

Tubulo-Interstitial Nephritis and Uveitis Syndrome: A Case SeriesSaid Kaddouri^{1*}, Zemraoui Nadir², Zakaria Chahbi¹, Hassan Qacif¹, Mohamed Zyani¹¹Department of Internal Medicine, Ibn Sina Military hospital, Marrakesh, Morocco²Department of Nephrology, Ibn Sina Military hospital, Marrakesh, Morocco***Corresponding author**

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Abstract: The tubulo-interstitial nephritis and uveitis syndrome (TINU syndrome) affects adolescent females preferentially, and it is typically characterized by the association of tubulo-interstitial nephritis and anterior bilateral uveitis. However, it may have different atypical presentations. It can be seen in male, in adults, without renal insufficiency or with a posterior uveitis. We report three cases of atypical TINU syndrome. We reported two out of three adult patients (16, 60 and 62 years of age), two of whom were female and one male. The first patient had a panuveitis of the left eye and a posterior uveitis of the right eye. The second patient presented bilateral panuveitis with retinal vasculitis. The third patient had a bilateral anterior uveitis recurrent. The three patients had proteinuria, glucosuria, aseptic leukocyturia without renal insufficiency. Renal biopsy showed Tubulo-interstitial nephritis with no sign of vasculitis or glomerular involvement. The etiological investigation did not find any cause (infection, medication, systemic illness). The patients received a local and general corticosteroid therapy associated in one case with Methotrexate, which has resulted in rapid improvement for all three patients. This clinical case report highlights some important features of TINU syndrome, including the increasing incidence of disease in male and adult patients, the possibility of a posterior involvement of uveitis, and clinical presentation without kidney failure. Extensive studies are needed to elucidate the cause and pathogenesis of this syndrome for better management.

Keywords: Tubulo-Interstitial Nephritis, Uveitis, TINU Syndrome, Corticosteroid

INTRODUCTION

Tubulo-interstitial nephritis and uveitis syndrome (TINU syndrome) is a rare disorder of unknown pathogenesis that affects adolescent females in particular. It is characterized by the association of tubulo-interstitial nephritis and anterior bilateral uveitis. However, it may have different atypical presentations. TINU syndrome can be seen in male, in adults, without renal insufficiency and with a posterior uveitis. We report three cases of atypical TINU syndrome followed at the department of internal medicine of Ibn Sina military hospital in Marrakech.

CASE PRESENTATION**Case 1**

A 16-year-old Moroccan girl, who had no significant past and family history, complained of a clinical presentation first made of ocular pain and redness with a decrease in visual acuity followed a few days later by an alteration of the general state; fatigue, anorexia, weight loss with myalgia and arthralgia of the lower limbs, then a pruritus that spares the trunk preceding a purpuric rash. Clinical examination on admission found an afebrile patient with mucocutaneous pallor and petechial purpura in the limbs. There was no peripheral lymph node swelling.

Peripheral edema was not observed. The rest of the physical examination was without special features. The ophthalmological examination revealed a panuveitis of the left eye and a posterior uveitis of the right eye, not granulomatous and non-synechiante. The initial assessment found a high erythrocyte sedimentation rate (ESR 100 mm /1st hour). C-reactive protein was 23mg / l. hemoglobin was 10g / dl. Plasma protein electrophoresis was normal. Serum creatinine and urea nitrogen concentrations were normal. The 24-hour urine protein excretion was 1.38 g / 24h. The urine examination revealed microscopic hematuria, glucosuria and aseptic leukocyturia. Renal Ultrasonography did not reveal any abnormality. Renal biopsy showed acute interstitial nephritis consistent with a TINU syndrome with no sign of vasculitis or glomerular involvement. The etiological investigation did not find any history of medication intake, dry syndrome or buccogenital aphthosis. Serum calcium, calciuria and angiotensin-converting enzyme (ACE) levels were all normal. The biopsy of the accessory salivary glands showed a discrete sialadenitis grade I of Chisholm. The search for autoantibodies (ANA, anti-DNA, anti-SSA / SSB, ANCA) was negative. Serologies (TPHA, VDRL, CMV, HIV, and toxoplasmosis) were negative. The search for

tuberculosis was negative as well as the tuberculin skin test. The serum complement CH50 and the fractions C3 and C4 were normal. There was no hilar adenopathy or abnormalities in pulmonary radiography and chest CT.

The diagnosis of TINU syndrome was retained in the absence of an etiology of this renal and ocular involvement. The patient received a local and general corticosteroid therapy (1mg / kg) enabling a favorable evolution with improvement of the general state, negativation of proteinuria and hematuria, normalization of the inflammatory assessment, improvement of the visual acuity and disappearance of ocular inflammatory signs.

Case 2

A 60-year-old Moroccan male, who had no significant pathological history, presented bilateral panuveitis with retinal vasculitis. On admission, the patient was in good general health, apart from the decrease in visual acuity. He was asymptomatic and the clinical examination was without abnormality. Initial assessment found C-reactive protein 6 mg / l. Eosinophilia rate was 910 / mm³. The rest of blood count was normal. Renal function was normal. The 24-hour urine protein excretion was between 1 and 2.5g / 24h. The urine examination revealed Microscopic hematuria, glucosuria and aseptic leukocyturia. Plasma protein electrophoresis and renal ultrasound were normal. Renal biopsy showed moderate and non-specific tubulo-interstitial inflammatory lesions, with no sign of vasculitis or glomerular involvement. The etiological investigation did not find any history of medication intake, dry syndrome or buccogenital aphthosis. The patient was asymptomatic. The infectious research was negative. The immunological assessment was negative. Serum calcium, calciuria, serum complement and angiotensin-converting enzyme levels were normal. The biopsy of the accessory salivary glands showed a discrete unspecific sialadenitis. The thoraco-abdomino-pelvic CT scan was without abnormality. The diagnosis of TINU Syndrome was retained in the absence of other cause. The patient received a bolus of corticosteroid of 500mg / day for three days relayed by 1mg / kg orally, and then at a decreasing dose associated with Methotrexate 15mg / week. The evolution was favorable with normalization of the eosinophilic ratio, a decrease in proteinuria to 0.4 g / 24h, and ophthalmological control showed an improvement in visual acuity and persistence of sequelae uveitis without signs of ocular inflammation.

Case 3

A 62-year-old Moroccan female, who had a long history of high blood pressure and total thyroidectomy for nodular goitre two years previously under Substitutive treatment, presented bilateral anterior uveitis followed one year later by a clinical presentation of asthenia, febrile sensation, arthromyalgia, and ocular pain and redness with a

decrease in visual acuity. Ophthalmologic examination revealed a recurrence of bilateral anterior uveitis with the presence of iridocrystalline synechiae. On admission, the patient was in fairly good general health. Her body temperature was 38°C. The physical examination was essentially normal. She had no edema or palpable lymph nodes. The biological evaluation found a C-reactive protein 80 mg / l, a preserved renal function, and hemoglobin 11 g / dl. The 24-hour urine protein excretion was 1 g / 24h. The urine examination revealed aseptic leukocyturia and glucosuria in the presence of normoglycemia. Renal Ultrasonography did not find any abnormality. Renal biopsy showed unspecific tubulo-interstitial nephritis lesions without signs of glomerular involvement. The diagnosis of TINU syndrome was retained after etiologic research that returned negative. Treatment with local and general corticosteroids has resulted in a rapid improvement, with an improvement in visual acuity, disappearance of ocular inflammatory signs, and a negativity of proteinuria and leukocyturia.

DISCUSSION

The TINU syndrome was described for the first time by Dobrin et al in 1975 [1]. Since then, hundreds of similar observations were reported. It is a systemic disorder that occurs most often in young female subjects. However, it can occur late in the adult and in the male sex [2,3]. We reported two out of three adult patients, two females versus one male. Its pathogenesis, although little known, has recently made significant progress by the demonstration of the presence of an antibody recognizing the modified CRP (mCRP), which is present in both tubular and uveal cells [4,5]. The TINU syndrome is characterized clinically by the association of a prodromal period made up of low-grade fever, weight loss, anorexia, asthenia, arthralgia, myalgia and abdominal pain, preceding the appearance of a renal insufficiency [6,7]. The ocular involvement is made of anterior uveitis, sometimes posterior, usually bilateral and may occur at different times in the course of renal disease [8]. Paraclinically, there is an impairment of renal function, with a description of cases with normal creatinemia [7,8], proteinuria, hematuria, aseptic leukocyturia, high β_2 microglobulin in the urine, high erythrocyte sedimentation rate, anemia, blood hypereosinophilia, hepatic cytolysis and tuberculin anergy [3]. We reported three patients without renal insufficiency and two out of three patients with posterior uveitis. Histologically, TINU syndrome is characterized by interstitial edema with a cellular infiltrate mainly composed of mononuclear cells, eosinophils and neutrophils and by tubular atrophy without glomerular or vascular involvement [3, 5]. TINU syndrome is a diagnosis of exclusion. It must eliminate the drug causes, infectious causes (syphilis, tuberculosis, brucellosis, HIV, toxoplasmosis) and systemic diseases in particular sarcoidosis, Sjogren's syndrome, lupus, Behçet's disease and Wegener's granulomatosis with Polyangiitis [3, 7].

There is no specific therapeutic consensus. However, general corticosteroids provide effective treatment in the vast majority of published cases. Nephritis is more corticosteroid sensitive than uveitis, which tends to be recurrent, sometimes requiring the use of immunosuppressants [9].

CONCLUSION

This clinical case report highlights some important features of TINU syndrome, including the increasing incidence of disease in male and adult patients, the possibility of a posterior involvement of uveitis, and clinical presentation without kidney failure. Extensive studies are needed to elucidate the cause and pathogenesis of this syndrome for better management.

ABBREVIATIONS

TINU: Tubulo-Interstitial Nephritis and Uveitis, ANA: Antinuclear antibody, ANCA: Antineutrophil cytoplasmic antibody, ACE: Angiotensin-converting enzyme, CMV: Cytomegalovirus, HIV: Human immunodeficiency virus, CT: Computed tomography, CRP: C-reactive protein, VDRL: Venereal Disease Research Laboratory, TPHA: Treponema Pallidum Hemagglutinations Assay

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