Case Report

Syndrome of Tubulointerstitial Nephritis and Uveitis

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Abstract

We report a case of acute tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) in an elderly Indian woman. TINU is one of the rare causes of acute tubulo interstitial nephritis and is likely to be missed as there is often temporal gap between the appearance of the renal and ocular manifestations.

Introduction

Acute Interstitial Nephritis (AIN) is not an uncommon cause of acute renal failure. Drugs and infections are the most common etiological agents. Idiopathic AIN is a rare entity and has been reported in association with uveitis especially in young females. They seem to share an immunological basis. It is important to be aware of this association as it has tendency to respond to immunosuppression and the diagnosis is likely to be missed in view of the temporal gap in the manifestations. In this case report we are presenting its occurrence in an elderly woman.

Case Report

61 year old Indian woman presented in March 2007 for evaluation of elevated serum creatinine. She had history of ischemic heart disease since 10 years and was on diet control for DM since 1 year. While undergoing evaluation for headache in January 2007, she was found to have 1+ proteinuria, bland urine sediment and serum creatinine 2.4mg/dl. Serum protein electrophoresis was normal and VDRL was non reactive. She was normotensive and otherwise asymptomatic then. There was no prior regular or OTC medicine intake nor was there any preceding or associated fever or other symptoms suggestive of active infection. There was no history of anorexia or weight loss.

Evaluation in March 2007 revealed normal blood pressure and no diabetic retinopathy. Laboratory investigations showed the following results: proteinuria (1.1 gram/24 hrs), 6-8 wbc's in urine, normocytic hypochromic anemia (Hemoglobin 9.9gm/dl), elevated ESR (75mm/hour), renal failure (Serum creatinine-2.4mg/dl) and normal serum albumin (Serum Total Protein 7.9gm/dl, albumin 5gm/dl, globulin 2.9gm/dl), serum cholesterol (195 mg/dl) and normal blood sugar (101 mg/dl). Serology for Hepatitis B, Hepatitis C and HIV were negative. Chest x ray was unremarkable except for mild increase in cardiothoracic ratio. USG abdomen revealed normal sized kidneys. She underwent renal biopsy in April 2007 which, under light microscope, revealed 4 normal glomeruli and diffuse interstitial edema and inflammation; tubules and vessels were unremarkable; Immunofluorescence was negative. ANA was negative.

A diagnosis of idiopathic acute interstitial nephritis was made in the absence of preceding drug intake and definite clinical features for infection or connective tissue disease and oral Prednisolone (1mg/kg/day) was started in April 2007 (as there was unresolved, persistent renal failure over 2 months duration). Subsequently there was steady decline in serum creatinine. When serum creatinine reached 1.3mg/dl, Prednisolone was tapered over 6 weeks and stopped in June 2007.

In November 2007 she had painful red eye on the left side. Anterior nongranulomatous uveitis was diagnosed.

Fig. 1: Renal Biopsy - Light Microscopy showing significant interstitial inflammation (white arrows) Haematoxylin & Eosin stain (High power).
and she was restarted on steroid eye drops. That time, she revealed that she had a similar episode in February 2007 and ophthalmology consult records showed that she had been treated for anterior non-granulomatous uveitis in the left eye with steroid eye drops. During her last visit a month back, serum creatinine was 1.2 mg/dl, urine protein was nil and she continued to have episodes of uveitis both eyes.

DISCUSSION

TINU is a distinct entity comprising of tubulo interstitial nephritis and uveitis in the absence of systemic illness associated with either condition and is very much likely to be under diagnosed in view of asynchronous development of these two features. Tubulo interstitial nephritis and uveitis (TINU) syndrome was first described in 1975 by Dobrin in two teen aged girls. In a review of three series of TINU (cytomegalovirus, herpes zoster, Epstein–Barr virus, Toxoplasmosis), and systemic diseases (hyperthyroidism, hypoparathyroidism, rheumatoid arthritis, Juvenile Rheumatoid Arthritis, Spondyloarthopathy, Behcet’s syndrome, Reiter’s syndrome, sarcoidosis).

The main differential diagnosis is sarcoidosis. Although uveitis associated with sarcoidosis is typically granulomatous, uveitis associated with TINU is mostly non-granulomatous and frequently relapsing despite treatment with local or systemic steroids. Sarcoidosis rarely causes acute interstitial nephritis and frequently affects the lungs, whereas lung involvement has not been reported with TINU. Sjögren’s syndrome is not a differential diagnosis because patients with Sjögren’s syndrome do not develop uveitis despite having sore eyes (sicca).

The pathogenesis of TINU syndrome is not clear though immunological cause is very much likely in view of numerous CD4+ and CD8+ cells in the interstitium of renal biopsies, hypergammaglobulinemia and favorable response to steroids in some instances. Abnormalities of both humoral and cellular immunity have been reported, including antineutrophil cytoplasmic antibodies (ANCA), immune complexes in the aqueous and serum, elevated serum IgG1 and suppressed T-cell function in vivo and in vitro during remission. Various HLA associations have also been described.

Patients with progressive renal insufficiency are typically treated with prednisone at a dose of 1 mg/kg per day (typically between 40 to 60 mg/day) for three to six months (duration of therapy depending upon the response). Most patients recover normal renal function. This regimen is similar to (but more prolonged) therapy in acute interstitial nephritis. However, relapses are more likely to occur in TINU syndrome because of the potential immunological basis of the disease and the lack of a possible culprit agent. Topical and systemic steroids have been used for uveitis with success. However, recurrences and relapses of uveitis are common; infrequently, steroid-sparing immunosuppressive agents, such as Cyclosporin, methotrexate and mycophenolate mofetil are needed.

To summarize, it is better to enquire specifically for episodes of uveitis in any patient presenting with unexplained acute interstitial nephritis.

REFERENCES


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