Dobrin syndrome: A case report and review of the literature

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ABSTRACT

Dobrin syndrome or tubulointerstitial nephritis and uveitis syndrome is a rare disease with excellent prognosis. We report a 60-year-old male of Indian origin who presented with acute interstitial nephritis (AIN) and unilateral anterior immune-mediated uveitis. The syndrome has been reported sporadically. This is only the third case from a patient of Indian origin. We highlight this case and evaluate the long-term use of nonsteroidal anti-inflammatory drug-induced AIN and uveitis as a potential causative factor.

Key words: NSAID, tubulointerstitial nephritis and uveitis syndrome, unilateral

Introduction

Dobrin syndrome, named after the US physician Robert S. Dobrin, (syn. tubulointerstitial nephritis and uveitis syndrome, TINU), was first described in 1975.[1] About 200 cases have been reported worldwide, including two each from India and Saudi Arabia.[2,3] People of Japanese, European, Hispanic, Asian and African descent are the most affected. In Japan, it is the second most frequently diagnosed disease in children with uveitis after sarcoidosis.[4,5] Cases have also been reported from the U.K.[4,6] A single case have been reported from Scandinavia, while many have been reported in Germany, where population has a similar genetic background to that of Scandinavians.[4]

This syndrome has two elements: acute idiopathic tubulointerstitial nephritis and uveitis, which can occur synchronously or metachronously.[6] The majority of patients are adolescents and young women.[7,8] There is a 3:1 female predominance. Long term ophthalmic and nephrology follow-up is essential to prevent organ damage.

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Case Report

A 60-year-old male presented with blurred vision, redness, floaters and pain in the left eye. An ophthalmologist diagnosed a keyhole type pupil and anterior unilateral idiopathic uveitis. During follow-up and optical coherence tomography imaging [Figure 1], he was found to have unilateral cystoid macular edema and cotton wool spots. He was treated initially with left orbital floor injection of triamcinolone acetonide 10 mg/mL, topical dexamethasone OD for 4 weeks, and ketorolac tromethamine ophthalmic solution for 6 weeks. His vision improved considerably, but there was no improvement in the macular edema [Figure 1]. Another left orbital floor corticosteroid injection was given after 3 months, but with no improvement, after which he was commenced on high dose (1 mg/kg) of prednisolone for 4 weeks with a subsequent reducing regime over 3 months The patient was also on regular diclofenac 50/100 mg for severe knee pain for over 6 months, and calcium antagonist, esomoprozole and simvastatin.

Two weeks after starting on prednisolone, he complained of shivering, fever and sharp pain in the flank. Urine output fell, and serum creatinine rose. Laboratory assessment results are shown in Table 1. Renal ultrasound

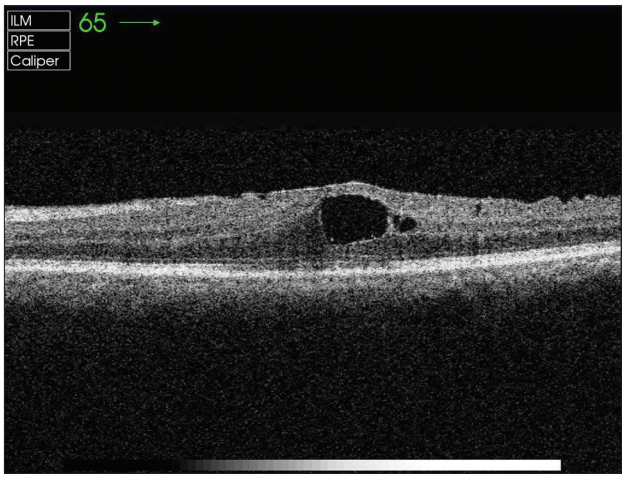

Figure 1: Optical coherence tomography image shows left eye optic swelling and cystoid macular edema – active inflammation

report showed normal sized kidneys. A kidney biopsy was performed, which showed tubulointerstitial nephritis, with no immune deposits. Oral prednisolone was continued, and diclofenac was withdrawn. There was an immediate and progressive improvement of the vision and renal function after the withdrawal of NSAID [Figure 2]. This was followed by complete resolution of the uveitis and kidney function. The renal function gradually returned to normal.

Discussion

The pathogenesis of Dobrin syndrome is not well understood. Limited evidence suggests that risk factors may include prior infection or drugs like antibiotics or NSAIDs.[9] Patients with uveitis usually present with bilateral and sometimes a unilateral alternating uveitis. Anterior uveitis is the predominant finding in the majority of cases, although a posterior uveitis can also be seen. It has been reported that uveitis occur before, concurrently, or up to 14 months after the onset of the interstitial nephritis. In majority of cases, uveitis usually presents after the silent onset of renal disease.[6,9]

It is estimated that in about 20% of patients with uveitis, intraocular complications like posterior synechiae, optic disc swelling, cystoids macular edema, chorioretinal scar formation, and later cataracts and glaucoma can develop.[7]

The diagnosis of Dobrin syndrome is suggestive of a combination of uveitis and renal involvement, with renal biopsy consistent with acute tubulointerstitial nephritis. There are no specific serum markers or laboratory findings that are unique to patients. Laboratory findings may include eosinophilia, anemia,

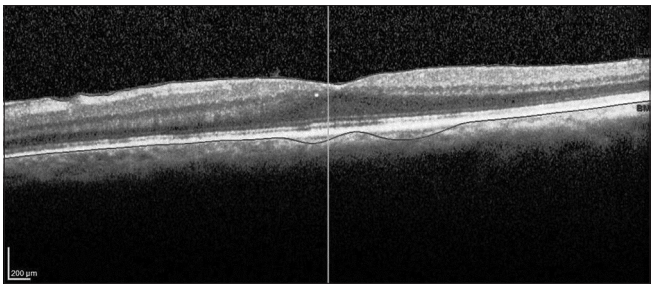

Figure 2: Optical coherence tomography image shows no evidence of active inflammation in the left eye after the withdrawal of nonsteroidal anti-inflammatory drug

Table 1: Laboratory investigations

Blood test	Results
Serum creatinine	6.5 mg/dL
Blood urea nitrogen	137.4 mg/dL
ACE	Normal
ESR	25 mm/h
Serum calcium	10.8 mg/dL
CRP	73 mg/L
Glucose (random)	259.2 mg/dL
ALT	1.71 µkat/L
Urine albumin-creatinine ratio	9 ratio
K+	3.0 mEq/L
ANA	Negative
DNA Abs	Negative
RF	Negative
VDRL	Negative
HBsAg	Negative
HCV Abs	Negative
FBC	Normal
Coagulation studies	Normal
Percutaneous left kidney renal biopsy	Tubulointerstitial nephritis with no glomerular or vascular lesions and the absence of immunoglobulin or complement deposits

ACE: Angiotensin-converting enzyme, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALT: Alanine Aminotransferase, VDRL: Venereal Disease Research Laboratory, FBC: Full blood count, ANA: Antinuclear antibody, DNA Abs: Anti-DNA antibody, RF: Rheumatoid factor, HBsAg: Hepatitis B surface antigen, HCV Abs: Anti-hepatitis C antibody

slightly abnormal liver function tests, and an elevated erythrocyte sedimentation rate, renal insufficiency or sudden ARF, multiple proximal and distal tubular defects resulting in aminoaciduria, acidification defects, glucosuria and phosphaturia.[9]

The differential diagnosis may include sarcoidosis, tuberculosis, Sjögren's syndrome, systemic lupus erythematosus, Wegener's granulomatosis and Behçet's disease. Other differentials include ocular infections associated with tuberculosis, brucellosis, toxoplasmosis, glomerulonephritis, histoplasmosis, hyperthyroidism and drug-induced interstitial nephritis in a small percent of cases.[6,10]

The distinction of Dobrin syndrome from sarcoidosis and Sjögren's syndrome may also be challenging. In addition

to uveitis and interstitial nephritis, Dobrin may also be associated with several systemic findings, including, fever, weight loss, fatigue, malaise, anorexia, arthralgia, myalgia, headache, polyuria, asthenia, abdominal and flank pain, and/or nocturia.[11,12]

There have been no definitive identified familial, genetic or geographic clustering, but in a particular published study, some HLA-DQ antigenic determinants have been associated, namely with HLA-DQA1 × 01, HLA-DQB1 × 05 and HLA-DQB1 × 01 antigens; thus, increasing the possibility of genetic risk factors.[13]

Patients with progressive renal insufficiency are typically treated with prednisone at a dose of 1 mg/kg/day for 3 to 6 months and then slowly tapered. Majority of the patients recover absolute normal renal function and sight. This regimen is similar to (but more prolonged) therapy for AIN. However, relapses are more likely to occur in Dobrin syndrome because of the potential immunologic basis of the disease.[6,11]

The acute tubulointerstitial nephritis in this case could be related to the NSAID use as well, since the condition resolved following withdrawal of the agent.

Conclusion

The renal disease in Dobrin syndrome seems to have an excellent prognosis, with complete resolution if treated early with selective corticosteroid therapy. A multidisciplinary approach is crucial for the prompt recognition, effective management and control of the disease activity and for drug regimen optimization.

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