



## Past Medical History

- None

## Ocular medications

- None

## Family history

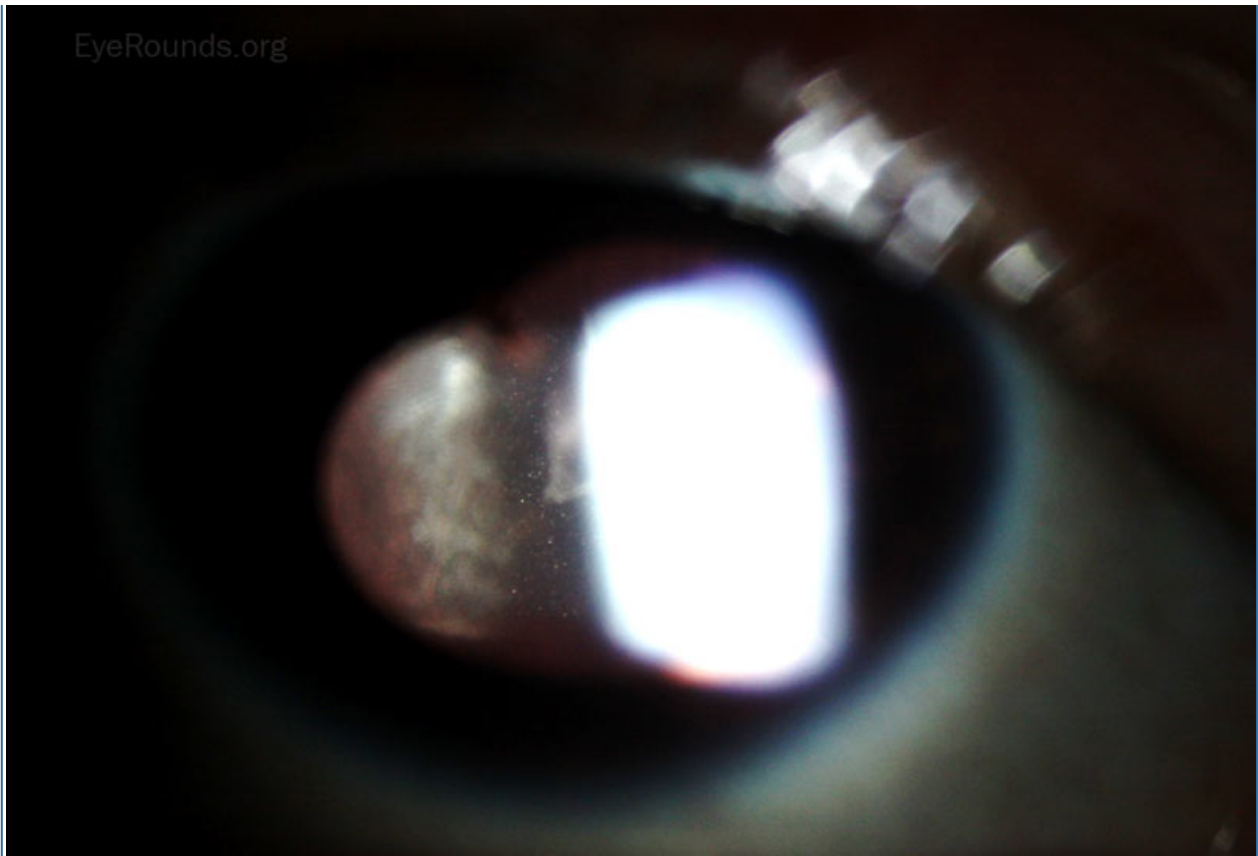
- Non-contributory

## Social History

- College student
- She lives with 15 cats and 1 dog
- Works part-time as a babysitter

## Ocular Examination

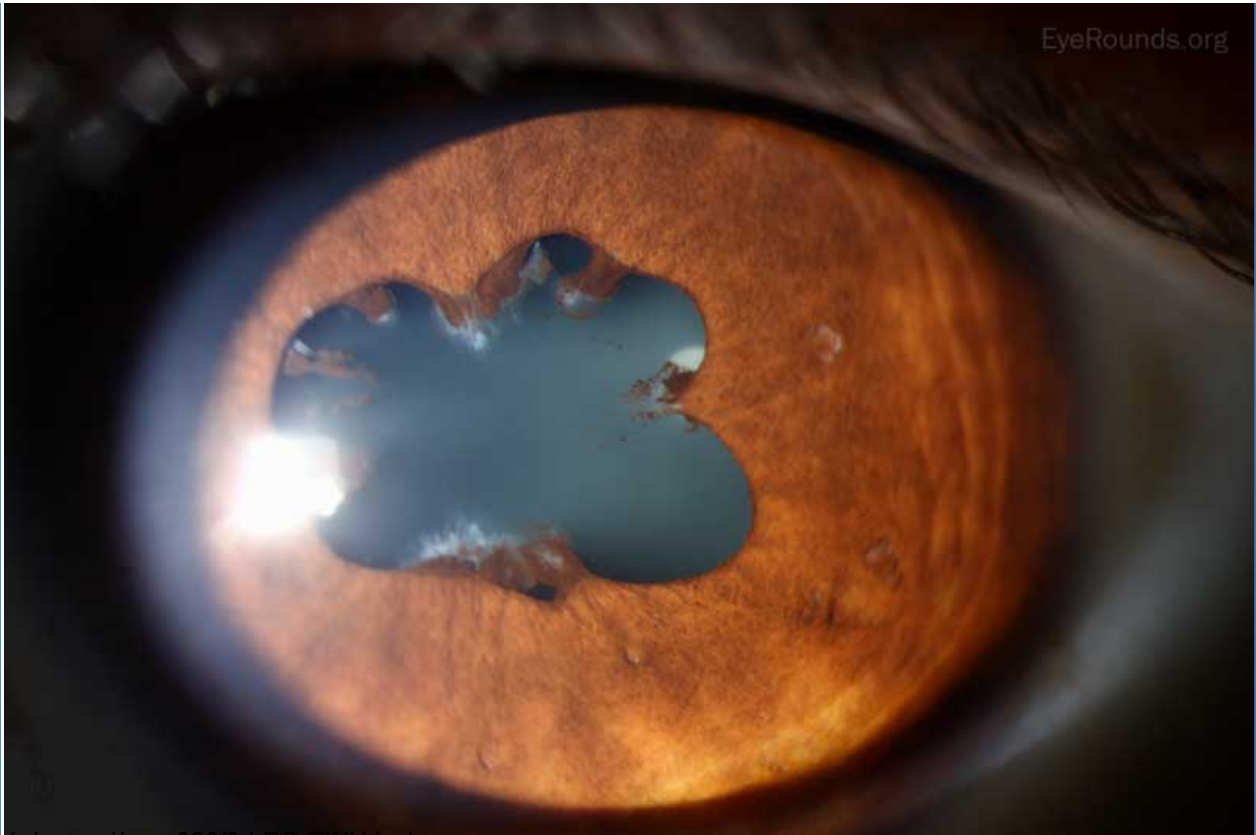
- Visual acuity without correction
  - Right eye (OD): 20/30, no improvement with pinhole testing
  - Left eye (OS): 20/25, no improvement with pinhole testing
- Intraocular pressure
  - OD: 12 mmHg
  - OS: 14 mmHg
- Ocular motility/alignment: Orthophoric in primary gaze and full motility OU
- Pupils
  - OU: Equal and briskly reactive to light; the left pupil had an irregular shape; no relative afferent pupillary defect OU
- Visual fields: Full to confrontation OU
- External: Normal OU
- Anterior segment
  - OD
    - Conjunctiva/sclera: Clear and quiet
    - Cornea: Many fine, non-mutton fat keratic precipitates centrally and inferiorly
    - Anterior chamber (AC): 2+ cell, 2+ flare [Figure 1]
    - Iris: Patchy central posterior synechia
    - Lens: Trace nuclear sclerosis with pigment flecks on the anterior capsule



(../cases-1/case226/1-LRG-T1NU.jpg)

**Figure 1: 2+ anterior chamber cell in the right eye**

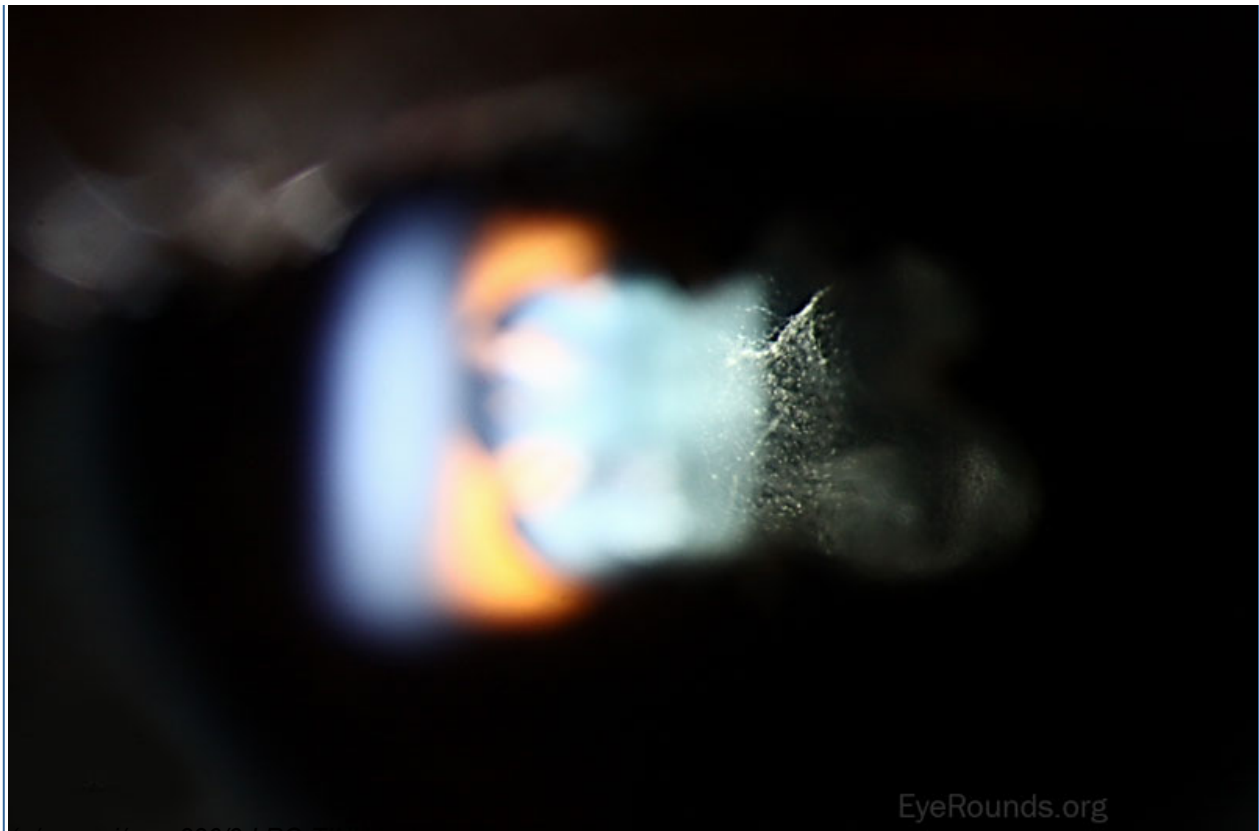
- OS
  - Conjunctiva/sclera: Clear and quiet
  - Cornea: Many fine, non-mutton fat keratic precipitates centrally and inferiorly
  - AC: 2+ cell, 2+ flare
  - Iris: Patches of central posterior synechiae for 360 degrees around the pupillary margin
  - Lens: Trace nuclear sclerosis



(../cases-1/case226/2-LRG-11NO.jpg)

**Figure 2. Patches of central posterior synechiae for 360 degrees around the pupillary margin of the left eye**

- Dilated fundus exam
  - OU
    - Vitreous: 2+ anterior vitreous cell with mild white vitreous opacities just posterior to the ora serrata
    - Optic Nerve: Normal and without edema
    - Macula: Normal contour, no cystoid macular edema
    - Vessels: Normal course and caliber without sheathing or neovascularization
    - Periphery: Normal and without lesions



(../cases-1/case226/3-LRG-TINU.jpg)

**Figure 3. 2+ anterior vitreous cell (present bilaterally)**

## Clinical Course

This young, previously healthy female had acute bilateral uveitis that was centered anteriorly, although there was prominent vitreous inflammation. We considered the following differential diagnosis.

- HLA-B27 related diseases such as ankylosing spondylitis and reactive arthritis syndrome
- Inflammatory bowel disease associated uveitis
- Psoriatic arthritis
- Tubulointerstitial nephritis and uveitis syndrome (TINU)
- Sarcoidosis
- Viral disease: Herpes simplex I&II, varicella zoster virus (VZV), cytomegalovirus (CMV)
- Syphilis
- Tuberculosis
- Lyme disease

Her laboratory studies showed a normal complete blood count. Her urinalysis demonstrated trace protein, 3+ leukocyte esterase, 8 white blood cells and 11 red blood cells. The urine protein-to-creatinine ratio was normal. Beta-2 microglobulin was elevated at 3169 and 1474, in urine and serum, respectively (normal: 0-300). Toxoplasma, bartonella, lyme, and syphilis serologies were negative. ANA and ANCA were normal. Purified protein derivative testing was non-reactive. The patient was referred to Nephrology, who performed a renal biopsy which demonstrated a focal tubulointerstitial inflammatory infiltrate containing lymphocytes and nonspecific histiocytes – confirming the diagnosis of TINU.

## Diagnosis

## DISCUSSION

Tubulointerstitial nephritis and uveitis syndrome (TINU) is a rare syndrome (less than 1-2% of all patients seen by ophthalmologists), that was first described in 1975 [1].

### Epidemiology

The true prevalence of this syndrome is unknown, likely secondary to poor recognition of the disease [2]. The largest case series review of 133 patients (as of this writing) demonstrated the median age of presentation to be between ages 14-15, with females three times more likely to have the disease compared to males [3]. There does not appear to be any racial or ethnic predilection.

### Pathology/Etiology

The precise pathophysiology is unknown, but one hypothesis describes auto-antibody formation against uveal and tubular cells from hapten-induced cytokine production to certain antibiotics and non-steroidal anti-inflammatory drugs [4]. A strong correlation between the HLA-DRB1 and HLA-DQA1 genes and biopsy-confirmed TINU syndrome has also been confirmed by independent groups [4].

### Signs/Symptoms/Testing

Patients with this disease typically present with eye redness, light sensitivity, decreased vision, new floaters, and intraocular inflammation. Patients with TINU will have elevated beta-2 microglobulin levels in their urine and serum. This should prompt referral to a nephrologist for consideration of a renal biopsy, the definitive method to diagnose TINU. Characteristic histologic findings include tubulointerstitial necrosis and/or fibrosis with preserved glomeruli, interstitial edema, and cellular infiltration of predominantly CD4-positive lymphocytes [4].

### Treatment

Ophthalmologists can manage the intraocular inflammation with topical corticosteroids (i.e., 1% prednisolone acetate) and long-acting cycloplegics (e.g., cyclopentolate, atropine); however, severe cases may necessitate the use of oral prednisone [2]. From a prognostic standpoint, patients tend to recover close to baseline visual acuity with treatment, which is typically less than one year in duration. The uveitic component of TINU can recur in up to 40% of patients, so periodic ophthalmologic monitoring is recommended; the nephritic component spontaneously resolves in most cases with a rare recurrence risk [6].

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<p><b>Epidemiology</b></p> <ul style="list-style-type: none"> <li>• Primarily affects young, female patients (median age 14-15, 3:1 female to male ratio), but has been diagnosed in adults up to age 74</li> <li>• No racial or ethnic predilection</li> <li>• Affects 1-2% of patients in specialized uveitis centers</li> <li>• Reported associations with HLA-DRB1 and HLA-DQA1</li> </ul>	<p><b>Signs/Symptoms</b></p> <ul style="list-style-type: none"> <li>• Conjunctival injection</li> <li>• Fine keratic precipitates</li> <li>• Anterior chamber cell/flare</li> <li>• Peripheral anterior synechiae</li> <li>• Central posterior synechiae</li> <li>• Anterior vitreous cell</li> <li>• Vitreous opacities</li> <li>• Cystoid macular edema</li> <li>• Epiretinal membrane</li> <li>• Decreased visual acuity</li> <li>• Photophobia</li> <li>• Floaters</li> </ul>
<p><b>Labs/Testing</b></p> <ul style="list-style-type: none"> <li>• Serum urea nitrogen and creatinine (potentially elevated if renal function is impaired)</li> <li>• Serum and urine beta-2 microglobulin (elevated)</li> <li>• Nephrology consultation for renal monitoring and biopsy to confirm tubulointerstitial involvement</li> </ul>	<p><b>Treatment</b></p> <ul style="list-style-type: none"> <li>• Topical steroids and cycloplegics</li> <li>• Oral steroids or other steroid-sparing immunomodulators may be required for severe inflammation</li> </ul>

## References

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2. Mackensen F, Smith JR, Rosenbaum JT. Enhanced recognition, treatment, and prognosis of tubulointerstitial nephritis and uveitis syndrome. *Ophthalmology* 2007;114(5):995-999. [PMID 17383731]
3. Mandeville JT, Levinson RD, Holland GN. The tubulointerstitial nephritis and uveitis syndrome. *Surv Ophthalmol* 2001;46(3):195-208. [PMID 11738428]
4. Abed L, Merouani A, Haddad E, Benoit G, Oligny LL, Sartelet H. Presence of autoantibodies against tubular and uveal cells in a patient with tubulointerstitial nephritis and uveitis (TINU) syndrome. *Nephrol Dial Transplant* 2008;23(4):1452-1455. [PMID 18156461]
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6. Takemura T, Okada M, Hino S, Fukushima K, Yamamoto S, Miyazato H, Maruyama K, Yoshioka K. Course and outcome of tubulointerstitial nephritis and uveitis syndrome. *Am J Kidney Dis* 1999;34(6):1016-1021. [PMID 10585310]

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