



Clinical Patterns, Complications, and Long-Term Visual Outcomes of Fuchs' Uveitis Syndrome in Turkish Population: Retrospective Study in a Tertiary Uveitis Referral Center

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Abstract

Objectives: In this study, we aimed to characterize the clinical presentation patterns, complications, and visual prognosis of Fuchs' uveitis syndrome (FUS) patients at a tertiary center in Türkiye.

Materials and Methods: Sixty-one FUS patients (64 eyes) were enrolled in this retrospective study. Detailed ophthalmic and systemic history was obtained from patients at the initial examination. Visual acuity measurement (decimal values, converted to logarithm of the minimum angle of resolution [logMAR]), slit lamp examination, dilated fundus examination, intraocular pressure measurement with Goldmann applanation tonometry were performed at each visit.

Results: Keratic precipitates (KP) were present in 57 eyes (89.06%) at initial examination. Diffuse small stellate greyish KPs were observed in 50 eyes (78.13%). Thirty eyes (46.88%) presented with heterochromia. Twenty-seven eyes (42.19%) had vitreous debris/fibrillary appearance or condensation. The most common complication was cataract (79.69%), of which the most common type was posterior subcapsular cataract. At presentation, anterior chamber cells were seen in 32 eyes (50%). The mean visual acuity was 0.28 ± 0.56 logMAR at the first examination and 0.25 ± 0.48 logMAR at the final examination ($p=0.542$).

Conclusion: According to our findings, unilateral uveitis accompanied by low-grade anterior chamber inflammation, diffuse small stellate KPs, and diffuse stromal iris atrophy, with or without vitreous debris, remains the most characteristic clinical presentation among patients with FUS. Iris findings such as heterochromia and iris nodules are less frequently observed in Turkish patients, likely due to ethnic variations.

Keywords: Fuchs' uveitis syndrome, keratic precipitates, cataract, glaucoma, uveitis

Introduction

Fuchs' uveitis syndrome (FUS) is a specific type of uveitis characterized by low-grade inflammation and generally unilateral involvement.¹ The hallmark signs of FUS include chronic mild intraocular inflammation, stellate and mostly diffuse keratic precipitates (KPs), and iris stromal atrophy, which frequently leads to heterochromia.² The absence of posterior synechiae (PS) is another diagnostic clue. The clinical presentation may also involve posterior segment findings such as inflammatory vitreous debris and chorioretinal scars. In the long term, FUS can lead to vision-threatening complications, including cataracts, glaucoma, and severe vitreous haze.

The diagnosis of FUS is primarily based on clinical examination, although no definitive diagnostic criteria have been established. The variable presentations and frequency of clinical signs make diagnosis challenging. The SUN Working Group proposed unilateral anterior uveitis, stellate KPs, and unilateral diffuse iris atrophy as key diagnostic criteria for FUS.³ However, some researchers have criticized the SUN criteria, arguing that they have low sensitivity

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and place undue emphasis on unilateral involvement.⁴ Atypical bilateral cases further complicate the diagnostic process.⁵ Additionally, the absence of diagnostic tests (ocular or systemic) increases the risk of misdiagnosis. The exact pathogenesis of FUS remains unknown, but several theories have been proposed. The detection of antibodies against the rubella virus and cytomegalovirus in aqueous humor samples,⁶ as well as the presence of chorioretinal scars resembling toxoplasmosis⁷ in some patients with FUS suggest a potential infectious etiology.

FUS is an important cause of anterior uveitis worldwide.⁸ Yang et al.⁹ reported that FUS was the most common cause of anterior uveitis in China. It is also a frequent cause of uveitis in Türkiye. A multicenter study identified FUS as the second most common diagnosis among Turkish patients with uveitis.¹⁰ Another study reported that FUS accounts for 6.3% of all uveitis cases in Türkiye, ranking as the third most common noninfectious uveitis etiology nationwide.¹¹

In this study, we aimed to characterize the presentation, frequency of clinical signs, complications, and visual prognosis of patients with FUS at a tertiary center in Türkiye. Our objective is to enhance the current understanding of the clinical patterns of this disease and the reasons for its misdiagnosis.

Materials and Methods

Sixty-one patients (64 eyes) diagnosed with FUS in the Uvea Division of the Department of Ophthalmology at İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine were enrolled in the present study. The medical records of patients with FUS who were examined between 2012 and 2022 were retrospectively reviewed. The study was conducted in accordance with the tenets of Declaration of Helsinki. Ethics approval was obtained from the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (number: E-83045809-604.01.02-134482, date: 09.07.2021).

A detailed ophthalmic and systemic history was obtained from all patients during the initial examination. Presenting symptoms, systemic diseases, systemic and ocular medications (e.g., corticosteroids, antiglaucoma agents), previous surgeries, and other noninvasive procedures were recorded. At each visit, patients underwent visual acuity measurement (decimal values were converted to logarithm of the minimum angle of resolution [logMAR]), slit-lamp examination, dilated fundus examination, and intraocular pressure (IOP) measurement by Goldmann applanation tonometry. The presence of anterior chamber and vitreous cells, the types and locations of KPs, and the presence of heterochromia, vitreous haze, and other fundus

findings were documented. Optical coherence tomography (OCT) and fundus fluorescein angiography (FA) were performed as needed for differential diagnosis in patients with confounding vitreous findings or suspected retinal vasculitis.

The diagnosis of FUS was based on the presence of clinical findings such as chronic uveitis with mild or low-grade intraocular inflammation, diffuse iris atrophy with or without heterochromia, predominantly small and stellate KPs, and the absence of PS (except in cases with history of previous intraocular surgery). The diagnosis was confirmed by a single clinician (D.U.). However, follow-up examinations were performed by different clinicians. To ensure diagnostic accuracy, patients with other types of uveitis (anterior, posterior, or intermediate) or systemic comorbidities that could mimic FUS were excluded. Cases presenting with heterochromia and sectorial/partial iris atrophy or corneal opacification were excluded due to their resemblance to viral uveitis. Patients with active chorioretinitis or a history of ocular toxoplasmosis were also excluded. In uncertain cases, a diagnostic workup was performed, including complete blood count, erythrocyte sedimentation rate, C-reactive protein and angiotensin-converting enzyme levels, chest X-ray, syphilis serology, pathergy test, QuantiFERON, high-resolution computed tomography of the lung, and magnetic resonance imaging of the brain.

Prior to receiving a definitive diagnosis, some patients were treated with topical corticosteroids, which are not typically indicated for the management of FUS. This treatment was discontinued in all patients following the confirmed diagnosis of FUS. The use of other systemic or peribulbar treatments administered at other centers was also documented. For patients presenting with elevated IOP or glaucoma, topical antiglaucoma agents were the first-line therapy, particularly combined beta-blockers and carbonic anhydrase inhibitors, or alpha agonists. Oral acetazolamide or intravenous mannitol was administered for effective IOP control in cases with IOP ≥ 40 mmHg. Patients with glaucoma refractory to medical treatment were evaluated for glaucoma surgery.

Statistical Analysis

All analyses were performed using SPSS version 22.0 software. The Shapiro-Wilk test was used to evaluate the distribution of continuous variables. Accordingly, descriptive statistics were expressed as mean and standard deviation for normally distributed quantitative data, and as median and interquartile range for non-normally distributed data. Categorical variables were presented as frequencies and percentages, with comparisons performed using the chi-square test. A paired t-test was used to

compare visual acuity values between the first and last examinations.

Results

Sixty-four eyes of sixty-one patients with FUS were included in the present study. Thirty-one patients (50.82%) were male and 30 (49.18%) were female. The mean age of the study group was 33.93 ± 10.03 years (33.00 ± 11.46 years for male patients and 34.90 ± 8.40 years for female patients). The patients' presenting symptoms are summarized in [Table 1](#). Fifty-eight patients (95.08%) presented with unilateral involvement and 3 patients (4.92%) had bilateral disease.

At initial examination, KPs were present in 57 eyes (89.06%). Diffuse small grayish stellate KPs were observed in 50 eyes (78.13%), whereas medium-sized nonpigmented globular KPs were observed in 6 eyes and a granulomatous mutton-fat-like KP appearance was seen in one eye. At presentation, anterior chamber cells were seen in 32 eyes (50.00%): 4 (6.25%) with +0.5, 16 (25.00%) with +1, 11 (17.19%) with +2, and 1 eye (1.56%) with +3 cells. All eyes exhibited some degree of iris atrophy. Thirty eyes (46.88%) presented with heterochromia. Iris nodules at the pupillary margin were observed in 3 eyes (4.69%).

Thirty-one eyes (48.44%) had cataract at presentation, of which 30 (96.77%) exhibited posterior subcapsular cataract (PSC) and 1 (3.23%) had nuclear cataract. Fourteen eyes (21.88%) were pseudophakic at initial presentation, while 19 eyes (29.69%) were phakic with no cataract. During follow-up, 11 eyes (17.19%) underwent cataract surgery with intraocular lens (IOL) implantation. Posterior capsular opacity (PCO) developed in 3 eyes (12.00% of all pseudophakic eyes) during follow-up, one of which underwent neodymium-doped yttrium aluminum garnet laser capsulotomy.

Twenty-seven eyes (42.19%) had vitreous debris, fibrillary appearance, or condensation. Epiretinal membrane was present in 2 eyes (3.13%). Chorioretinal

scars were observed in 3 eyes (4.69%). Snowball-like vitreous opacities were seen in one patient with multiple sclerosis. This patient exhibited the classic FUS phenotype, characterized by unilateral uveitis, stellate KPs, iris stromal atrophy, and debris in anterior vitreous.

The mean IOP at presentation was 14.09 ± 4.68 mmHg. Six eyes (9.38%) had elevated IOP requiring the use of topical antiglaucoma therapy (a single agent in 4 eyes [6.25%] and a combination of two agents in 2 eyes [3.13%]). Glaucoma was diagnosed in 2 eyes (3.13%). In two eyes, IOP was uncontrolled despite topical therapy. One of these patients was treated with oral acetazolamide alone (once daily), while the other received oral acetazolamide (three times daily) along with intravenous mannitol during follow-up, and subsequently underwent trabeculectomy with mitomycin-C (MMC).

Twenty-seven eyes (42.19%) received topical medication either before presentation or during the follow-up period. Topical steroids, cycloplegics, peribulbar steroids, oral corticosteroids, or other immunosuppressive agents had been administered in other centers before a definitive diagnosis was made in our department.

Complications observed during follow-up are presented in [Table 2](#). The most common complication was cataract (79.69%), with PSC being the most predominant type. Nuclear cataract was observed in only one eye during follow-up. FA was performed in 14 eyes, revealing optic disc staining in 4 eyes (6.25%) and cystoid macular edema (CME) in 3 eyes (4.69%). CME was also observed on OCT in these three eyes, all of which developed the condition after phacoemulsification surgery. FA findings were normal in the other 7 eyes (10.94%).

The mean visual acuity was 0.28 ± 0.56 logMAR at the initial examination and 0.25 ± 0.48 logMAR at the final examination ($p=0.542$). Visual acuity remained stable in

Presenting symptom	Number of patients (%)
Blurred vision	36 (59.02)
Floaters	16 (26.23)
Ocular pain with decreased vision	2 (3.28)
Ocular pain	1 (1.64)
Incidental finding	6 (9.84)
During general examination	3
During glaucoma screening	2
During workup for Behçet disease	1

Complication	Number of eyes (%)
Cataract	51 (79.69)
Cumulative rate at the end of follow-up	31 (48.44)
At presentation	
Vitreous debris or condensation	27 (42.19)
Elevated IOP	6 (9.38)
Posterior capsular opacity	3 (4.69)
Cystoid macular edema	3 (4.69)
Glaucoma	2 (3.13)
Epiretinal membrane	2 (3.13)
Optic disc membrane	2 (3.13)
IOP: Intraocular pressure	

31 eyes (48.44%), improved in 17 eyes (26.56%), and worsened in 16 eyes (25.00%). The decrease in visual acuity during follow-up was associated with cataract formation or progression in all 16 eyes. Improved visual acuity was attributed to cataract surgery in 11 eyes (17.19%) and resolution of vitreous opacities in 4 eyes (6.25%).

Discussion

FUS is among the main etiologies of uveitis worldwide. Its prevalence varies according to ethnicity and geographic region. Yang et al.⁹ reported that FUS is the second most common type of anterior uveitis in China, following idiopathic anterior uveitis. Another study similarly showed that FUS is the second most common etiology of anterior uveitis in China, noting a higher prevalence among women.⁸ According to a multicenter study, FUS accounts for 6.3% of all uveitis cases in Türkiye, ranking as the third most common noninfectious uveitis etiology, with a male-to-female ratio of 0.79.¹¹ However, no sex-based difference was observed in the present study.

The diagnosis of FUS can sometimes be quite challenging, and patients may receive inappropriate treatment for years until the correct diagnosis is established. The SUN Working Group proposed specific diagnostic criteria for FUS.³ However, even with these criteria, the wide spectrum of atypical presentations can make it difficult to distinguish FUS from other entities. In particular, atypical and bilateral cases may require additional diagnostic procedures.⁵ Alternative essential findings have also been proposed in contrast to the SUN criteria. Yang et al.⁴ argued that the SUN criteria had lower sensitivity than their own proposed criteria and overemphasized the unilaterality of the disease. They suggested diffuse iris depigmentation, the absence of PS, and mild inflammation as the essential diagnostic findings.

In the present study, the most common presenting symptom was blurred vision (59.02%). Most previous studies have also reported decreased vision as the primary presenting symptom,^{12,13,14,15} although others identified floaters as the most frequent symptom of FUS.¹⁶ Nevertheless, these studies noted that visual impairment was the main reason patients sought ophthalmic care. Unilaterality rates in the literature range from 84.4% to 96.0%.^{12,15,17,18,19} Similarly, 95.1% of our patients had unilateral involvement.

The KPs in FUS are usually described as diffuse, white, stellate endothelial precipitates with characteristic fibrillary extensions. Most previous reports have documented this KP morphology in the majority of patients.^{13,15,16,18} In contrast, Tugal-Tutkun et al.¹⁷ reported that medium-sized, nonpigmented, globular KPs are the most common type

observed in FUS. In our study, KPs were predominantly small and stellate, consistent with the general literature.

Iris stromal atrophy was present in all patients across the majority of previous studies.^{12,16,18} Reported rates of heterochromia range from 13.9% to 90.3% in the literature. In the present study, heterochromia was observed in 46.9% of eyes. Despite the disease's historical name, "Fuchs heterochromic iridocyclitis," heterochromia is not a principal sign. This feature may be absent or difficult to detect, particularly in darkly pigmented eyes, which are highly prevalent among the population in our region. Other studies from Türkiye noted similar rates of heterochromia.^{15,17}

Iris nodules have also been recognized as an important finding in some cases, with reported prevalence rates ranging from 13% to 37.7%.^{12,14,15,17,19} However, iris nodules were observed in only 4.69% of the eyes in our study. Ethnic variations or difficulties in clinical detection during examination may account for this relatively low rate.

Chronic low-grade anterior chamber inflammation is also characteristic of FUS. Fifty percent of the eyes in our study had some degree of anterior chamber cells, mostly mild (+1 cells). Jones¹³ reported +1 cells in 44.1% and no cellular activity in 53.1%, whereas Tugal-Tutkun et al.¹⁷ observed anterior chamber cells in 74% of cases, mostly graded as less than +2. Other studies have reported mild to moderate anterior chamber inflammation in all cases.¹²

Cataract was the most frequent complication of FUS in our study, consistent with the literature.¹⁵ PSC has been reported previously as the most frequent type.^{15,17} However, the prevalence of PSC among cataract types in our study was exceptionally high at 97%. Our results suggest that PSC is highly characteristic of FUS in this population.

Thirty-nine percent of the eyes in the current study were pseudophakic at the end of follow-up. Higher rates have been noted in other reports.^{12,13} In our cohort, the PCO rate was 12% among eyes with cataract surgery and 4.7% overall. PCO has been identified as the most common postoperative complication across various types of IOL.²⁰ Nalçacıoğlu et al.¹⁵ reported a higher PCO rate (19.8%) in patients with FUS who underwent cataract surgery. The varying rates among studies may be related to differences in follow-up duration or IOL materials.

Chorioretinal scars, inflammatory vitreous debris, and epiretinal membrane are among the posterior segment findings reported in FUS. The frequency of chorioretinal scars in patients with FUS ranges between 2.3% and 20% in the literature.^{12,13,15,17,18,19} Vitreous opacification or debris is another important finding, with a reported prevalence spanning a wide spectrum of 15.7% to 84%.^{12,13,15,17,18,19}

In the present study, inflammatory vitreous debris was observed in 42.2% of eyes, a rate consistent with other studies from Türkiye.¹⁷ Epiretinal membrane has been reported in a minority of patients in previous reports, similar to our results.¹⁵ The definitive cause of epiretinal membrane and vitreal changes remains unknown.

Glaucoma is the leading cause of severe visual loss in FUS.¹⁴ In our study group, 6 eyes (9.38%) developed elevated IOP during the course of the disease, and 2 eyes (3.13%) were diagnosed with glaucoma during follow-up. The prevalence of elevated IOP or glaucoma has been reported to range from 11.1% to 27.6% in various studies.^{12,15,16,18} Tugal-Tutkun et al.¹⁷ reported rates of elevated IOP and glaucoma similar to our results (12.7% and 1.1%, respectively). One patient in our series required trabeculectomy with MMC. Nalçacıoğlu et al.¹⁵ noted an 18% glaucoma prevalence, with trabeculectomy performed in 25.8% of those cases. Furthermore, Tugal-Tutkun et al.¹⁷ reported that in the majority of patients, elevated IOP could be managed successfully with medical therapy alone. The findings of the present study are consistent with these reports.

Study Limitations

The present study has several limitations. The sample size was relatively small because of the single-center study design. In addition, although the diagnosis of FUS was confirmed by a single clinician (D.U.), follow-up examinations and documentation were performed by different clinicians, potentially introducing bias in the evaluation of clinical findings. Furthermore, laser flare photometry and intraocular fluid sampling were not performed. Finally, some patients were treated with topical corticosteroids prior to a definitive diagnosis, which may have impacted the incidence and progression of cataract and glaucoma in these individuals.

Conclusion

The findings of the present study are largely consistent with those previously reported for Turkish patients with FUS, with some minor differences. Iris findings such as heterochromia and iris nodules seem to be less frequent among Turkish patients, which is likely attributable to ethnic variations. Furthermore, PSC was a highly characteristic finding in our study, whereas the PCO rate after cataract surgery was lower than that reported in other studies from Türkiye. According to our results, the presentation of unilateral uveitis with low-grade anterior chamber inflammation, diffuse small stellate KPs, and diffuse stromal iris atrophy with or without vitreous debris remains the most accurate clinical description of FUS.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the tenets of Declaration of Helsinki. Ethics approval was obtained from the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (number: E-83045809-604.01.02-134482, date: 09.07.2021).

Informed Consent: Retrospective study.

Declarations

Authorship Contributions

Surgical and Medical Practices: O.K., A.Y.Ç., D.U., Concept: O.K., Design: A.Y.Ç., Data Collection or Processing: O.K., A.Y.Ç., Analysis or Interpretation: D.U., Literature Search: O.K., Writing: O.K.

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