagnosis marker for this syndrome.

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Case Report

## INTRODUCTION

Tubulointerstitial nephritis and uveitis (TINU) is a rare syndrome which was first reported in 1975.[1] Nearly, 200 cases are reported in the world with unknown pathogenesis. This syndrome is more prevalent in women than men (3:1).[2] Here, we present a 23-year-old man with uveitis and interstitial nephritis. This report is the first report of a male patient with TINU syndrome and antitubular antibody in Iran.

## CASE REPORT

A 23-year-old man presented with nausea and vomiting and blurring of vision. He also had weight loss. The ophthalmologist detected anterior uveitis in both eyes and referred him for

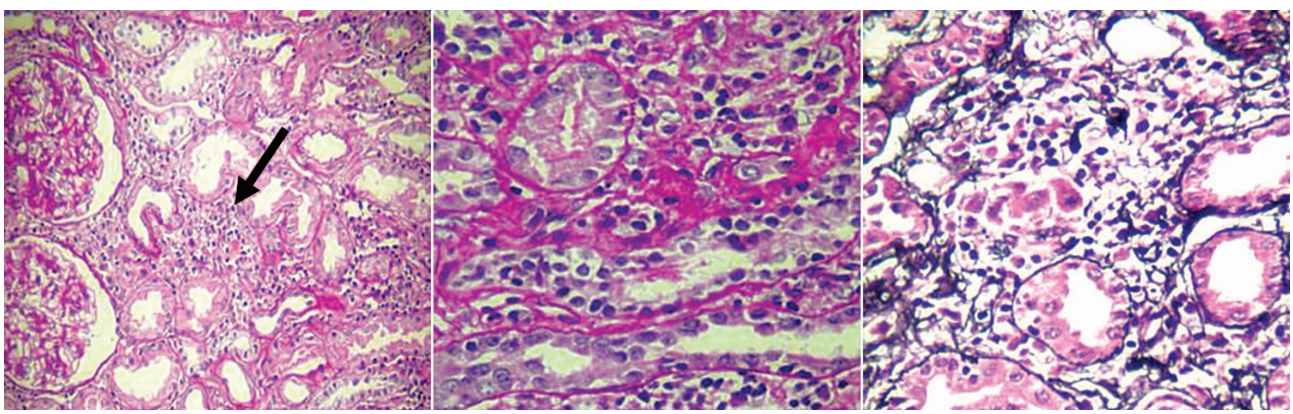

**Figure 1. Left,** lymphocytic infiltration in the interstitium and tubulitis (arrow). Note the normal looking glomeruli (periodic acid-Schiff, × 100). **Middle,** lymphocytic infiltration of interstitium, making tubulitis (periodic acid-Schiff, × 400). **Right,** histiocytic aggregation in the interstitium compatible with granuloma formation (Jones, × 400).

Laboratory Results

| Test | Result |
|---|---|
| Complete blood count | |
| Hemoglobin, g/dL | 11 |
| Leukocyte count, × $10^9$/L | 9.4 |
| Polymorphonuclear cell, % | 67 |
| Eosinophil, % | 20 |
| Monocyte, % | 4 |
| Basophil, % | 4 |
| Platelet count, × $10^9$/L | 283 |
| Erythrocyte sedimentation rate, mm/h | 35 |
| C-reactive protein | Negative |
| Blood urea nitrogen, mg/dL | 18 |
| Creatinine, mg/dL | 2.1 |
| Urinalysis | |
| Leukocyte, /HPF | 6 to 8 |
| Protein | Trace |
| 24-hour urine protein, mg | 325 |
| Thyroid function test | Normal |
| Antinuclear antibody | Negative |
| C4, mg/dL | 92 |
| C4, mg/dL | 14 |
| CH50, mg/dL | 140 |
| Protein electrophoresis (gamma ), g/dL | 2.6 |
| Perinuclear cytoplasmic antineutrophil antibody | Negative |
| Cytoplasmic antineutrophil antibody | Negative |
| Angiotensin-converting enzyme activity, IU/L | 34 (8 to 52) |
| Rheumatoid Factor, IU/m | < 8 |
| Cryoglobin | Negative |
| Hepatitis B surface antigen | Negative |
| Hepatitis C antibody | Negative |
| Human immunodeficiency virus antibody | Negative |
| Venereal disease research laboratory test | Negative |
| Tuberculosis skin test | Negative |
| Human leukocyte antigenB27 | Negative |

systemic evaluation. He had no complaint of fever, arthralgia, mucosal aphthous ulcerations, skin eruption, sinusitis, cough, or dyspnea. His blood pressure was 120/80 mm Hg, and no abnormal finding was detected on physical examination. Laboratory results are reported in the Table.

Imaging studies, including chest radiography, chest computed tomography, and gallium scan were unremarkable. On ultrasonography, the right kidney was 10.5 × 3.5 cm and the left kidney was 11.5 × 3.5 cm, with no evidence of obstruction. Percutaneous kidney biopsy showed inflammatory cell infiltration in the interstitium, composed of lymphocytes, polymorphonuclear cells, and also eosinophils (3 to 4per high-power field) with foci of tubulitis and also histiocytic aggregation, making noncaseating granuloma formation, suggestive of granulomatous interstitial nephritis (Figure 1). On the basis of our clinical and pathological findings, the patient was diagnosed tubulointerstitial nephritis and uveitis syndrome. After adding the patient's and a control sera on normal renal tissue of a nephrectomy specimen (taken for renal tumor in another patient), indirect immunofluorescence with anti-immunoglobulin G (IgG), anti-IgM, and anti-IgA antibody was performed. Indirect immunofluorescence with anti-IgG antibody showed focal cytoplasmic staining in cortical tubular cells, and therefore, the patient's serum for antitubular antibody was positive (Figure 2).

The patient received 1 mg/kg of prednisolone for 1 month. Interstitial nephritis and uveitis were well controlled (serum creatinine, 1.3 mg/

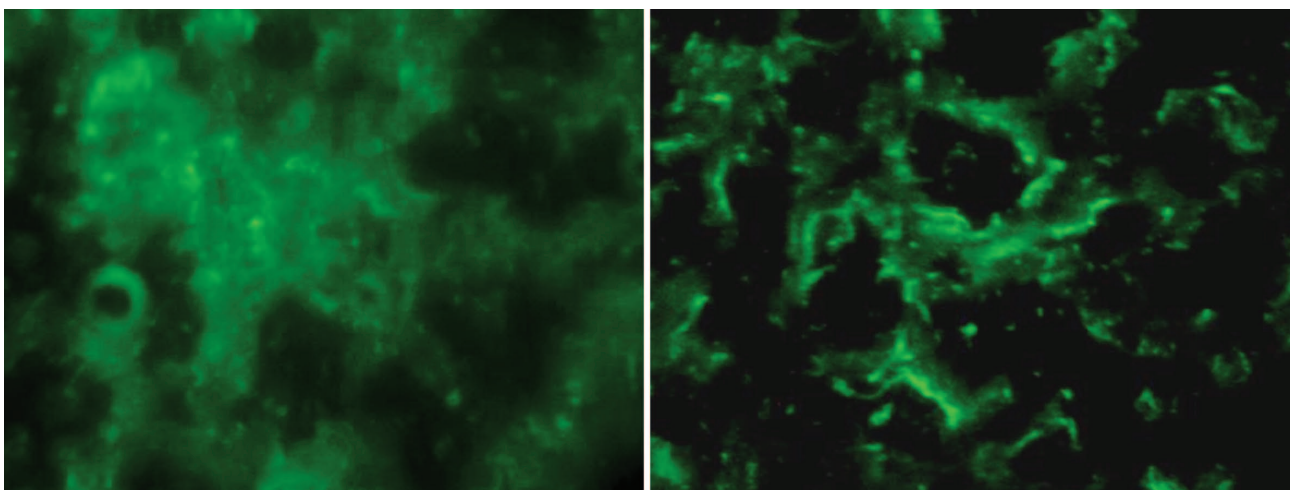

**Figure 2. Left,** indirect immunofluorescence with anti-IgG antibody in control specimen showing no positivity (× 200). **Right,** indirect immunofluorescence with anti-IgG antibody with focal cytoplasmic staining in cortical tubular cells (× 200).

dL; 24-hour urine protein, 137 mg). There was no recurrence in 1-year follow-up.

## DISCUSSION

The pathogenesis of TINU syndrome has not been well known. There are reports of recent infections by organisms such as Epstein-Barr virus, herpes zoster virus, and *Chlamydia trachomatis*, medications such as nonsteroidal agents and antibiotics, and co existence of other autoimmune conditions.[2-4] Levinson and coworkers noted that the haplotype of human leukocyte antibody DQA1*01/DQB1*05/DRB1*01 was identified in 13 of their patients (72.2%) with TINU.[5] Some patients with this syndrome have antitubular antibody with localization on proximal tubule and lesser-extent distal tubule and Bowman capsule.[2] However, these antibodies are not specific for this syndrome and have been detected in kidney transplant recipients and consumption of drugs.

Kase and colleagues[6] showed a significant increase in serum Krebs von den Lunge-6 levels, a human glycoprotein which has been used to monitor the activity of sarcoidosis in this syndrome. They noted that the Krebs von den Lunge-6 level is not increased in age-matched patients with uveitis from other causes. Another potential diagnostic marker is urine β2-microglobulin level. Goda and colleagues[7] noted that in 11 of 12 patients with TINU syndrome, urinary β2-microglobulin was increased.

Clinical presentation is varied. Systemic symptoms such as weight loss, fatigue, arthralgia, and fever may predominate. Renal manifestations include sterile pyuria, hematuria, subnephrotic proteinuria, and renal insufficiency. Ocular symptoms can precede (20%) or follow (65%) the renal diagnosis.[2] There is no single diagnostic test available for TINU syndrome. Diagnosis is based on exclusion of systemic diseases such as Wegener granulomatosis, systemic lupus erythematosus, Sjorgren syndrome, sarcoidosis, rheumatoid arthritis, Behcet disease, tuberculosis, toxocariasis, and toxoplasmosis.

Tubulointerstitial nephritis can resolve spontaneously and dialysis therapy is not usually required. In the case of progressive renal impairment, reducing dose of oral prednisolone, starting at 1mg/kg/d, is usually recommended.[7] On the basis of our data patient's diagnosis was TINU Syndrome. He received prednisolone for 1 month. Interstitial nephritis and uveitis were well controlled. There was no recurrence in 1-year follow-up.

This case is the first report of a male patient with TINU syndrome in Iran, with antitubular antibody in the patient's serum. Our patient had a benign course. Due to increasing number of TINU reports in the world, we suggest that TINU syndrome should be considered in differential diagnosis of patients with interstitial nephritis and uveitis. Antitubular antibody may be used as a diagnostic marker for this syndrome.

## CONFLICT OF INTEREST

None declared.

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Correspondence to:
Shokoufeh Savaj, MD
Firouzgar Hospital, Behafarin St, Karim Khan Ave, Valiasr Sq,
Postal code: 1593748711, Tehran, Iran
Tel: +98 21 2290 0008
Fax: +98 21 2227 6951
E-mail: ssavaj@hotmail.com



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