

The etiological features of anterior uveitis in a Turkish population

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Purpose: To identify any patterns in the cause of anterior uveitis in a Turkish population and compare them with results from previous studies.

Methods: The clinical records of 75 patients between January 2009 and January 2010 were retrospectively analyzed and classified as anterior uveitis according to Standardization of Uveitis Nomenclature criteria. Complete blood count, sedimentation rate, chest radiography, purified protein derivative skin test, and venereal disease research laboratory test were done on all patients. Additional serologic and radiographic tests were performed when indicated.

Results: Forty-one (54.6%) were male and 34 (45.3%) were female patients. The mean age at presentation was 39.1 ± 12.6 years. Fifty-six (74.6%) had unilateral and 19 (25.3%) had bilateral disease at presentation. A specific diagnosis was able to be established in 54 (72%) patients. The most common diagnoses were anterior uveitis associated with human leukocyte antigen B27 (14.6%) and Fuchs uveitis syndrome (14.6%). The second most common diagnosis was uveitis associated with herpes simplex virus (13.3%), followed by Behcet's uveitis (6.6%). Systemic disease associations were noted in 15 (20%) patients, and the most commonly associated systemic disease was Behcet's disease (6.6%).

Conclusion: Fuchs uveitis syndrome and anterior uveitis associated with human leukocyte antigen B27 were the most common form of anterior uveitis in this study. Using a systematic approach, a diagnosis was able to be established in 72% of the anterior uveitis cases.

Keywords: anterior uveitis, differential diagnosis, etiology, laboratory investigations

Introduction

Anterior uveitis is the most common form of uveitis.¹ Although anterior uveitis is usually the most easily managed form of uveitis, associated complications such as cataract, glaucoma, and cystoid macular edema may result in severe visual loss. Several studies have reported different referral patterns of anterior uveitis in different countries.²⁻⁸ In order to identify specific ocular and systemic conditions and decide on treatment strategies, diagnosis of anterior uveitis is essential. With a systematic approach, diagnoses can be established in up to 70% of cases.⁹

The purpose of this study was to identify any patterns in the cause of anterior uveitis compared with results from previous studies.

Materials and methods

In the uveitis department of the Ophthalmology Clinic at Umraniye Research and Training Hospital (Istanbul, Turkey), the clinical records of all anterior uveitis patients between January 2009 and January 2010 were analyzed retrospectively. Each patient

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underwent a complete ophthalmic examination including best corrected visual acuity (Snellen scale), slit lamp bio microscopy, tonometry, and indirect ophthalmoscopy. Age at presentation, gender, previous ophthalmologic examination, and systemic disease association were recorded for all patients.

Laboratory investigations including complete blood count, sedimentation rate, chest radiography, purified protein derivative skin test, and venereal disease research laboratory test were done on all patients. Additional serologic and radiographic tests such as sacroiliac spine X-rays or thorax computed tomography were performed when indicated. In patients presented with nongranulomatous uveitis, human leukocyte antigen (HLA)-B27 typing, and pathergy test were performed also. HLA-B5 and HLA-B51 could not be evaluated due to financial reasons. Systemic disease associations were investigated with an internist, rheumatologist, or pulmonologist whenever it was required to document the etiological diagnosis.

Patients were classified as anterior uveitis according to the recommendations of the Standardization of Uveitis Nomenclature group.¹⁰ Patients with large “mutton-fat” keratic precipitates, Koeppe nodules, and/or Busacca nodules were classified as granulomatous uveitis. Patients who were HLA-B27 positive and proved to be negative on radiographic testing and/or rheumatologic evaluation were classified as having anterior uveitis associated with HLA-B27. The diagnosis of seronegative spondyloarthritis was established after rheumatologic consultation. Diagnosis of Behcet’s disease was made in patients fulfilling the diagnostic criteria of the International Study Group for Behcet’s disease.¹¹ The diagnosis of herpetic uveitis was based on clinical findings. The presence of herpetic or dendritic keratitis, stromal scars, edema, decreased corneal sensation, acutely elevated intraocular pressure, or sectoral iris atrophy with unilateral uveitis were the strongest diagnostic findings.¹²

The diagnosis of Fuchs uveitis syndrome (FUS) was established by the constellation of clinical findings also. These findings were diffuse, small to medium sized keratic precipitates, chronic low grade anterior chamber reaction, diffuse iris stromal atrophy, lack of posterior synechia, and the absence of cystoid macular edema, retinal vasculitis, snowbanks, and chorioretinal infiltrates despite the presence of vitreous cells and debris.¹³ The diagnosis of bilateral acute depigmentation of the iris (BADI) was based on ocular findings including an acute onset of bilateral symmetrical depigmentation of the iris stroma, pigment discharge into the anterior chamber, and pigment accumulation in the trabecular meshwork.¹⁴

The clinical diagnosis of sarcoidosis was made using the criteria proposed by the International Workshop on Ocular Sarcoidosis.¹⁵ The diagnosis of the patients was confirmed by transbronchial lung biopsy and classified as “definite sarcoidosis.”

Patients in which a specific diagnosis could not be made were classified as “undetermined.”

Informed consent was obtained from all patients.

Results

In a 1-year period, there were 131 cases of uveitis – with an incidence of 0.4% – among 32,468 new cases that were seen at the authors’ clinic. Of those 131 patients, 75 (57.5%) were diagnosed as anterior uveitis, 27 (20.6%) were diagnosed as panuveitis, 18 (13.7%) were diagnosed as posterior uveitis, and eleven (8.3%) were diagnosed as intermediate uveitis. All patients were Turkish Caucasians. Of the 75 patients included in the study, 61 (81.3%) patients were seen in the authors’ clinic, nine (12%) were referred from other disciplines at the hospital with an established systemic diagnosis, and five (6.6%) were seen by an ophthalmologist before referral. Forty-one (54.6%) were male and 34 (45.3%) were female patients. The male to female ratio was 1.2:1. The mean age at presentation was 39.1 ± 12.6 years; 64 (85.3%) were aged 20–60 years. As mentioned in Table 1, 56 (74.6%) had unilateral and 19 (25.3%) had bilateral disease at presentation. A total of 94 eyes had uveitis. Nongranulomatous uveitis was seen in 70 (74.4%) eyes and granulomatous uveitis was seen in 24 (25.5%) eyes. Nongranulomatous uveitis was seen in 57 (76%) patients and granulomatous uveitis was seen in 18 (24%) patients. The most common granulomatous forms of anterior uveitis were FUS (25%) and anterior uveitis associated with herpes simplex virus (HSV) (12.5%). Twenty-five percent of the granulomatous cases were classified as undetermined. The most frequent nongranulomatous forms of uveitis were anterior uveitis associated with HLA-B27 and Behcet’s disease. Anterior uveitis associated with HSV and anterior uveitis associated with varicella zoster virus

Table 1 Age and sex distribution of anterior uveitis

	Male	Female	Total
Number of patients	41 (54.6%)	34 (45.3%)	75
Age			
Range	8–59	7–74	7–74
Mean	37.3 (± 12)	41 (± 12.6)	39.1 (± 12.6)
Eye involvement			
Unilateral	35 (46.6%)	21 (28%)	56 (74.6%)
Bilateral	6 (8%)	13 (17.3%)	19 (25.3%)

were referred to as infectious anterior uveitis, and was diagnosed in 13 (17.3%) patients.

A specific diagnosis was able to be established in 54 (72%) patients. The most common diagnoses were anterior uveitis associated with HLA-B27 (14.6%) and FUS (14.6%). The second most common diagnosis was anterior uveitis associated with HSV (13.3%), followed by Behcet's disease (6.6%). All cases with BADI had bilateral disease and all cases with herpetic keratouveitis had unilateral disease (Table 2). Male predominance was obvious among patients with Behcet's disease (80%) and FUS (72.7%). All the patients with BADI and sarcoidosis were female, and anterior uveitis associated with HLA-B27 (63.6%) was more common among female patients (Table 3). Systemic disease associations were noted in 15 (20%) patients, and the most commonly associated systemic disease was Behcet's disease (6.6%). Of the total 75 patients, 64 (85.3%) were presented to the clinic at 16–60 years of age. Table 4 provides data on the distribution of etiology and uveitis diagnosis by age.

Visual acuity of the eyes was assessed at initial presentation (Table 5). Of the 94 eyes, eight (8.5%) had visual acuity less than 20/200. The most common etiology for visual acuity

Table 2 Diagnosis of uveitis patients and distribution according to ocular involvement (N = 75)

Diagnosis	Number (%) of patients	Bilateral (n = 19)	Unilateral (n = 56)	Mean age at presentation (years)
AU associated with HLA-B27	11 (14.6%)	1 (9%)	10 (90.9%)	41.6
AU associated with AS	4 (5.3%)	1 (25%)	3 (75%)	33.2
AU associated with UC	1 (1.3%)	–	1 (100%)	35
AU associated with psoriasis	1 (1.3%)	–	1 (100%)	31
Fuchs uveitis syndrome	11 (14.6%)	3 (27.2%)	8 (72.7%)	33.8
AU associated with HSV	10 (13.3%)	–	10 (100%)	41
AU associated with VZV	3 (4%)	–	3 (100%)	56
Behcet's uveitis	5 (6.6%)	2 (40%)	3 (60%)	29.2
BADI	4 (5.3%)	4 (100%)	–	38.5
JIA associated AU	2 (2.6%)	2 (100%)	–	7.5
AU associated with sarcoidosis	2 (2.6%)	2 (100%)	–	36.5
Undetermined	21 (28%)	4 (19%)	17 (81%)	43.9

Abbreviations: AU, anterior uveitis; AS, ankylosing spondylitis; BADI, bilateral acute depigmentation of the iris; HLA, human leukocyte antigen; HSV, herpes simplex virus; JIA, juvenile idiopathic arthritis; UC, ulcerative colitis; VZV, varicella zoster virus.

Table 3 Diagnosis of patients according to sex

Diagnosis	Number of patients (N = 75)	Sex distribution n (%)	
		Male 41 (54.6%)	Female 34 (45.3%)
AU associated with HLA-B27	11	4 (36.3%)	7 (63.6%)
AU associated with AS	4	3 (75%)	1 (25%)
AU associated with UC	1	1 (100%)	–
AU associated with psoriasis	1	1 (100%)	–
Fuchs uveitis syndrome	11	8 (72.7%)	3 (27.2%)
AU associated with HSV	10	5 (50%)	5 (50%)
AU associated with VZV	3	3 (100%)	–
Behcet's uveitis	5	4 (80%)	1 (20%)
BADI	4	–	4 (80%)
JIA associated AU	2	1 (50%)	1 (50%)
AU associated with sarcoidosis	2	–	2 (100%)
Undetermined	21	11 (53.4%)	10 (47.6%)

Abbreviations: AU, anterior uveitis; AS, ankylosing spondylitis; BADI, bilateral acute depigmentation of the iris; HLA, human leukocyte antigen; HSV, herpes simplex virus; JIA, juvenile idiopathic arthritis; UC, ulcerative colitis; VZV, varicella zoster virus.

less than 20/200 was FUS-induced cataract and corneal scarring associated with HSV.

Discussion

In the present study, the aim was to establish the etiologic distribution of anterior uveitis. The present series mostly studied patients who attended the authors' clinic directly; only 19.7% of the patients were referrals.

A specific diagnosis was able to be established in 72% of patients, meaning the etiology remained undetermined in 28%. According to different reports, diagnosis can be made in 54%–80% of cases with anterior uveitis.^{3–8} Systemic disease associations were found in 20% of patients, of which Behcet's disease – due to the geographical distribution – comprised a great proportion. Systemic disease associations in anterior uveitis have been previously reported to be 13%–42%.^{3,5–7}

All patients were Caucasians born in Turkey. The mean age at presentation was 39.1 ± 12.6 years (range 7–74 years), which is in agreement with other reports that state uveitis to be most common in the third decade of life.^{16,17} Males and females were almost equally represented. Unilateral non-granulomatous involvement was found to be more common. The majority of patients were aged between 16–60 years (85.3%). Herpetic uveitis was the leading cause of anterior

Table 4 Distribution of etiology and diagnosis of uveitis according to age

Diagnosis	Age distribution n (%)		
	< 6 years	16–60 years	> 60 years
AU associated with HLA-B27	–	11 (17%)	–
AU associated with AS	–	4 (6%)	–
AU associated with UC	–	1 (2%)	–
AU associated with psoriasis	–	1 (2%)	–
Fuchs uveitis syndrome	–	11 (17%)	–
AU associated with HSV	–	8 (13%)	2 (29%)
AU associated with VZV	–	2 (3%)	1 (14%)
Behcet's uveitis	–	5 (8%)	–
BADI	–	4 (6%)	–
JIA associated AU	2 (50%)	–	–
AU associated with sarcoidosis	–	2 (3%)	–
Undetermined	2 (50%)	15 (23%)	4 (57%)

Abbreviations: AU, anterior uveitis; AS, ankylosing spondylitis; BADI, bilateral acute depigmentation of the iris; HLA, human leukocyte antigen; HSV, herpes simplex virus; JIA, juvenile idiopathic arthritis; UC, ulcerative colitis; VZV, varicella zoster virus.

uveitis in patients older than 60 years. The most common diagnosis among males was FUS, and anterior uveitis associated with HLA-B27 was the most common among females. In the present series, BADI and anterior uveitis associated with sarcoidosis were predominantly seen in females, which is similar to other reports,^{3,5,6,14} and anterior uveitis associated with varicella zoster virus was predominantly seen in males.

In the present series, the most frequent diagnoses were anterior uveitis associated with HLA-B27 (14.6%) and FUS, followed by anterior uveitis associated with HSV (13.3%) and Behcet's uveitis (6.6%). However, Behcet's disease was diagnosed in 31.3% of eyes with anterior uveitis and was the most common cause of anterior uveitis in Kazokoglu et al's recent multicenter Turkish study.³ Their high percentage of Behcet's uveitis may be explained by

Table 5 Visual acuity for the most common diagnoses

Diagnosis	Visual acuity		
	20/20–20/40	20/50–20/200	≤20/200
AU associated with HLA-B27	10 (91%)	1 (9%)	–
Fuchs uveitis syndrome	10 (72%)	1 (7%)	3 (21%)
AU associated with HSV	4 (40%)	3 (30%)	3 (30%)
Behcet's uveitis	6 (86%)	1 (14%)	–
Undetermined	18 (72%)	6 (24%)	1 (4%)

Abbreviations: AU, anterior uveitis; HLA, human leukocyte antigen; HSV, herpes simplex virus.

the referral characteristics of centers that participated in that multicenter study. In Turkey, patients with Behcet's disease have been mostly followed up in university clinics, which may be related to overestimated ratios of Behcet's disease among anterior uveitis. In the present study, only 6.6% of patients were seen by an ophthalmologist before referral, the majority of whom were habitants of Umraniye county and were seen by the study clinic's ophthalmology department first. Additionally, Kazokoglu et al related their high percentage of anterior uveitis among patients with Behcet's disease to inadequate comprehensive examination of the posterior vitreous, which may lead to posterior segment involvement being overlooked. Therefore, the data reported in the present study may show more reliable incidence. In the present study, anterior uveitis associated with HLA-B27 was seen more often than reported in previous studies from Turkey.^{3,18} This may be due to the fact that, unlike the previous studies, the HLA-B27 typing test was performed on all patients with nongranulomatous and noninfectious uveitis.

The high frequency of noninfectious anterior uveitis, including anterior uveitis associated with HLA-B27 and FUS, in the present study was found to be similar to that reported by Cimino et al from Italy,⁴ Jakob et al from Germany,⁸ and Soheilian et al from Iran.⁵ Of the total 75 patients, 13 (17.3%) were diagnosed as infectious anterior uveitis. This finding was similar to that found in the studies from Italy, Germany, and Iran, which ranged between 7%–19%. However, infectious anterior uveitis was predominantly seen in studies from Saudi Arabia, India, and Tunisia, with percentages up to 35% reported.^{6,7,17}

At initial presentation, 8.5% of the eyes had visual acuity less than 20/200. The most common causes were mature cataract formation associated with FUS and corneal scars associated with HSV uveitis. In previous reports, Kazokoglu et al reported rates of visual acuity less than 20/200 as 14%³ and Oruc et al reported them as 18%.¹⁹

Conclusion

FUS and anterior uveitis associated with HLA-B27 were the most common diagnoses among anterior uveitis. Unlike other reports, only a small percentage of the patients in this study were referrals. Therefore, this study presents a more reliable incidence of anterior uveitis. Since specific ocular and systemic etiology were established in 72% of the cases, all anterior uveitis cases deserve further investigation. With an insistent approach, the causes of anterior uveitis could be expected in the majority of cases.

Disclosure

The authors report no conflicts of interest in this work.

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