Tubulointerstitial nephritis and uveitis: The first report from the ophthalmology perspective in India

Gazal Patnaik, Parthopratim Dutta Majumder[1], Jyotirmay Biswas[2]

A 16-year-old boy presented with uveitis in both eyes with recurrent febrile illness and renal ailments. The patient was referred to a nephrologist. Subsequent investigations revealed acute tubulointerstitial nephritis in a renal biopsy and raised urinary beta-2 microglobulin (B2M). Based on his clinical findings and laboratory investigations, a diagnosis of tubulointerstitial nephritis and uveitis (TINU) syndrome was made. Since, the literature on TINU through India is sparse, the two available case reports were published through nephrology setup. Our case illustrates how ophthalmologist can aid in the diagnosis of such a rare clinical entity using interdisciplinary approach.

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_1461_19

Departments of Uvea and Medical Retina, [1]Uvea and [2]Uvea and Ocular Pathology, Medical and Vision Research Foundations, Sankara Nethralaya, Chennai, Tamil Nadu, India

Correspondence to: Dr. Jyotirmay Biswas, Department of Uvea and Ocular Pathology, Sankara Nethralaya, 18, College Road, Nungambakkam, Chennai - 600 006, Tamil Nadu, India. E-mail: drjb@snmail.org

Received: 10-Aug-2019 Revision: 12-Dec-2019
Accepted: 18-Jan-2020 Published: 20-Aug-2020

Key words: Acute tubulointerstitial nephritis, immunomodulatory therapy, oculo-renal syndrome, tubulointerstitial nephritis and uveitis syndrome, urinary beta-2-microglobulin

Tubulointerstitial nephritis and uveitis (TINU) syndrome is a well-known, yet rarely reported oculo-renal inflammatory condition. The diagnosis of TINU requires a high index of suspicion and detailed clinical as well as laboratory workup. Delay in diagnosis increases ocular morbidity. Hence, early recognition of this rare syndrome is a necessity. Although 300 cases on TINU have been reported worldwide, literature from India still remains sparse. Till date, only 2 cases have been reported from India and both from nephrology setup.[1,2] The present case illustrates the role of ophthalmologist in narrowing down the diagnosis and proper management of ocular manifestations to reduce relapses and hence preserve vision.

Case Report

A 16-year-old boy presented with a history of recurrent attacks of redness, pain, and blurring of vision in both eyes for 5 months. His ocular complains preceded through a history of recurrent febrile illness which was associated with systemic hypertension. He was investigated locally for his febrile illness, which revealed elevated serum creatinine, glycosuria, and trace albuminuria. Urine culture did not yield growth of any organism and ultrasound of kidney was within normal limits. He was treated with intravenous antimicrobial agents, the details of which were not available with the patient. He had been prescribed oral prednisolone (1 mg/kg/day) along

Cite this article as: Patnaik G, Dutta Majumder P, Biswas J. Tubulointerstitial nephritis and uveitis: The first report from the ophthalmology perspective in India. Indian J Ophthalmol 2020;68:1993-5.

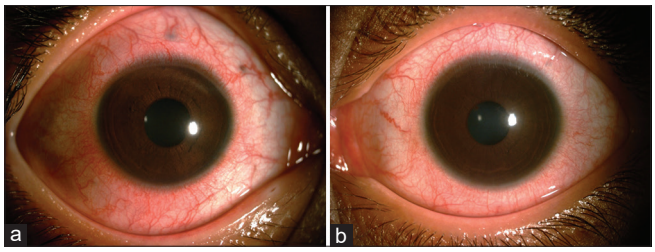

Figure 1: Slit-lamp photograph of (a) Right eye and (b) Left eye at presentation showing circumcorneal congestion and anterior segment inflammation

with topical nonsteroidal anti-inflammatory eye drops by the ophthalmologist. On presentation to us, he was afebrile, and his recent serum creatinine report was borderline (1.3 mg/dL). There was no change in subjective symptoms and his redness, ocular pain, and blurring of vision were persistent. On examination, best-corrected visual acuity (BCVA) was 20/20 in the right eye and 20/40 in the left eye. Slit-lamp evaluation of both eyes showed circumcorneal congestion, anterior chamber cells of grade 1+, flare 1+, and plenty of cells in anterior vitreous [Fig. 1].

A detailed investigation to rule out other causes of uveitis including Mantoux test and interferon-gamma release assay were normal. Based on the history of recurrent uveitis and deranged renal function, a provisional diagnosis of TINU was made. He was referred to a nephrologist and a diagnosis of acute interstitial nephritis was confirmed based on renal biopsy report [Fig. 2]. His urinary beta-2 microglobulin (B2M) was highly elevated (14646 ng/mL).[3,4] In accordance to Mandeville's proposed diagnostic criteria, he was diagnosed as definite TINU syndrome recalcitrant to oral corticosteroids.[5]

He was started on topical steroid and cycloplegic in both eyes and was advised oral mycophenolate mofetil and oral prednisolone. He showed a marked improvement in his symptoms and ocular features. After a month follow-up, there was significant improvement in his subjective symptoms and BCVA of both eyes were 20/20. Slit-lamp evaluation revealed quiet anterior chamber with a clear anterior vitreous face. Fundus examination of both eyes were normal. At present, he is under regular follow-up with us without any recurrence of ocular inflammation and his renal parameters are within normal limit.

Discussion

TINU syndrome remains largely a disease of exclusion. TINU accounts for 0.1–2% of uveitic patients seen in tertiary eye care centres in western world; however, none of such case series related to TINU have been reported from India.[6,7] Diagnosis of TINU requires high index of suspicion. In addition, ruling out other causes of inflammation involves establishing the diagnosis of acute interstitial nephritis (AIN) in uveitis. Often, this is further compounded by heterogenicity of clinical phenotypes of oculo-renal inflammation. TINU may account for 9–22% of all cases of AIN in adults.[8] In a prospective study, 84% of TINU were found to have uveitis.[9] However, there are chances that when these patients are presented to ophthalmologist, the renal parameters may all be well within normal limits. On the other hand, some uveitis labelled as idiopathic did not undergo further laboratory evaluation to

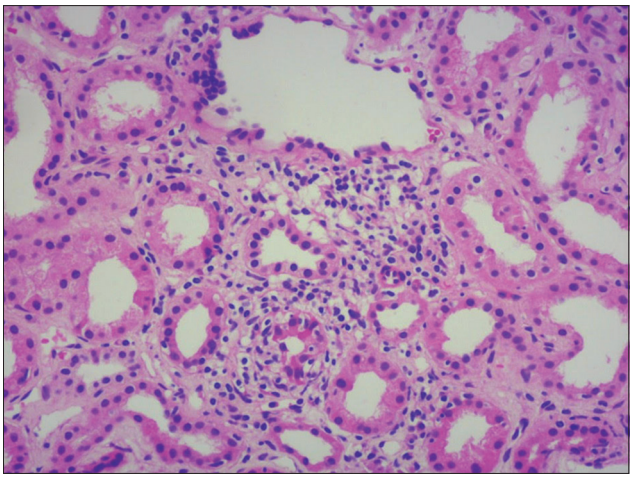

Figure 2: Microphotograph showing renal tubules with diffuse lymphocytic infiltration (hematoxylin and eosin stain, 200× magnification)

rule out or confirm this entity. Elevated urinary B2M level, a marker of interstitial nephritis, was reported in about 87% cases of TINU and hence, it has been suggested as a sensitive and specific noninvasive diagnostic test.[3] However, it is a marker of tubular injury of any etiology and not specific for TINU. It may remain elevated for months even after the urine analysis and serum creatinine has returned to normal, as was evidenced in our case[3] With steroid therapy, recovery of renal function is the rule, and relapses are infrequent but uveitis tends to persist or relapse in 50% of the TINU patients. Uveitis in the setting of TINU syndrome appears to be more persistent and troublesome than the nephritis. Immunomodulatory agents may be used when uveitis is unresponsive to systemic steroids or to reduce ocular or systemic toxicity from corticosteroids.[5] Commonly used agents include azathioprine, methotrexate, cyclosporine, and mycophenolate mofetil.[4]

The diagnosis of TINU syndrome can be a challenge especially in young patients, as symptoms are nonspecific, physical examination findings are evasive, blood and urine, and imaging tests are not always helpful. It is important to be aware of this association as diagnosis is likely to be missed in view of the temporal gap in the manifestations. Although the long-term outcomes are generally good for both eyes and kidney, ocular disease frequently determines the need for ongoing systemic therapy as this recurs in up to half of patients after corticosteroid withdrawal.[4]

Conclusion

Recurrent uveitis in presence of deranged renal parameters in adolescent and young adults warrants detailed workup along with a nephrologist and one must rule out TINU in such patients. An investigation like urinary B2M might help in diagnosis, without any need for an invasive procedure like a renal biopsy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Parameswaran S, Mittal N, Joshi K, Rathi M, Kohli HS, Jha V, *et al*. Tubulointerstitial nephritis with uveitis syndrome: A case report and review of literature. Indian J Nephrol 2010;20:103-5.
2. Ramakrishnan S, Dilip R. Syndrome of tubulointerstitial nephritis and uveitis. J Assoc Physicians 2009;57:177-9.
3. Hettinga YM, Scheerlinck LME, Lilien MR, Rothova A, de Boer JH. The value of measuring urinary β2- microglobulin and serum creatinine for detecting tubulointerstitial nephritis and uveitis syndrome in young patients with uveitis. JAMA Ophthalmol 2015;133:140-5.
4. Pakzad-Vaezi K, Pepple KL. Tubulointerstitial nephritis and uveitis. Curr Opin Ophthalmol. 2017;28:629-35.
5. Mandeville JT, Levinson RD, Holland GN. The tubulointerstitial nephritis and uveitis syndrome. Surv Ophthalmol. 2001;46:195-208.
6. Rathinam SR, Namperumalsamy P. Global variation and pattern changes in epidemiology of uveitis. Indian J Ophthalmol 2007;55:173-83.
7. Biswas J, Narain S, Das D, Ganesh SK. Pattern of uveitis in a referral uveitic clinic in India. Int Ophthalmol 1996-1997;20:223-8.
8. Su T, Gu Y, Sun P, Tang J, Wang S, Liu G, *et al*. Etiology and renal outcomes of acute tubulointerstitial nephritis: A single-center prospective cohort study in China. Nephrol Dial Transplant 2017;32:1-9.
9. Saarela V, Nuutinen M, Ala-Houhala M, Arikoski P, Ronnholm K, Jahnukainen T. Tubulointerstitial nephritis and uveitis syndrome in children: A prospective multicenter study. Ophthalmology 2013;120:1476-81.