doi: 10.5262/tndt.2016.11

Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome: A Case Report

Tübülointerstisyel Nefrit ve Üveit (TINU) Sendromu: Olgu Sunumu

Şiyar ERDOĞMUŞ
Serkan AKTÜRK
Zeynep KENDİ ÇELEBİ
Kenan KEVEN
Şule ŞENGÜL
Neval DUMAN

Ankara University School of Medicine, Department of Nephrology, Ankara, Turkey

ABSTRACT

Tubulointerstitial nephritis and uveitis syndrome is characterized by a combination of acute tubulointerstitial nephritis and uveitis. This syndrome is an uncommon cause of acute tubulointerstitial nephritis and is an exclusion diagnosis. Most patients with this syndrome are young women and adolescents although it may occur adults and old age. The uveitis can occur concurrently, precede or follow the onset of the tubulointerstitial nephritis. The vast majority of cases present after the onset of renal disease. The underlying mechanisms of the disease are still unknown. Renal disease tends to be self-limited, whereas uveitis tends to recur and relapse. A collaborative approach between nephrologists and ophthalmologists is crucial for the early diagnosis, treatment and management of disease. In this report, we describe a 31-year-old woman with tubulointerstitial nephritis and uveitis syndrome.

KEY WORDS: Acute tubulointerstitial nephritis, Tubulointerstitial nephritis and uveitis (TINU) syndrome, Uveitis

ÖZ

Tübülointerstisyel nefrit ve üveit sendromu akut tübülointerstisyel nefrit ve üveitin kombinasyonu ile karakterizedir. Bu sendrom akut tubulointerstisyel nefritin nadir bir nedeni ve ekartasyon tanısıdır. Hastalık sıklıkla genç kadınlar ve adölesanlarda görülmesine rağmen yetişkin ve ileri yaşlarda da ortaya çıkabilir. Üveit, tübülointerstisyel nefritin öncesinde ve sonrasında ortaya çıkabildiği gibi eş zamanlı olarak da saptanabilir. Olguların büyük çoğunluğu renal hastalığın başlangıcından sonra prezente olur. Hastalığın altında yatan mekanizmalar henüz bilinmemektedir. Renal hastalık kendini sınırlama eğilimindeyken, üveit nükslerle seyretmektedir. Hastalığın erken tanısında, tedavisinde ve yönetiminde nefrologlar ve oftalmologlar arasındaki işbirliği çok önemlidir. Bu olgu sunumunda, tübülointerstisyel nefrit ve üveit sendromu olan 31 yaşında kadın hasta tanımlanmaktadır.

ANAHTAR SÖZCÜKLER: Akut tübülointerstisyel nefrit, Tübülointerstisyel nefrit ve üveit (TINU) sendromu, Üveit

INTRODUCTION

The tubulointerstitial nephritis and uveitis (TINU) syndrome, which is characterized by acute tubulointerstitial nephritis (ATIN) along with uveitis, is an uncommon disease. It was first described in 1975 by Dobrin and colleagues (1) and many cases have been reported (2,3). Most patients with the TINU syndrome are adolescents and young women, with a median onset age of 15 years and a female predominance (4) but it has also been reported in adults and the elderly (5). The uveitis can develop concurrently, preceded or follow the onset of tubulointerstitial nephritis but it is most often seen after the onset of the renal disorder (4). The pathogenesis of the TINU syndrome is still not well understood. However, some studies have recently indicated that the TINU syndrome has an immunological origin. For instance, the presence of autoantibodies against both tubular and uveal cells (6) and autoantibodies against modified C-reactive protein (mCRP-Ab) has been demonstrated (2,7). We report the case of a 31-year-old woman who presented with the TINU syndrome.

Received : 30.07.2015
Accepted : 31.12.2015

Correspondence Address:
Şiyar ERDOĞMUŞ
Ankara Üniversitesi Tıp Fakültesi,
İbni Sina Hastanesi, Nefroloji Bilim Dalı,
Ankara, Turkey
Phone : +90 312 508 21 68
E-mail : si.yar21@hotmail.com

CASE PRESENTATION

A 31-year-old woman was referred to our clinic for further investigation due to acute kidney injury. On admission, her vital signs were within the normal range and physical examination findings were unremarkable. She complained of nonspecific constitutional symptoms such as fatigue, malaise, anorexia and headache. There was no medical history of toxic agents, fever, weight loss, rash and arthralgias or any other health problem. Three months prior, she had suffered from sore throat and was treated with antibiotics. Laboratory tests revealed a white blood cell count of 9.2 X 10^9/L, hemoglobin 11.4 g/dL, platelet count 348 X 10^9/L, blood urea nitrogen level 21 mg/dL, serum creatinine level 1.8 mg/dL, estimated glomerular filtration rate 43 ml/min/1.73 m^2 and 24-hour urine protein level 1.2 g/day. Other laboratory tests including serum levels of electrolytes, liver function tests and thyroid function tests were within the normal range. Urinalysis revealed a density of 1018, pH 5, protein 30 mg/dL, glucose 150 mg/dL (normoglycemic glycosuria), and 4 leukocytes and 8 erythrocytes per high-power field. Erythrocyte sedimentation rate (ESR) was 76 mm/h and C-reactive protein (CRP) level was 55 mg/L. Antinuclear antibodies (ANA) were positive at 1:100. Anti-neutrophil cytoplasmic antibodies (ANCA), anti-double-stranded DNA (Anti-ds DNA), rheumatoid factor (RF), antibodies to SS-A/Ro, and SS-B/La tests were all negative. Serum complement levels were within the normal range. Renal ultrasonography demonstrated normal kidney sizes and slightly elevated echogenicity of renal parenchyma.

Subsequently, percutaneous renal biopsy was performed. On light microscopy, the renal interstitium showed intense infiltration with inflammatory cells, predominantly composed of plasma cells, eosinophils, and lymphocytes, together with moderate tubulitis. Glomerular and vascular structures were normal. Immunofluorescence microscopy was negative for immunoglobulins and complement components in the glomeruli. Consequently, a diagnosis of ATIN was made and administration of systemic prednisone 60 mg (1mg/kg) per day was started. During follow-up, her serum creatinine returned to normal and treatment was slowly tapered for three months.

Four months after admission, she presented with bilateral eye pain, redness and photophobia. Ophthalmological consultation documented bilateral anterior uveitis. The patient was treated with topical corticosteroids and her ocular symptoms subsided within one week. To exclude the other systemic diseases that can cause uveitis such as Sjögren's syndrome, sarcoidosis, IgG4-related autoimmune disease, systemic lupus erythematosus, Wegener's granulomatosis, Behçet's syndrome and infectious diseases including tuberculosis, brucellosis, toxoplasmosis, herpes virus, cytomegalovirus and syphilis, further testing were performed (4,8). ANA, ANCA, Anti-ds DNA, Anti SSA/Ro, and Anti SSB/La, serum IgG4 level, PPD skin tests, serum angiotensin-converting enzyme level, and viral and bacterial serologic tests were all negative or within normal limits. Chest X-ray and tomography findings were unremarkable. Based on these findings, a diagnosis of TINU syndrome was made. Furthermore, at the time of the diagnosis, her creatinine level, urinary beta-2 microglobulin level and urinalysis were normal. During the follow-up of six months, recurrences of uveitis did not occur.

DISCUSSION

The TINU syndrome is defined as a combination of tubulointerstitial nephritis and uveitis and is a rare disorder. Some risk factors have been associated with TINU syndrome such as drugs (antibiotics and nonsteroidal anti-inflammatory drugs), infectious agents, toxins and autoimmune diseases. In one-half of the patients with TINU syndrome, no identifiable risk factors have been found. Patients with TINU syndrome can present with nonspecific systemic features including fever, weight loss, fatigue, malaise, anorexia, weakness or asthenia, abdominal or flank pain, arthralgias or myalgias, headache and polyuria or nocturia. The most common ocular complaints in patients with the TINU syndrome are eye pain or redness, decreased visual activity and photophobia. The ocular disease is most often a bilateral anterior uveitis, although posterior uveitis can be observed. The uveitis usually occurs after the onset of tubulointerstitial nephritis but it has been observed to occur two months before, concurrently, and up to 14 months after the onset of the renal dysfunction (4).

Renal manifestations with TINU syndrome are typical for ATIN. These may contain flank pain, sterile pyuria, hematuria, proteinuria (usually subnephrotic range), renal insufficiency and acute kidney injury. Renal biopsy is required for the definitive diagnosis of ATIN (2,9). Standard treatment has not been established for the TINU syndrome. It is essential that the potentially causative agent be immediately discontinued. If there is no subsequent improvement in kidney function, prednisone therapy is employed. Laboratory findings in patients with TINU syndrome are not specific. Laboratory findings may include anemia, eosinophilia, leukocyturia and elevation of the serum creatinine levels, ESR, CRP and urinary beta-2 microglobulin levels (4). In recent years, serum Krebs Von Den Lunge-6 (KL-6) glycoprotein and mCRP-Ab levels have been found to be potentially for the diagnosis of the TINU syndrome (2).

A diagnosis of TINU syndrome should be considered in patients with tubulointerstitial nephritis in combination with uveitis. A number of diseases can cause both interstitial nephritis and uveitis. Therefore, the TINU syndrome is a diagnosis by exclusion. The TINU syndrome has a good prognosis generally, but recurrences and relapses of uveitis are common. Thus, long-term ophthalmological follow-up is required (4).

In conclusion, we described a 31-year-old woman with TINU syndrome who presented with acute kidney injury due to ATIN by confirmed renal biopsy. The patient was treated with prednisone for three months and this was then slowly tapered.

Four months later, she presented with bilateral anterior uveitis. A diagnosis of the TINU syndrome was made after the differential diagnosis for uveitis. The patient had no recurrences in the following six months.

REFERENCES

1. Dobrin RS, Vernier RL, Fish AL: Acute eosinophilic interstitial nephritis and renal failure with bone marrow-lymph node granulomas and anterior uveitis. A new syndrome. Am J Med 1975;59:325-333
2. Li C, Su T, Chu R, Li X, Yang L: Tubulointerstitial nephritis and uveitis in Chinese adults. Clin J Am Soc Nephrol 2014;9:21-28
3. Matsumoto K, Fukunari K, Ikeda Y, Miyazono M, Kishi T, Matsumoto R, Fukuda M, Uchiumi S, Yoshizaki M, Nonaka Y, Kanaya A: A report of an adult case of tubulointerstitial nephritis and uveitis (TINU) syndrome, with a review of 102 Japanese cases. Am J Case Rep 2015;16:119-123
4. Mandeville JT, Levinson RD, Holland GN: The tubulointerstitial nephritis and uveitis syndrome. Surv Ophthalmol 2001;46:195-208
5. Ungprasert P, Kue-A-Pai P, Surakiatchanukul T, Rassameehiran S, Knight EL: Tubulointerstitial nephritis and uveitis syndrome in an older adult: A case report and review of the literature. J Am Geriatr Soc 2013;61:1840-1842
6. Abed L, Merouani A, Haddad E, Benoit G, Oligny LL, Sartelet H: Presence of autoantibodies against tubular and uveal cells in a patient with tubulointerstitial nephritis and uveitis (TINU) syndrome. Nephrol Dial Transplant 2008;23:1452-1455
7. Tan Y, Yu F, Qu Z, Su T, Xing GQ, Wu LH, Wang FM, Liu G, Yang L, Zhao MH: Modified C-reactive protein might be a target autoantigen of TINU syndrome. Clin J Am Soc Nephrol 2011;6: 93-100
8. Yoneda K, Murata K, Katayama K, Ishikawa E, Fuke H, Yamamoto N, Ito K, Shiraki K, Nomura S: Tubulointerstitial nephritis associated with IgG4-related autoimmune disease. Am J Kidney Disease 2007;50:455-462
9. Abdelghany M, Nasser S, Frem G, Goldblatt C: Tubulointerstitial nephritis and uveitis syndrome in an elderly woman. Clin Kidney J 2014;7:420-421