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**SHORT COMMUNICATION**

# Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) with unilateral neuroretinitis: A case report

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PURPOSE. *To report a case of tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) with unusual unilateral neuroretinitis.*
METHODS. *An 11-year-old girl who developed anterior uveitis 3 months after acute tubulointerstitial nephritis, without any etiologic factors for either nephritis or uveitis, is presented.*
RESULTS. *Several days after the anterior uveitis, the patient presented with unilateral optic disk edema associated with a serous retinal detachment of the posterior pole, never previously described in TINU syndrome, leading to the formation of perifoveal intraretinal exudates.*
CONCLUSIONS. *In spite of these posterior lesions, clinical course confirmed the previously reported favorable visual outcome of TINU syndrome treated with corticosteroids. It appeared that ocular impairment in TINU syndrome could be more diffuse and more extensive than previously described. As well as the whole uveal tract, the retina and the optic nerve may also be the ocular targets of the idiopathic inflammatory response in TINU syndrome. (Eur J Ophthalmol 2004; 14: 334-7)*

KEY WORDS. *Neuroretinitis, Optic disk edema, Serous retinal detachment, Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome)*

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## INTRODUCTION

Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome), first described by Dobrin et al (1), is a rare idiopathic renal and ocular disease, where acute tubulointerstitial nephritis (AIN) occurs typically in association with a bilateral anterior uveitis. TINU syndrome is usually benign (2). The aim of this report is to describe a case of TINU syndrome associated with unilateral neuroretinitis, to our knowledge never previously reported in TINU syndrome.

## Case report

An 11-year-old girl presenting with anorexia and daily vomiting for 3 weeks was hospitalized for acute renal failure, with normal diuresis. The patient had no previous medical history. Laboratory investigations revealed increased uremia (16 mmol/L), increased creatininemia (535 µmol/L), normocytic anemia (5.6 mmol/L), increased C-reactive protein (10 mg/L), hyperproteinemia, and hypergammaglobulinemia. Urinalysis showed elevated beta-2-microglobulin level,

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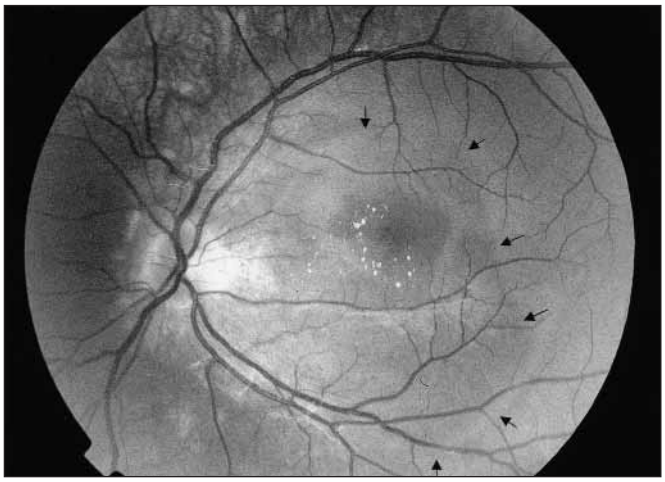

**Fig. 1 -** *Late phase fluorescein angiography of the right eye showing optic disk fluorescein leakage and fluorescein pooling in the subretinal space, revealing the limits of the serous retinal detachment (arrows), which largely involves the posterior pole.*

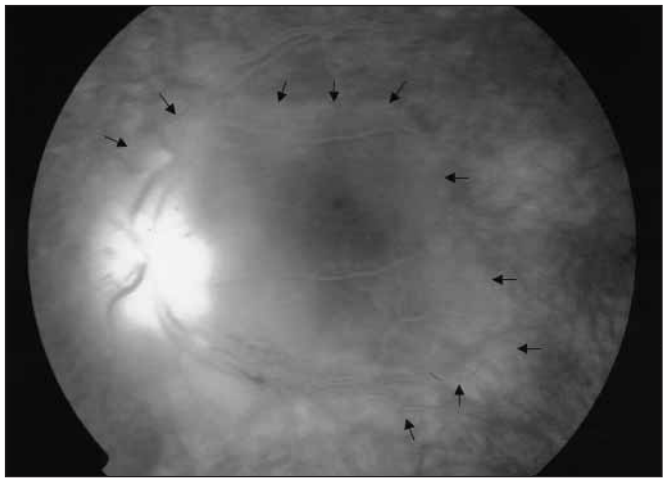

**Fig. 2 -** *Red-free retinal fundus of the right eye showing thin perifoveal intraretinal exudates, which became visible after the gradual resolution of the serous retinal detachment and persisted for 5 months. The previous edges of the serous retinal detachment can still be clearly seen (arrows).*

low-grade proteinuria (1.5 g/24 hr), and normoglycemic glucosuria. Renal ultrasonography was normal. The renal biopsy revealed a tubulitis and interstitial lymphohistiocytosis infiltration consistent with tubulointerstitial nephritis, with neither glomerular nor vascular alterations, or granuloma. Investigations did not reveal any systemic or infectious diseases. There was no evidence for toxic or drug-related etiologies. Evolution showed spontaneous and progressive improvement of renal function.

Three months after the onset of systemic symptoms, the patient developed a bilateral nongranulomatous anterior uveitis, with normal ocular tonus. Ocular examination showed a best-corrected visual acuity of 20/25 in each eye. The patient was treated by topical mydriatics and topical corticosteroids. A few days later, right best-corrected visual acuity strongly decreased to 20/125. An optic disk edema with a large peripapillary serous retinal detachment involving the posterior pole had appeared on the right eye, associated with a moderate hyalitis. Neither retinal vasculitis nor chorioretinitis was observed. Fluorescein angiography revealed leakage from the right optic disk and pooling of fluorescein in the subretinal space, and confirmed the absence of retinal vasculitis (Fig. 1). Laboratory tests showed persistent elevated uremia (13 mmol/L) and creatininemia (237 µm/L). Oral corticosteroids, 60 mg daily for 1 month, followed by 60 mg every other day, were prescribed. Two months after the onset of systemic corticosteroids, visual acuity was 20/40 in the right eye, the serous retinal detachment had resolved, and thin resorptive perifoveal intraretinal exudates had appeared, without retinal macular thickening (Fig. 2). Oral corticosteroids were progressively reduced (reduction of 10 mg each week), and finally stopped.

However, 4 days after the end of oral corticosteroid therapy, bilateral anterior uveitis recurred, and a bilateral optic disk edema, associated with a hyalitis, was observed. Ocular inflammation was predominant in the right eye. Subconjunctival injections of delayed effect followed by short-effect corticosteroids were performed on the right eye, associated with topical corticosteroids bilaterally. As anterior and posterior uveitis slowly resolved, topical corticosteroids were progressively decreased and stopped, with no recurrence of ocular inflammatory signs. Right intraretinal perifoveal exudates disappeared 5 months after they occurred.

One year after the onset of systemic symptoms, visual acuities were 20/25 bilaterally. With the exception of anterior micro Tyndall phenomenon on the left eye, ocular examination was normal. Laboratory findings showed normal renal function.

## DISCUSSION

The diagnosis of TINU syndrome requires the presence of both AIN and uveitis without other known systemic diseases that can cause either AIN or uveitis (2). TINU syndrome is considered definite when AIN is histopathologically diagnosed or clinically diagnosed with complete criteria, and associated with typical uveitis. Typical uveitis of TINU syndrome is a bilateral anterior uveitis, with an onset up to 2 months before, or up to 12 months after the beginning of systemic symptoms (2). TINU syndrome typically occurs in adolescent women, initially presenting with general impairment, moderate fever, abdominal pain, and vomiting. Urinalysis shows a tubular syndrome, and renal histologic examination demonstrates inflammatory interstitial lesions (diffuse cellular infiltration of mononuclear cells, including lymphocytes, plasma cells, and histiocytes). Renal disease usually resolves in a few months, either spontaneously or with corticosteroid treatment. Uveitis also improves with topical or systemic corticosteroids, but tends to recur. The course of the uveitis appears to be independent from that of the renal disease (2).

In the present case, the renal biopsy of the patient was consistent with tubulointerstitial nephritis. Acute tubulointerstitial nephritis can be caused by different factors: drugs (diuretics, antimicrobial and anti-inflammatory medication), infectious diseases (streptococci infection, toxoplasmosis), systemic and autoimmune diseases (sarcoidosis, Sjögren syndrome, Behçet disease, systemic lupus erythematosus) (3). These etiologies were not found in the present case.

Three months later, the patient presented with unilateral panuveitis, with neuroretinitis. The main causes of panuveitis in adolescents are sarcoidosis, Behçet disease, Vogt-Koyanagi-Harada syndrome, and Lyme disease (2-4). However, sarcoidosis is usually associated with granulomatosis anterior uveitis and retinal venous periphlebitis; Behçet disease is associated with occlusive vasculitis; and Vogt-Koyanagi-Harada syndrome with multiple serous retinal detachments. None of these ocular characteristics was present in this patient. Autoimmune diseases such as lupus erythematosus, periarteritis nodosa, scleroderma, or dermatomyositis, and infectious diseases such as tuberculosis, VIH disease, or syphilis, can also be associated with panuveitis (2-4). Neuroretinitis was defined as swelling of the optic disk associated with peripapillary and macular hard exudates, often occurring in the setting of mild vitreous inflammation (5). Bartonella henselae infection appears to be the most common cause for neuroretinitis, but less frequent causes such as toxoplasmosis, syphilis, leptospirosis, Lyme disease, toxocariasis, measles, mumps, tuberculosis, varicella zoster virus infection, or herpes simplex virus infection should also be considered (5). Investigation did not reveal these systemic or infectious diseases. As no etiology for uveitis or nephritis was observed, the patient was considered to have TINU syndrome.

Most of the cases reported as TINU syndrome presented anterior ocular characteristics (2). Only a small number of patients with TINU syndrome have been previously reported to present posterior ocular lesions, including two cases of retinal edema, one case of retinal exudates, and seven cases of optic disk swelling (2). The interest of the present report is in the occurrence of a unilateral papillitis with a large unilateral peripapillary serous retinal detachment involving the posterior pole, to our knowledge never previously described in TINU syndrome, leading to the formation of perifoveal intraretinal exudates. Therefore, panuveitis associated with neuroretinitis should be considered as a possible ocular lesion leading to the diagnosis of TINU syndrome. However, in spite of these ocular posterior lesions, visual prognosis remained good, with no persistent macular edema and subsequently any macular sequelae.

The pathogenesis of TINU syndrome remains unknown and an immune mechanism has been proposed (2). A role for cell-mediated immunity is supported by cytologic studies revealing a preponderance of T-lymphocytes in the renal interstitium (2). Mycoplasma-like organisms have been reported to be able to directly infect both kidneys and eyes. The kidneys and eyes may also be the leading targets of an inflammatory response toward similar but not yet identified antigenic stimulus (2).

We report an additional case of TINU syndrome, with an unusual ophthalmologic manifestation: unilateral papillitis associated with serous retinal detachment involving the major part of the posterior pole, leading to the formation of perifoveal intraretinal exudates. However, in spite of these posterior lesions, the clinical course confirmed the previously described favorable visual outcome of TINU syndrome. It appears that oc-

ular impairment in TINU syndrome could be more diffuse and more extensive than previously reported. As well as the entire uveal tract, the retina and the optic nerve may also be the ocular targets of the idiopathic inflammatory response in TINU syndrome.

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