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On the Cover

What's the diagnosis? A 19 year-old healthy male presented with 3 weeks of worsening bilateral red eyes, blurry vision and pain with eye movement. Ophthalmologic exam was consistent with anterior uveitis as seen on the upper panel. Oral prednisone 60 mg daily with rapid taper, and topical prednisolone and cyclopentolate eye drops were administered. Symptoms improved; however, review of lab-work obtained on initial evaluation noted serum creatinine of 3.2 mg/dl. He was admitted for further workup. Vital signs were within normal limits while physical examination revealed minimal scleral injection, but no skin rash, or joint tenderness or edema. Repeat serum creatinine measured 2 weeks later was 1.8 mg/dl and urinalysis revealed pH 7.5, +1 glucose (serum glucose 105 mg/dl), negative blood and protein with bland manual urine microscopy. Spot urine protein/creatinine ratio was 0.1 mg/mg Cr and urinary beta-2 microglobulin 8749 mcg/L (normal range 0-300). Workup was negative for the following: ANA, ENA, rheumatoid factor, ANCA, SPEP, HIV, HLA-B27, gonorrhea/ chlamydia cultures, complement levels, and ACE levels. A clinical diagnosis of tubulointerstitial nephritis and uveitis (TINU) was made. However, 2 weeks later, serum creatinine remained elevated (1.7 mg/dl) on oral prednisone 30 mg daily. Repeat urine microscopy revealed 1-2 WBC casts/LPF. Kidney biopsy revealed a lymphocyte predominant tubulointerstitial nephritis (lower panel). TINU syndrome was confirmed and oral steroids were escalated to 60 mg daily with a plan for a slower taper.

TINU is a relatively rare syndrome with only approximately 250 published cases. It can occur at any age, but is more common in adolescents. Ocular symptoms may precede, coincide, or occur up to 14 months after tubulointerstitial nephritis is noted. Fever, weight loss, fatigue, abdominal/flank pain, arthralgias, and polyuria may be seen. Uveitis is typically bilateral and manifests as painful red eyes, which may also be associated with photophobia and decreased visual acuity. Uveitis is most often anterior, but can be posterior with intraretinal hemorrhage, cotton wool spots, and retinal edema. TINU should be considered in any patient presenting with unexplained interstitial nephritis. An ocular workup is warranted if symptoms develop. Supportive laboratory data include eosinophilia, anemia, mildly abnormal LFTs, and elevated CRP. Normoglycemic glycosuria, leukocyturia, and increased urinary beta-2 microglobulin may also be seen. Typical kidney biopsy findings include interstitial edema with an inflammatory cell infiltrate composed of lymphocytes, plasma cells, histiocytes, and eosinophils. Noncaseating granulomas may also be seen. Treatment includes prednisone 1 mg/kg/day for 3-6 months (depending on renal response) with a slow taper. *Images and text provided by Barry Gorlitsky, MD; John Huang, MD; Gilbert Moeckel, MD and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut.*