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Polyuric Kidneys and Uveitis: An Oculorenal Syndrome

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: Female, 32
Final Diagnosis: Nephrogenic diabetes inspidus secondary to tubulointerstitial nephritis and uveitis (TINU) syndrome
Symptoms: —
Medication: —
Clinical Procedure: Kidney biopsy
Specialty: Nephrology

Objective: Rare disease

Background: Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) is a diagnosis of exclusion based on the presence of uveitis and acute tubulointerstitial nephritis in the absence of other disease entities known to cause both of these disorders. The proximal tubule is frequently affected by this syndrome, resulting in a wide range of presentations that vary from proteinuria to full picture of Fanconi syndrome. However, distal tubular involvement is not common.

Case Report: A 32-year-old female patient presented with polyuria, polydipsia and painful red eyes. Her water deprivation test and desmopressin test results were consistent with nephrogenic diabetes insipidus. Her kidney biopsy showed acute tubulointerstitial nephritis. Her eye exam was consistent with uveitis. To our knowledge, this is the first reported case of nephrogenic diabetes insipidus due to tubulointerstitial nephritis and uveitis syndrome.

Conclusions: Tubulointerstitial nephritis and uveitis syndrome (TINU) syndrome can present with multiple renal tubular defects, including nephrogenic diabetes insipidus.

MeSH Keywords: Acidosis, Renal Tubular • Diabetes Insipidus, Nephrogenic • Nephritis, Interstitial

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/892060

Background

Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) is a diagnosis of exclusion, based on the presence of clinical and histological evidence of tubulointerstitial process in addition to the presence of eye symptoms, provided that other diseases are excluded.

TINU syndrome has a wide range of renal manifestations, ranging from asymptomatic pyuria to multiple renal tubular defects. Eye manifestations include blurred vision, photophobia, foreign body sensation, floaters, itching dry eyes, and superficial keratitis.

Case Report

A 32-year-old African-American female presented to the emergency department with a 2-month history of polyuria, polydipsia, and generalized weakness. She also complained of pain and watering in both eyes that started 1 week after the onset of polyuria. Her past medical history was significant for Graves' disease, for which she had a subtotal thyroidectomy 3 years prior to her presentation. Her only home medication was levothyroxine 100 Mcg daily. There was no family history of polyuria or renal diseases. She denied any tobacco, alcohol, or recreational drug use.

On presentation, the patient had a heart rate of 90 beats per min, a blood pressure of 135/77 mm Hg, a respiratory rate of 16 breaths per min, and a temperature of 98.2°F. Slit lamp examination showed ocular keratic precipitates and flare and leukocytes in anterior chambers bilaterally. The remainder of the physical examination was unremarkable.

Table 1. Laboratory findings at presentation and 8 weeks after treatment with prednisone.

	At presentation	After treatment
Sodium (mMol/L)	140	138
Potassium (mMol/L)	3.3	3.9
Carbon dioxide (mMol/L)	18	23
Chloride (mMol/L)	111	101
Blood urea nitrogen (mg/dl)	18	13
Creatinine (mg/dl)	2.2	1.3
Urine PH	7	5
Urine osmolality (mosm/kg)	119	325
Thyroid stimulating hormone mIU/L	2	

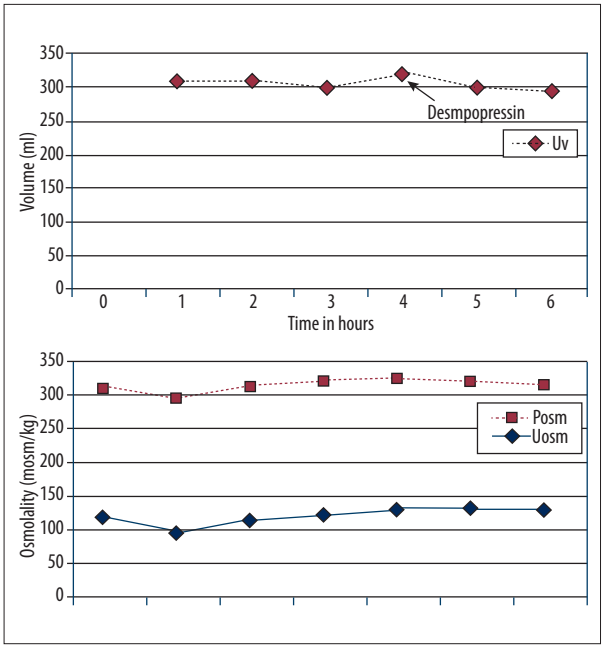

Figure 1. Water deprivation test followed by desmopressin challenge with hourly measurements of urine osmolality (Uosm), plasma osmolality (Posm) and urine volume (Uv). There are no significant changes in Uosm and Uv after water deprivation or desmopressin administration, consistent with nephrogenic diabetes insipidus.

Her pertinent laboratory studies showed a moderate degree of acute kidney injury with metabolic acidosis and hypokalemia (Table 1). Her 24-h urine output was 6.5 liters with a urine analysis showing pH 7.0, specific gravity 1.002, and a white cell count 9/high power field, but no glucosuria, proteinuria, or hematuria. Her urine culture showed no growth of bacteria. Urine anion gap was +21 mEq/L (Urine Na, K, and Cl were 43, 5, and 27 mEq/L, respectively), indicating a low urinary ammonium concentration due to renal tubular acidosis. Serological work-up including complements, anti-nuclear antibodies, anti-double-stranded DNA, and anti-neutrophil cytoplasmic antibodies, were all within normal limits. Renal sonographic examination showed normal-sized kidneys without hydronephrosis or masses. Chest radiography was normal.

Discussion

Because of her polyuria and polydipsia, we performed a water deprivation test followed by a desmopressin challenge (4 mcg, intravenously). As shown in Figure 1, she continued to produce a high volume of urine during the testing period, and

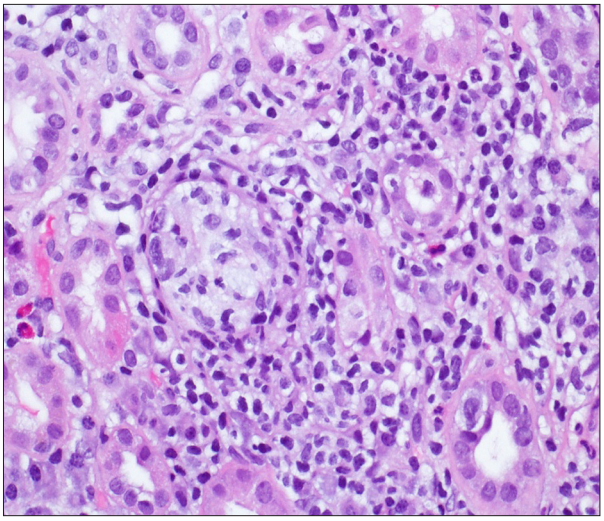

Figure 2. Renal biopsy (light microscopy – hematoxylin and eosin stain, 400× magnification). Interstitial inflammation (predominantly mononuclear) is present and focally dense. Several tubules show marked infiltration by inflammatory cells and epithelial cell injury.

her urine osmolality was unaffected by water deprivation or desmopressin treatment. These findings are consistent with nephrogenic diabetes insipidus.

Our patient had multiple renal manifestations – acute kidney injury with a high urine output due to nephrogenic diabetes insipidus. In addition, she had distal renal tubular acidosis, which accounts for the hypokalemia, metabolic acidosis, positive urine anion gap, and inability to acidify urine (her urine pH was 7 in the presence of metabolic acidosis). The multiple renal tubular defects together with a sterile pyuria suggest a renal tubulointerstitial disease. The absence of proteinuria or hematuria essentially eliminated glomerular involvement. A renal biopsy was performed and demonstrated marked tubulitis with inflammatory cells and injured epithelial cells inside renal tubules (arrow in Figure 2) and patchy interstitial infiltration of mononuclear cells (Figure 2).

Our patient developed bilateral anterior uveitis a week after her renal symptoms, the so-called "oculorenal syndrome". The differential diagnoses included systemic lupus, Sjögren syndrome, sarcoidosis, granulomatosis with polyangiitis, Behçet's disease, and infections including tuberculosis, toxocariasis, and toxoplasmosis, and tubulointerstitial nephritis and uveitis syndrome [1]. Our patient did not have joint or skin involvement, and serology studies were negative for lupus. She did not have dry eyes or mouth, and thus was unlikely to have Sjögren syndrome. She did not have hypercalcemia, renal stones, or abnormal chest radiography, which ruled out sarcoidosis. Given no sinus or pulmonary symptoms and negative anti-neutrophil cytoplasmic antibodies, granulomatosis with polyangiitis was unlikely. Behçet's disease was unlikely because she did not have genital aphthae, skin lesion, arthritis, or neurological disorders. Lastly, she did not have any symptoms or signs of the above-mentioned infections sufficient to cause oculorenal syndrome. By exclusion, we diagnosed her as having tubulointerstitial nephritis and uveitis syndrome.

This syndrome was first described as a distinct entity by Dobrin et al. in 1975 [2]. It mainly affects young females, with a median age of onset at 15 years. Uveitis frequently occurs after the onset of tubulointerstitial nephritis, but can occur prior to renal symptoms. Currently, the pathogenesis of tubulointerstitial nephritis and uveitis syndrome remains unclear [3]. As for renal manifestations, the most common finding is acute kidney injury, followed by proteinuria and normoglycemic glucosuria [3,4]. There are 4 published cases of Fanconi syndrome associated with tubulointerstitial nephritis and uveitis syndrome [5–8]. It appears that the proximal tubule is frequently affected by this syndrome, resulting in proteinuria and normoglycemic glucosuria, and occasionally a full-blown Fanconi syndrome with renal loss of glucose, phosphorus, bicarbonate, and amino acids. Our patient is unique because she had distal tubular dysfunction, including distal renal tubular acidosis and nephrogenic diabetes insipidus. In fact, this is the first reported case of nephrogenic diabetes insipidus due to tubulointerstitial nephritis and uveitis syndrome. Nephrogenic diabetes insipidus has been reported in other tubulointerstitial diseases, including Sjögren syndrome [9], and drug-induced acute interstitial nephritis [10,11]. The ability to produce concentrated urine depends on the countercurrent multiplier system and the responsiveness of the collecting duct to vasopressin. In the presence of tubulointerstitial nephritis, cellular damage in the collecting duct decreases responsiveness to vasopressin. Diffuse interstitial infiltration of lymphocytes in the medulla may interfere with the countercurrent multiplier system and impair urinary concentration ability.

Spontaneous remission of tubulointerstitial nephritis has been reported in children and adolescents; however, permanent renal damage may occur if the diagnosis is delayed [3,12,13]. Patients with progressive renal injury are typically treated with prednisone at a dose of 1 mg/kg per day up to 60 mg daily [14]. Depending on the response, therapy is given for 3–6 months followed with a slow taper. The early literature reports full recovery of renal function after steroid treatment, particularly in children and young adults [3,12], but a recent study on adult onset tubulointerstitial nephritis and uveitis syndrome reveals that 80% of patients developed chronic kidney stage 3 and 4 by 1 year after the diagnosis [13]. Mycophenolate mofetil [14] or cyclophosphamide [13] has been used for patients who are steroid resistant or dependent, with variable outcomes. Uveitis also responds well to steroid, but relapse is common [3]. The course of the renal disease appears to be independent from that of the ocular condition.

Our patient was started on oral prednisone 60 mg daily and tapered over a period of 6 months. Following 8 weeks of steroid therapy, the patient's uveitis resolved. Her glomerular filtration rate improved, and hypokalemia and metabolic acidosis resolved with restoration of her urinary acidification (urine pH 5.0) and concentration (urine osmolality 325 mOsm/kg) abilities (Table 1). These results further confirm that her distal renal tubular acidosis and nephrogenic diabetes insipidus were induced by tubulointerstitial nephritis. Nine months after her initial presentation, she showed no recurrence of uveitis or tubulointerstitial nephritis.

Conclusions

Tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) can present with multiple renal tubular defects, including nephrogenic diabetes insipidus.

Declaration of interest

The authors of this manuscript have no conflicts of interest. The authors alone are responsible for the content and writing of the paper. There was no financial support or funding for this manuscript.

References:

1. Izzedine H: Tubulointerstitial nephritis and uveitis syndrome (TINU): a step forward to understanding an elusive oculorenal syndrome. Nephrol Dial Transplant, 2008; 23(4): 1095–97
2. Dobrin RS, Vernier RL, Fish AL: Acute eosinophilic interstitial nephritis and renal failure with bone marrow-lymph node granulomas and anterior uveitis. A new syndrome. Am J Med, 1975; 59(3): 325–33
3. Mandeville JT, Levinson RD, Holland GN: The tubulointerstitial nephritis and uveitis syndrome. Surv Ophthalmol, 2001; 46(3): 195–208
4. Ren H, Wang WM, Chen XN et al. Renal involvement and followup of 130 patients with primary Sjögren's syndrome. J Rheumatol, 2008; 35(2): 278–84
5. Lessard M, Smith JD: Fanconi syndrome with uveitis in an adult woman. Am J Kidney Dis, 1989; 13(2): 158–59
6. Igarashi T, Kawato H, Kamoshita S et al: Acutetubulointerstitial nephritis with uveitis syndrome presenting as multiple tubular dysfunction including Fanconi's syndrome. Pediatr Nephrol, 1992; 6(6): 547–49
7. Koike K, Lida S, Usui M et al: Adult-onset acute tubulointerstitial nephritis and uveitis with Fanconi syndrome. Case report and review of the literature. Clin Nephrol, 2007; 67(4): 255–59
8. Yao YH, Lin CC, Chung YM et al: Tubulointerstitial nephritis and uveitis syndrome (TINU) with Fanconi's syndrome. Clin Nephrol, 2011; 75(Suppl.1): 75–78
9. Ren H, Wang WM, Chen XN et al: Renal involvement and followup of 130 patients with primary Sjögren's syndrome. J Rheumatol, 2008; 35(2): 278–84
10. Vigeral P, Kanfer A, Kenouch S et al: Nephrogenic diabetes insipidus and distal tubular acidosis in methicillin-induced interstitial nephritis. Adv Exp Med Biol, 1987; 212: 129–34
11. Quinn BP, Wall BM: Nephrogenic diabetes insipidus and tubulointerstitial nephritis during continuous therapy with rifampin. Am J Kidney Dis, 1989; 14(3): 217–20
12. Takemura T, Okada M, Hino S et al: Course and outcome of tubulointerstitial nephritis and uveitissyndrome. Am J Kidney Dis, 1999; 34(6): 1016–21
13. Li C, Su T, Chu R et al: Tubulointerstitial nephritis with uveitis in Chinese adults. Clin J Am Soc Nephrol, 2014; 9(1): 21–28
14. Clarkson MR, Giblin L, O'Connell FP et al: Acute interstitial nephritis: clinical features and response to corticosteroid therapy. Nephrol Dial Transplant, 2004; 19(11): 2778–83