

ONLINE FIRST

Bilateral Simultaneous-Onset Nongranulomatous Acute Anterior Uveitis

Clinical Presentation and Etiology

Andrea D. Birnbaum, MD, PhD; Yi Jiang, MD; Roshni Vasaiwala, MD; Howard H. Tessler, MD; Debra A. Goldstein, MD

Objective: To describe the etiology and outcome of patients with simultaneous-onset nongranulomatous bilateral acute anterior uveitis.

Methods: The medical records of patients who presented to a single tertiary care center with simultaneous-onset nongranulomatous bilateral acute anterior uveitis between January 1990 and May 2010 were retrospectively reviewed; the clinical presentation, results of diagnostic testing, and outcome data are described.

Results: A total of 4288 new patients with uveitis were evaluated by the Uveitis Service at the University of Illinois at Chicago Eye and Ear Infirmary between January 1990 and May 2010. Of these new patients, 44 (1%) presented with simultaneous-onset nongranulomatous bilateral acute anterior uveitis. The most common etiologies were postinfectious or drug-induced uveitis (23 of 44 patients [52%]) and idiopathic uveitis (15 patients [34%]). Tubulointerstitial nephritis and uveitis syndrome, HLA-B27-associated uveitis, inflammatory bowel disease, and Kawasaki disease each made up fewer than 5% of diagnoses. Overall, this group of patients was

younger than the entire cohort of new patients with uveitis who were evaluated during the same time period ($P=.002$). For 14 of the 15 patients with at least a year of follow-up (93%), the disease duration was limited (<3 months). Of these 14 patients, 7 (50%) developed recurrent disease, with an average time to first recurrence of 20 months (range, 7.5-40 months) after resolution of the initial inflammatory episode.

Conclusions: Simultaneous-onset nongranulomatous bilateral acute anterior uveitis is a rare clinical entity that is more common in younger patients and is most frequently associated with recent infection and/or systemic antibiotic use. Tubulointerstitial nephritis and uveitis syndrome should also be considered as a diagnosis. Diagnostic evaluation should include serum antistreptolysin-O titers, HLA-B27 antigen, and urine β_2 microglobulin levels because these may reveal systemic disease that requires therapy.

Arch Ophthalmol. 2012;130(11):1389-1394.

Published online July 9, 2012.

doi:10.1001/archophthalmol.2012.2006

ANTERIOR UVEITIS REFERS TO inflammation located in the anterior chamber (iritis) or with associated anterior vitreous involvement (iridocyclitis), and is the most common presentation of uveitis.¹⁻³ Frequent diagnoses, aside from idiopathic disease, include HLA-B27-associated disease, Fuchs heterochromic iridocyclitis, juvenile idiopathic arthritis, and herpetic disease.¹⁻³

Acute anterior uveitis describes episodic inflammation of sudden onset and limited duration (<3 months).⁴ Patients are symptomatic, usually experiencing pain, redness, photophobia, and decreased vision. The disease typically presents unilaterally, although episodes may alternate between eyes. Less well described is acute anterior uveitis that presents with bilateral, simultaneous onset. We present data on a series of patients with

simultaneous-onset nongranulomatous bilateral acute anterior uveitis (BAAU) evaluated by the Uveitis Service at the University of Illinois at Chicago Eye and Ear Infirmary between 1990 and 2010.

METHODS

We were granted permission by the institutional review board of the University of Illinois at Chicago to retrospectively review existing medical records of patients evaluated by the Uveitis Service between January 1990 and May 2010 with a diagnosis of acute anterior uveitis. The charts of patients with acute anterior uveitis were then reviewed to identify those patients who presented with symptomatic simultaneous-onset BAAU. Patients with granulomatous inflammation (based on the presence of mutton fat keratic precipitates or granulomatous iris nodules) were excluded. To be considered symptomatic, patients had to have at least 1 ocular complaint consistent with

Author Affiliations:

Department of Ophthalmology, Northwestern University (Dr Birnbaum), Rush University Medical School (Dr Jiang), and Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago (Drs Vasaiwala, Tessler, and Goldstein), Chicago, Illinois.

acute anterior uveitis (pain, redness, or photophobia) at presentation. *Simultaneous onset* was defined as onset of symptomatic disease in the second eye within 4 weeks of the first. Patients with unilateral inflammation or bilateral anterior uveitis symptomatic in only 1 eye were excluded.

Demographic information collected included age at presentation, self-reported race, and sex. The classification of uveitis was based on the Standardization of Uveitis Nomenclature criteria.⁴ A diagnosis of postinfectious or drug-induced uveitis was made in patients who developed symptomatic inflammation in both eyes within 4 weeks of either documented systemic infection or treatment with systemic antibiotics, or in a patient with an elevated antistreptolysin-O (ASO) titer after vague systemic complaints. A diagnosis of HLA-B27-associated anterior uveitis was made for any patient who tested positive for the HLA-B27 antigen, either by serological testing or polymerase chain reaction (PCR). Tubulointerstitial nephritis and uveitis (TINU) syndrome was diagnosed in patients with elevated urine β_2 microglobulin and associated kidney dysfunction or with confirmation of diagnosis by a nephrologist.

Any patient younger than 17 years at initial presentation was considered part of the pediatric population. Comparisons between pediatric and adult patients were performed using the Fisher exact test. Additional comparisons of age at presentation were calculated using a 2-tailed *t* test. $P < .05$ was considered statistically significant.

Table 1. Demographic Distribution of Patients With BAAU

Characteristic	No. (%)		
	Nongranulomatous BAAU (n=44)	Nongranulomatous Unilateral Acute Uveitis (n=643)	All Patients Without BAAU (n=4244)
Age at presentation, y			
Mean	34	42	43
Median (range)	37 (4-81)	41 (1-91)	43 (1-93)
Female sex	28 (64)	361 (56)	2594 (61)
Racial distribution ^a	(n = 44)	(n = 633)	(n = 4184)
White	26 (59)	420 (66)	2426 (58)
African American	11 (25)	110 (17)	1090 (26)
Hispanic	4 (9)	64 (10)	462 (11)
Asian	3 (7)	39 (6)	206 (5)

Abbreviation: BAAU, bilateral acute anterior uveitis.

^aSelf-reported (based on uveitis questionnaire). Race was not reported in all patients. Patients with BAAU presented at a younger age relative to those with unilateral acute uveitis ($P = .002$) and when compared with all other patients with uveitis who were evaluated during the same time period ($P = .002$).

A total of 4288 new patients were evaluated by the Uveitis Service between January 1990 and May 2010. Acute nongranulomatous anterior uveitis was diagnosed in 687 patients (23 patients with granulomatous disease were excluded). Of these, 44 presented with simultaneous-onset nongranulomatous BAAU (1% of the total number of new patients [n=4288] and 6% of patients with nongranulomatous acute anterior uveitis [n=687]). All patients with BAAU developed symptomatic inflammation in the second eye within 7 days of the first eye; 36 patients (82%) presented with symptomatic bilateral inflammation at onset. The most common complaints at presentation included redness (38 patients [86%]), pain (35 patients [80%]), and photophobia (32 patients [73%]). Less common complaints were sudden-onset blurred vision (13 patients [30%]) and floaters (4 patients [9%]). Children younger than 17 years comprised 25% of BAAU patients (n=11), compared with 3% of all patients with unilateral acute anterior uveitis ($P < .001$) and 10% of all new patients with uveitis evaluated during the same time period ($P < .001$). Patients with BAAU were younger than the cohort of other new patients with uveitis evaluated during the same time period ($P = .002$) and the cohort of new patients with unilateral acute anterior uveitis ($P = .002$). There was no difference in age at presentation between patients with postinfectious or drug-induced uveitis and patients with other diagnoses in the BAAU cohort ($P = .74$). For all patients, BAAU was the first documented episode of ocular inflammation. Two patients reported previous episodes of bilateral anterior uveitis that had resolved in less than 3 months with topical and oral corticosteroids. For the other 42 patients, the presentation with BAAU to the Uveitis Service at the University of Illinois at Chicago Eye and Ear Infirmary represented the first episode of ocular inflammation. For all patients, follow-up time was based on the episode for which they were treated at the University of Illinois at Chicago Eye and Ear Infirmary.

Demographic data are presented in **Table 1**. Comparison data are provided for patients with unilateral nongranulomatous acute anterior uveitis and for all other patients evaluated by the Uveitis Service during the same time period. Aside from age at presentation, the demographic profiles were similar between the patients with BAAU and the patients with unilateral acute anterior uveitis.

Table 2. Results of Diagnostic Testing^a

Test	No. Positive/Total No. (%), Patients From Each Group				
	Total	Adult	Children	Postinfectious or Drug-Induced Uveitis	Idiopathic Uveitis
Angiotensin-converting enzyme	3/36 (8)	1/27 (4)	2/9 (22)	2/19 (11)	1/13 (8)
Lysozyme	2/29 (7)	1/21 (5)	1/8 (13)	2/19 (11)	0/8 (0)
Antistreptolysin-O	4/13 (31)	1/8 (13)	3/5 (60)	4/11 (36)	0/0 (0)
HLA-B27	5/34 (15)	5/30 (17)	0/4 (0)	2/17 (12)	0/12 (0)
Urine β_2 microglobulin	3/17 (18)	2/12 (17)	1/5 (20)	0/12 (0)	1/2 (50)
Chest radiography	0/33 (0)	0/25 (0)	0/8 (0)	0/17 (0)	0/12 (0)

^aAntistreptolysin-O titers were elevated in 60% of children tested, and 36% of all patients diagnosed with postinfectious or drug-induced uveitis. Three patients had elevated urine β_2 microglobulin levels; these elevated levels were associated with tubulointerstitial nephritis and uveitis syndrome in 2 patients and a kidney stone in 1 patient.

Diagnostic testing was variable, and no test result was positive for more than 30% of patients (**Table 2**). Serum angiotensin-converting enzyme was elevated in 3 of 36 patients tested (8%), and lysozyme was elevated in 2 of 29 patients tested (7%). Five of 34 patients (15%) tested were positive for HLA-B27. None of the 33 patients undergoing chest radiography had a significant finding, such as hilar lymphadenopathy, suggestive of sarcoidosis. An-

Table 3. Etiologies of Simultaneous-Onset Bilateral Acute Anterior Uveitis^a

Etiology	No. (%)		
	Total (n=44)	Adults (n=33)	Children (n=11)
Postinfectious or drug-induced uveitis	23 (52)	16 (48)	7 (64)
Postinfectious or drug-induced uveitis with HLA-B27 positivity	2 (5)	2 (6)	0 (0)
Idiopathic uveitis	15 (34)	13 (39)	2 (18)
TINU syndrome	2 (5)	1 (3)	1 (9)
TINU syndrome with HLA-B27 positivity	1 (2)	1 (3)	0 (0)
HLA-B27-associated uveitis	2 (5)	2 (6)	0 (0)
HLA-B27-associated uveitis with other diagnosis	3 (7)	3 (9)	0 (0)
Inflammatory bowel disease	1 (2)	1 (3)	0 (0)
Kawasaki disease	1 (2)	0 (0)	1 (9)

Abbreviation: TINU, tubulointerstitial nephritis and uveitis.

^aThe majority of cases were attributed to recent infection, and many patients were treated with oral antibiotics. Three of the HLA-B27-positive patients fit into other categories: 2 with postinfectious or drug-induced disease and 1 with TINU syndrome.

tistreptolysin-O titers were elevated in 4 of 13 patients tested (31%). Elevated urine β_2 microglobulin was present in 3 of 17 patients tested (18%). This test was not obtained for the 15 patients evaluated before 2004.

The etiologies of BAAU are shown in **Table 3**. The most common association was postinfectious or drug-induced uveitis (23 patients [52%]). The profile of these patients is shown in **Table 4**. Of these 23 patients, 10 (43%) had received systemic antibiotics prior to presentation, and 13 (57%) had systemic infection without antibiotic therapy. No difference was noted between adults and children ($P = .75$). Seven patients (30%) with this diagnosis had only 1 evaluation by the Uveitis Service. Two patients were positive for HLA-B27, and both had recently been treated with oral antibiotics for throat infections (1 patient with confirmed infection with group A *Streptococcus*). The median duration from the onset of illness to the onset of eye symptoms for patients with postinfectious uveitis was 7 days (range, 1-30 days). Six patients specifically recalled the onset of eye symptoms after the termination of treatment with antibiotics at a mean duration of 8.5 days (range, 4-14 days). Two patients were taking oral antibiotics when ocular symptoms began: 1 patient on the fifth day of treatment and the other on the seventh. The other 5 patients did not recall their treatment timeline.

The second most common diagnosis was idiopathic disease (15 of 44 patients [34%]). Tubulointerstitial nephritis and uveitis syndrome was diagnosed in 2 of 14 patients tested, one at 5 years of age and one at 51 years of age. Both had elevated urine β_2 microglobulin and con-

Table 4. Profile of Patients Diagnosed With Postinfectious or Drug-Induced Uveitis^a

Patient No./Sex	Age at Presentation to Uveitis Service, y	Race	Site	Antibiotics	ASO	B ₂
1/F	4	White	Cellulitis (MRSA)	Sulfamethoxazole/trimethoprim sulfate	-	-
2/F	4	White	URI	Unspecified	-	-
3/M	5	Black	URI		+	-
4/F	8	White	Throat (S)		+	-
5/M	11	Asian	Throat			
6/F	11	Hispanic	URI		+	-
7/F	16	White	Sinus			-
8/M	17	Black	Throat (S)	Penicillin	+	-
9/M	18	Hispanic	Ear	Levaquin	-	-
10/M	35	White			-	-
11/F	38	Asian			-	-
12/F	39	White			-	-
13/M	39	White	Throat (S)	Amoxicillin, erythromycin stearate		
14/F	41	White	URI		-	-
15/F	41	Hispanic				
16/M	43	White	Throat			-
17/F	43	White	Throat	Erythromycin		
18/F	55	Asian	Lung	Unspecified intravenous antibiotics	-	-
19/M	56	White				
20/F	58	White	Throat	Penicillin		
21/M	59	Black	Prostate	Sulfamethoxazole/trimethoprim		
22/M	60	White	Middle ear			
23/M	62	White	Cellulitis	Moxifloxacin	-	-

Abbreviations: ASO, antistreptolysin-O antibody; B₂, urine β_2 microglobulin; MRSA, methicillin-resistant *Staphylococcus aureus*; S, confirmed streptococcal throat infection; URI, upper respiratory tract infection; -, negative (laboratory value within the normal range); +, positive (elevated laboratory value).

^aA specific site of infection was identified in all but 5 patients (ie, patients 10, 11, 12, 15, and 19). These patients all reported generalized malaise and/or flu-like symptoms prior to the development of ocular symptoms. Ten patients also received systemic antibiotic therapy. All antibiotics were given orally, unless specified otherwise.

Table 5. Systemic Complaints of Patients at Initial Presentation to Uveitis Service

Disease	No. (%)			
	Rash	Oral Ulcers	Back Pain	Arthritis
Total (n=44)	7 (16)	7 (16)	9 (20)	3 (7)
Postinfectious or drug-induced uveitis (n=23)	2 (9)	4 (17)	6 (26)	2 (9)
Idiopathic uveitis (n=15)	3 (20)	3 (20)	3 (20)	1 (7)
TINU syndrome (n=2)	1 (50)	0 (0)	0 (0)	0 (0)
Kawasaki disease (n=1)	1 (100)	0 (0)	0 (0)	0 (0)
Inflammatory bowel disease (n=1)	0 (0)	0 (0)	0 (0)	0 (0)

Abbreviation: TINU, tubulointerstitial nephritis and uveitis.

Table 6. Disease Course in Patients With Simultaneous-Onset Nongranulomatous BAAU^a

Etiology	Patients, Total No.	Patients, No./Total No. (%)		
		Acute		
		Total	Recurrent	Chronic
All	15	14/15 (93)	7/14 (50)	1/15 (7)
Postinfectious or drug-induced uveitis	7	6/7 (86)	3/6 (50)	1/7 (14)
Idiopathic uveitis	7	7/7 (100)	3/7 (43)	0/7 (0)
HLA-B27-associated uveitis	2	2/2 (100)	1/2 (50)	0/2 (0)

Abbreviation: BAAU, bilateral acute anterior uveitis.

^aFifteen patients had at least 1 year of follow-up, and only one of these patients had chronic disease. Of the patients whose disease was initially acute in duration, 50% subsequently developed recurrences of inflammation between 7.5 to 40 months after resolution of first episode.

firmation of diagnosis by a nephrologist. One patient with TINU syndrome tested positive for HLA-B27. Kawasaki disease and inflammatory bowel disease were each diagnosed in 1 patient, and both of these patients had been referred with the diagnosis.

Systemic symptoms at presentation are shown in **Table 5**. The most common complaint was back pain, which was present in 9 of 44 patients with BAAU (20%) and 6 of 23 patients with postinfectious or drug-induced uveitis (26%). Of the 44 patients with BAAU, 8 (18%) had a history of oral ulcers, and 7 (16%) had a recent rash. Only 3 of the 44 patients (7%) reported arthritis or joint pain, 2 of whom were diagnosed with postinfectious or drug-induced uveitis.

Fifteen patients had at least 1 year of follow-up, with a mean follow-up time of 33.5 months (range, 12-67 months) (**Table 6**). Of these 15 patients, 14 (93%) had acute disease that resolved within 3 months, and 1 (7%) had chronic disease with ultimate resolution by 6 months. Of the 14 patients with acute disease and at least a year of follow-up, 7 (50%) developed recurrent inflammation. The second episode of inflammation was bilateral in 6 of the 7 patients and occurred, on average, 20 months (range, 5-49 months) after resolution of the initial episode. Finally, 9 of the patients had more than 2 years of follow-up (range, 24-67 months). None had active chronic disease. Four of the 8 patients with acute disease (50%) developed a recurrent but limited episode of inflammation.

COMMENT

Nongranulomatous acute anterior uveitis with bilateral simultaneous onset is a rare presentation of ocular in-

flammation, even at our tertiary referral service. In this series, it comprised 44 of 4288 new patients with uveitis (1%), which was only 6% of the 687 new patients with nongranulomatous acute anterior uveitis. Other series⁵⁻⁷ have reported somewhat higher percentages of simultaneous-onset BAAU. In one study⁵ from the United States, 4% of all patients with uveitis had this presentation, although this study⁵ included patients who developed bilateral involvement within 16 weeks of initial onset of unilateral inflammation vs 4 weeks in our study. In Turkey, simultaneous-onset BAAU was reported in 7% of patients who tested positive for HLA-B27 and in 26% of patients who tested negative.⁶ This patient population was different, however, because only those retrospectively determined to have iridocyclitis of sudden onset and limited duration were included in the study,⁶ whereas our series included patients with uveitis of both limited and persistent duration. Finally, a study⁷ of patients with uveitis in Spain reported 2.7% of patients with this presentation (ie, BAAU), which is similar to that reported in our study.

More than half (52%) of the patients in this series were diagnosed with postinfectious or drug-induced anterior uveitis. Within the spectrum of postinfectious disease is the clinical entity poststreptococcal syndrome uveitis. First described in 1991, the syndrome is common in younger patients (<40 years) and usually presents 1 to 6 weeks after onset of systemic symptoms.⁸ The disease is typically bilateral and associated with elevated serum ASO titers in more than 95% of cases.⁸ Titers are normally elevated 1 week after infection with group A *Streptococcus* and peak between 3 to 6 weeks. A decrease begins after 6 to 8 weeks, but some patients maintain elevated levels for longer periods of time.⁹ Posterior segment involve-

ment has been described, including vitritis, vascular sheathing, and retinitis.¹⁰ Interestingly, approximately 12% of patients deny a preceding systemic illness.⁸ In this series, patients without systemic complaints did not have ASO titers measured; therefore, this condition may have been underdiagnosed. Also, cutaneous streptococcal infection is not always associated with increased ASO titers.¹¹ One patient with postinfectious or drug-induced uveitis in our series had a history of cellulitis and normal ASO titers. This patient may, in fact, have had recent streptococcal skin infection without an increase in ASO titers.

Postinfectious uveitis is not limited to anterior segment inflammation, as was shown in a series of patients with poststreptococcal inflammation.¹⁰ Frosted branch angiitis is a type of retinal vasculitis that is often associated with inflammation in the anterior segment and vitreous. Much like the patients with postinfectious or drug-induced BAAU in our study, the condition is often bilateral (75% of patients) and may be preceded by a systemic illness.¹²

Simultaneous-onset nongranulomatous BAAU was more common in young patients in our series. The younger age cannot be attributed entirely to a presumed increased risk of infection associated with the immature immune systems of younger patients leading to a predominance of postinfectious or drug-induced uveitis. The ages at presentation between the group of patients with postinfectious or drug-induced uveitis and the group of patients with BAAU were not different. However, as stated previously, our results may underestimate cases of postinfectious or drug-induced disease because ASO titers were not obtained for patients who did not present with a history of a recent infection. Perhaps more of the younger patients had a preceding subclinical infection.

The HLA-B27 allele is present in approximately 50% of patients with acute anterior uveitis.^{13,14} HLA-B27-associated uveitis is most often characterized by recurrent anterior ocular inflammation in one eye at a time. Bilateral simultaneous disease is much less common and behaves differently from unilateral disease, with fewer recurrences.¹⁵ In our series, HLA-B27 was not a common etiology of BAAU; only 5 of 35 patients tested (14%) were positive for the allele. Two of these patients had postinfectious or drug-induced uveitis, and one was classified as having TINU syndrome. It is possible that this association occurred by chance because approximately 8% of whites and 2% of African Americans are positive for HLA-B27.^{16,17} However, bacterial infection is known to be a trigger for acute anterior uveitis in patients with the HLA-B27 allele. Antibodies targeting endotoxin lipopolysaccharides of gram-negative bacteria have been found to be elevated in patients positive for HLA-B27 during their first attack of anterior acute uveitis, relative to levels during relapses.¹⁵ Patients with bilateral disease had higher antibody levels but lower recurrence rates than patients with unilateral disease.¹⁸ This is in keeping with our finding that the HLA-B27-positive patient with acute disease and 15 months of follow-up did not have a relapse. Also, endotoxin-induced uveitis, characterized by transient bilateral anterior segment inflammation, is a disease that was originally described in an animal model after injection of

lipopolysaccharides or endotoxin of gram-negative bacteria into foot pads of rats.¹⁸ The similarity in presentation (bilateral acute inflammation with eventual resolution) may suggest a similar triggering mechanism to what is seen clinically in HLA-B27-positive patients.

Of the 15 patients with more than a year of follow-up, 14 (93%) had a disease course of limited duration. Of these 14 patients, 7 (50%) developed recurrent acute disease. With longer clinical follow-up, the number of patients with recurrent disease would likely have increased. However, the real rate of recurrence may be much lower than ascertained because many patients with acute disease (sudden onset, limited duration) did not come for follow-up after disease resolution. This may be because they had no further episodes. Depending on the outcomes of the patients who did not return for follow-up, the true recurrence rate could be anywhere from 26% (10 of 39 patients) to 82% (32 of 39 patients). The actual recurrence rate for patients with BAAU would thus be better assessed in a prospective fashion. In our study, patients with bilateral inflammation tended to have a recurrence of disease at approximately 20 months, similar to or slightly earlier than reported in a series¹⁹ of patients with acute anterior uveitis, with a median time to first recurrence of 24 months. This same study¹⁹ also reported a significant decrease in time to first recurrence for patients with bilateral disease.

A diagnosis of TINU syndrome was made for 2 patients. First described in 1975,²⁰ TINU syndrome is a rare cause of uveitis originally thought to be more common in young women,²⁰ with a more recent series reporting an equal sex distribution or even a preponderance of male patients.²¹ Urine β_2 microglobulin is often used as a screening test and was elevated in 11 of 12 patients in a series of patients with biopsy-confirmed TINU syndrome.²² HLA-DRB1*0102 has also been associated with TINU syndrome,²³ and the allele may be an independent risk factor for simultaneous-onset BAAU.⁵ This marker was not tested for in our series.

Although TINU syndrome is a diagnosis of exclusion, diagnostic criteria have been proposed.^{20,22} A series by Mackensen et al²¹ from a tertiary referral center identified TINU syndrome in 1.7% of all new uveitis referrals and 10% of patients presenting with BAAU. A subgroup analysis on patients 20 years of age or younger identified TINU syndrome in 32% of them.²¹ These rates are higher than reported in the present study. However, only 40% of our patients underwent urine analysis for β_2 microglobulin, and we suspect that TINU syndrome may have been underdiagnosed. Three of the 17 patients tested had elevated urine β_2 microglobulin levels. One of these patients was presumed to have an elevated level owing to a kidney stone. The other 2 patients had confirmation of the diagnosis of TINU syndrome by a nephrologist, resulting in a diagnosis of TINU syndrome in 12% of the tested patients with BAAU, similar to the rate reported by Mackensen et al.²¹

Tubulointerstitial nephritis and uveitis syndrome is associated with the use of numerous systemic drugs. In one review of TINU syndrome,¹⁷ 24% of cases occurred in patients after antibiotic use, often to treat respiratory infections, and 18% of patients reported recent use of a non-

steroidal anti-inflammatory drug. A spectrum of postinfectious and drug-induced uveitis may therefore exist that includes postinfectious or drug-induced uveitis without renal disease and TINU syndrome. In our study, the use of systemic nonsteroidal anti-inflammatory drugs prior to presentation was not documented. However, in light of their possible role as a trigger for inflammation, we now ask all uveitis patients about recent use of systemic nonsteroidal anti-inflammatory drugs.

The other diagnoses in this series were inflammatory bowel disease and Kawasaki disease, and both were diagnosed prior to the onset of uveitis. Up to 14% of patients with inflammatory bowel disease develop ocular inflammation,²⁰ but, unlike the patient in our study, the most common presentation is chronic anterior uveitis. Kawasaki disease is a known cause of BAAU. One study²⁴ reported that 66% of children with Kawasaki disease developed anterior uveitis; 97% of them had bilateral disease. This type of systemic vasculitis typically presents with high fevers and a red tongue, which has been coined "strawberry tongue."²⁴ Patients with this presentation should be referred for immediate care to decrease the risk of coronary artery aneurysm.

In summary, symptomatic BAAU is an unusual presentation of uveitis that is more common in young patients. It must be distinguished from the insidious onset of anterior uveitis seen in children with juvenile idiopathic arthritis. Obtaining a detailed and thorough history, including queries regarding recent infection and use of systemic antibiotics or nonsteroidal anti-inflammatory drugs, may help elucidate a diagnosis. A complete review of systems, specifically focusing on possible systemic infection, gastrointestinal dysfunction, or signs of systemic vasculitis in a child, should be included. Diagnoses to consider include postinfectious or drug-induced uveitis and TINU syndrome. Diagnostic testing should include urine β_2 microglobulin testing, HLA-B27 antigen testing, and ASO titers. Making an appropriate diagnosis is important in these young patients because each disease has its own set of associated systemic implications.

Submitted for Publication: February 21, 2012; final revision received April 24, 2012; accepted May 1, 2012.

Published Online: July 9, 2012. doi:10.1001/archophthalmol.2012.2006

Correspondence: Debra A. Goldstein, MD, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, 1855 W Taylor St, Chicago, IL 60612 (debgold@uic.edu).

Financial Disclosure: None reported.

Funding/Support: This work was supported by an unrestricted grant from Research to Prevent Blindness, New York, New York (to Dr Goldstein).

- McCannel CA, Holland GN, Helm CJ, Cornell PJ, Winston JV, Rimmer TG; UCLA Community-Based Uveitis Study Group. Causes of the general practice of ophthalmology. *Am J Ophthalmol*. 1996;121(1):35-46.
- Suhler EB, Lloyd MJ, Choi D, Rosenbaum JT, Austin DF. Incidence and prevalence of uveitis in Veterans Affairs Medical Centers of the Pacific Northwest. *Am J Ophthalmol*. 2008;146(6):890.e8-896.e8.
- Rodriguez A, Calonge M, Pedroza-Seres M, et al. Referral patterns of uveitis in a tertiary eye care center. *Arch Ophthalmol*. 1996;114(5):593-599.
- Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data: results of the First International Workshop. *Am J Ophthalmol*. 2005;140(3):509-516.
- Mackensen F, David F, Schwenger V, et al. HLA-DRB1*0102 is associated with TINU syndrome and bilateral, sudden-onset anterior uveitis but not with interstitial nephritis alone. *Br J Ophthalmol*. 2011;95(7):971-975.
- Tuncer S, Adam YS, Urgancioglu M, Tugal-Tutkun I. Clinical features and outcomes of HLA-b27-positive and HLA-B27-negative acute anterior uveitis in a Turkish patient population. *Ocul Immunol Inflamm*. 2005;13(5):367-373.
- Bañares A, Jover JA, Fernández-Gutiérrez B, et al. Patterns of uveitis as a guide in making rheumatologic and immunologic diagnoses. *Arthritis Rheum*. 1997;40(2):358-370.
- Cokington CD, Han DP. Bilateral nongranulomatous uveitis and a poststreptococcal syndrome. *Am J Ophthalmol*. 1991;112(5):595-596.
- Shet A, Kaplan EL. Clinical use and interpretation of group A streptococcal antibody tests: a practical approach for the pediatrician or primary care physician. *Pediatr Infect Dis J*. 2002;21(5):420-426, quiz 427-430.
- Ur Rehman S, Anand S, Reddy A, et al. Poststreptococcal syndrome uveitis: a descriptive case series and literature review. *Ophthalmology*. 2006;113(4):701-706.
- Amigo MC, Martínez-Lavín M, Reyes PA. Acute rheumatic fever. *Rheum Dis Clin North Am*. 1993;19(2):333-350.
- Walker S, Iguchi A, Jones NP. Frosted branch angiitis: a review. *Eye (Lond)*. 2004;18(5):527-533.
- Feltkamp TE. Ophthalmological significance of HLA associated uveitis. *Eye (Lond)*. 1990;4(Pt 6):839-844.
- Mapstone R, Woodrow JC. HL-A 27 and acute anterior uveitis. *Br J Ophthalmol*. 1975;59(5):270-275.
- Misiuk-Hojto M, Miedzobrodzki R, Grzybowski A, et al. Elevated levels of anti-endotoxin antibodies in patients with bilateral idiopathic acute anterior uveitis. *Acta Ophthalmol*. 2011;89(3):e283-e288.
- Khan MA, Braun WE, Kushner I, Grecek DE, Muir WA, Steinberg AG. HLA B27 in ankylosing spondylitis: differences in frequency and relative risk in American Blacks and Caucasians. *J Rheumatol Suppl*. 1977;3:39-43.
- 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):325-333.
- Rosenbaum JT, McDevitt HO, Guss RB, Egbert PR. Endotoxin-induced uveitis in rats as a model for human disease. *Nature*. 1980;286(5773):611-613.
- Natkunarahaj M, Kaptoge S, Edelsten C. Risks of relapse in patients with acute anterior uveitis. *Br J Ophthalmol*. 2007;91(3):330-334.
- Mandeville JT, Levinson RD, Holland GN. The tubulointerstitial nephritis and uveitis syndrome. *Surv Ophthalmol*. 2001;46(3):195-208.
- Mackensen F, Smith JR, Rosenbaum JT. Enhanced recognition, treatment, and prognosis of tubulointerstitial nephritis and uveitis syndrome. *Ophthalmology*. 2007;114(5):995-999.
- Goda C, Kotake S, Ichiishi A, Namba K, Kitaichi N, Ohno S. Clinical features in tubulointerstitial nephritis and uveitis (TINU) syndrome. *Am J Ophthalmol*. 2005;140(4):637-641.
- Levinson RD, Park MS, Ridders SM, et al. Strong associations between specific HLA-DQ and HLA-DR alleles and the tubulointerstitial nephritis and uveitis syndrome. *Invest Ophthalmol Vis Sci*. 2003;44(2):653-657.
- Burns JC, Joffe L, Sargent RA, Glode MP. Anterior uveitis associated with Kawasaki syndrome. *Pediatr Infect Dis*. 1985;4(3):258-261.