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# Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) associated with Epstein-Barr virus

Beatriz Jiménez, MD[1]; Juan Ibáñez-Alperte, MD, PhD[1]; Diana Pérez-García, MD[1]; Enrique Mínguez, MD[1]; José A. Cristóbal, MD, PhD[1]; Manuel Moros, MD[2].

[1]Department of Ophthalmology, "Lozano Blesa" University Clinic Hospital, Zaragoza, Spain.
[2]Department of Pathological Anatomy, "Lozano Blesa" University Clinic Hospital, Zaragoza, Spain.

## Abstract

**Purpose.** To report a case of tubulointerstitial nephritis associated with uveitis (TINU) syndrome associated with Epstein-Barr virus, which presented aggressive bilateral uveitis.

**Methods.** Clinical evaluation, serologic testing, and renal biopsy were performed on a 16 year-old boy who presented with bilateral visual loss and constitutional symptoms.

**Results.** Slit lamp biomicroscopy revealed bilateral anterior uveitis with posterior synechiae in both eyes. He was commenced on topical and systemic corticoid treatment. Systemic evaluation revealed renal failure. Renal biopsy confirmed the diagnosis of TINU syndrome. IgM serology was positive for Epstein-Barr virus. While the renal response was good, the uveitis required immunosuppression which resulted in resolution.

**Conclusions.** There have been only 3 previously reported cases of TINU syndrome associated with acute Epstein-Barr infection. In TINU syndrome, it has been reported that microorganisms may act as triggers of the disease in patients who are genetically predisposed. TINU syndrome should be considered in the differential diagnosis of uveitis with constitutional symptoms.

## Introduction

Tubulointerstitial nephritis associated with uveitis (TINU) syndrome is a rare syndrome of unknown etiology that affects young patients, with a median age of 15 years at the time of presentation, and affects women three times more frequently than men.[1] It has been reported that there are only approximately 300 cases published in the medical literature since the first report in 1975.[2] Systemic symptoms usually appear as fatigue, weight loss and fever, typically followed by ocular involvement (65%). Upon examination, patients often have bilateral anterior uveitis (77%) that may precede or follow simultaneous renal pathology.[1] The renal prognosis is excellent because nephritis tends to be self-limiting, whereas the uveitis may become chronic or recurrent.[3]

## Case Report

A 16-year-old African boy was referred to our department for loss of visual acuity, photophobia and pain in both eyes, accompanied with constitutional symptoms. Examination revealed a visual acuity of 20/50 in the right eye and hand motions in the left eye. Slit lamp biomicroscopy revealed the presence of bilateral anterior non-granulomatous uveitis with

Correspondence:
Juan Ibáñez Alperte, MD, PhD
Department of Ophthalmology
"Lozano Blesa" University Clinic Hospital
San Juan Bosco 15, ES-50009 Zaragoza, Spain
Email: juanibanezalperte@msn.com
Phone: +34 665802084

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posterior synechiae (Figure 1). He was started on topical prednisolone, topical cyclopentolate, and oral prednisone.

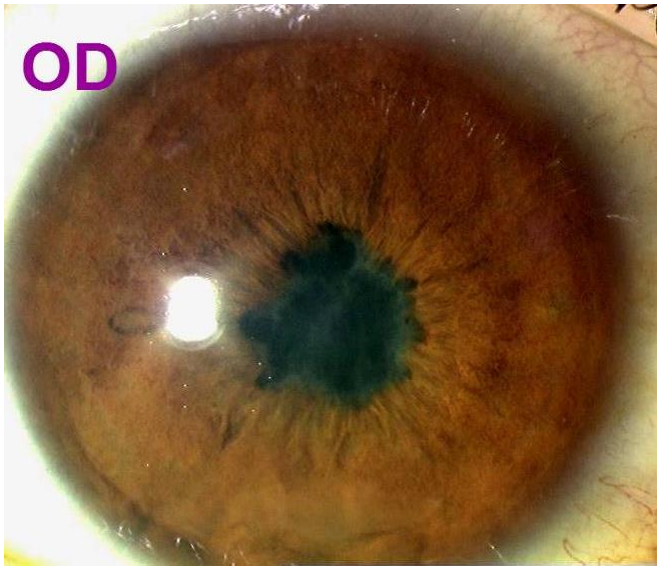


**Figure 1**
*Slit-lamp examination of the right eye with an anterior non-granulomatous uveitis demonstrates extensive posterior synechiae.*

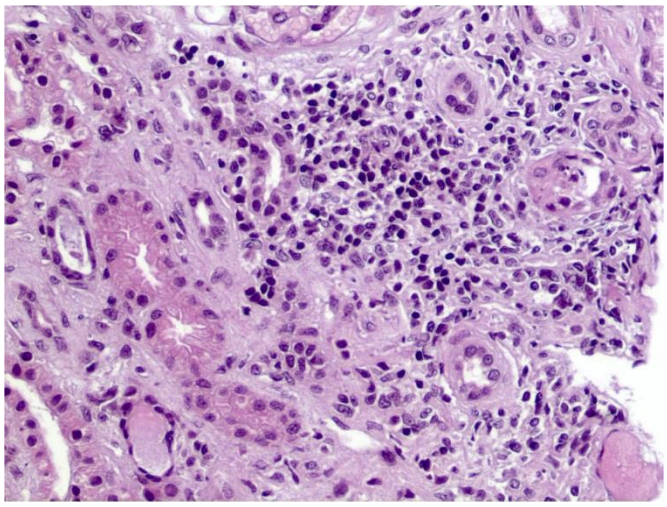

**Figure 2**
*Renal biopsy demonstrates interstitial inflammatory infiltration without glomerular involvement.*

Upon systemic evaluation, renal function studies disclosed glucosuria and proteinuria, as well as marked decreases in creatinine clearance and urea. IgM serology was positive for Epstein-Barr virus. Given the evidence of concomitant renal failure with bilateral anterior uveitis and our suspicion of a systemic syndrome involving the eye and kidney, we requested a percutaneous renal biopsy. The results revealed acute tubulointerstitial nephritis (Figure 2).

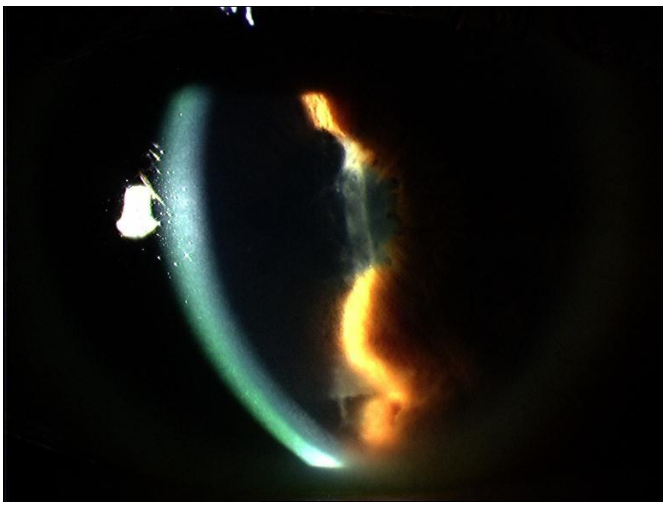

**Figure 3**
*A YAG-laser iridotomy was performed as seen in this slit-lamp biomicroscopic image, which also reveals the pupillary seclusion.*

Within weeks of initiation of the topical and systemic corticosteroid therapy, the uveitis resolved as did the renal dysfunction; however, the patient demonstrated persistent irido-lens-synechiae, for which a YAG-laser iridotomy was performed in both eyes (Figure 3). Cataract formation developed and six months after the initial presentation, the patient underwent therapeutic phacoemulsification of the lens with intraocular lens placement in both eyes. There were no postoperative complications. Currently, at the time of publication, the patient remains asymptomatic with visual acuity of 20/25 in each eye.

## Discussion

TINU syndrome is a rare but well-documented disease. Ocular and kidney manifestations do not

always coincide in time; moreover, not all reported cases present with obvious impairment of renal function: for example, only 25% of the patients in one small reported series of patients showed an increase in serum creatinine.[4]

The diagnosis is one of exclusion; acute tubulointerstitial nephritis can be caused by a reaction to drugs, an infection, or accompanying systemic disease.[5] In TINU syndrome, it has been reported that microorganisms may act as triggers of the disease in patients who are genetically predisposed. In a computerized search utilizing the online bibliographic database of the U.S. National Library of Medicine and in the referenced literature, we found only 3 cases of TINU syndrome associated with acute Epstein-Barr infection. In the first reported case, the presence of antigens against the Epstein-Barr virus was found in a young child with classic symptoms of infectious mononucleosis.[6] Though our patient did not present with the lymphadenopathy and atypical lymphocytosis associated with acute Epstein-Barr infection, the second reported case, of a 48 year-old woman, also presented Epstein-Barr IgM antibodies with the classic symptoms of infectious mononucleosis.[7] The third reported case was also of an older patient, a 43 year-old man, who also demonstrated hepatitis and interstitial pneumonitis, though his Epstein-Barr infection was chronic active disease.[8]

Ocular involvement is usually limited to the anterior segment in the form of non-granulomatous uveitis but can also affect the vitreous, with posterior uveitis; the retina, with macular edema, choroiditis, and/or choroidal neovascularization; and, the optic nerve, with optic disc swelling and/or glaucoma.[1,2,9]

Because our patient did not present until the uveitis was highly progressed, he did not receive early medical treatment. One is therefore left to wonder whether his presentation would be the natural evolution of the disease if it were left to its natural course. The renal involvement tends to resolve spontaneously without sequelae, but the uveitis in some patients may relapse with exacerbations and remissions.[1] In such cases, the use of topical and/or systemic corticosteroids or even immunosuppression may be required to control inflammation.[9] In our case, topical and systemic steroids were needed for resolution.

We emphasize the importance of early diagnosis of TINU syndrome. The presence of uveitis with systemic constitutional symptoms should raise the suspicion and renal function should be evaluated. TINU syndrome should be considered in the differential of a pediatric patient with uveitis and renal disease, along with the following other diagnoses that also may demonstrate combined renal involvement and uveitis: juvenile idiopathic arthritis, sarcoidosis, Wegener granulomatosis, systemic lupus erythematosus, IgA nephropathy, Sjogren syndrome, Adamantiades-Behcet disease, poststreptococcal glomerulopheritis, syphilis, tuberculosis, brucellosis, leptospirosis, and viral epidemic nephropathy.[2,9]

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