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ORIGINAL ARTICLE

# Clinical features and treatment results of Fuchs uveitis syndrome

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#### Abstract

**Purpose:** The study aims to evaluate the clinical features and treatment results of patients with Fuchs uveitis syndrome (FUS). **Methods:** A retrospective chart review was carried out for all the FUS patients who were treated and followed up at the Uvea Unit of our clinic between 2008 and 2019. Demographic data of all patients and best corrected visual acuity (BCVA), intraocular pressure (IOP) values, anterior and posterior segment examination findings at the time of diagnosis, and the complications along with medical and surgical treatments were analyzed.

**Results:** The mean age of 56 patients included in the study was 40.19±9.69 (20–66) years and the mean follow-up period was 25.91±33.86 (1–154) months. The mean BCVA was 0.43±0.73 (0–3.1) LogMAR, and the mean IOP value was 17.75±9.64 (8–52) mmHg. At the time of admission, 19.6% patients were under systemic immunosuppressive treatment with corticosteroid and/or immunomodulator agents. The most common presenting symptoms were visual disturbance and blurriness (39.2%). Moreover, the most common complications were cataracts (53.5%) and IOP elevation (26.7%). Phacoemulsification was performed in 50% of eyes with cataracts, and BCVA showed a statistically significant increase postoperatively (p<0.0001). While pressure could be controlled with medical treatment in 73.3% of eyes with high IOP, 26.7% of eyes required glaucoma surgery. BCVA was found <2.10 logMAR in 20% eyes with glaucoma at the last visit.

**Conclusion:** In eyes with FUS, the most common presenting symptom was visual loss and blurriness and the most common complications were cataract and IOP elevation. While the surgical treatment of cataracts can be successfully performed, blindness may develop in eyes with glaucoma despite treatment. Therefore, early diagnosis is essential to prevent unnecessary steroid use in these cases.

Keywords: Fuchs syndrome; heterochromia; iridocyclitis.

Fuchs uveitis syndrome (FUS) was first described by Ernst Fuchs in 1906 as a triad of heterochromia, cataract and low grade anterior chamber reaction.<sup>[1]</sup> This syndrome is also called Fuchs heterochromic iridocyclitis or Fuchs syndrome. The course of FUS is typically unilateral, chronical and often asymptomatic, characterized by low grade anterior chamber and vitreous inflammation. Anterior segment findings of this syndrome are small, white, stellate like diffuse ker-

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atic precipitates (KPs) (fuchs precipitates), heterochromia and iris atrophy. Heterochromia as often seen on light colored eyes it can also be seen on dark colored eyes and it is called "inverse heterochromia."<sup>[2–4]</sup> Alongside of the iris atrophies, iris nodules and rarely anormal iridocorneal angle vascularization and anormal iris vascularization can be seen. Posterior segment findings can be listed as; vitreous degeneration, retinal tears, peripheral retinal scars, and vitreous membranes.

Etiological factors for FUS have been pointed as genetic factors, infectious agents such as rubella, cytomegalovirus, toxoplasma, immunologic pathologies, trauma and dysfunction of the sympathetic system yet any proof has not been stated.<sup>[5–13]</sup>

The most encountered complications on FUS are glaucoma and cataract. Follow-up of the patients is important for these complications as well as inflammation. The outcome of cataract surgery is excellent. Glaucoma can be seen at the time of diagnosis and close monitoring is needed.<sup>[5]</sup>

The aim of this study is to evaluate the clinical features, treatment results and complication rates of patients with FUS.

## **Materials and Methods**

A retrospective chart review was carried out for all the anterior uveitis patients who were treated and followed up at the Uvea Unit of our clinic between 2008 and 2019. Among all anterior uveitis, FUS patients were identified and enrolled in the study. Besides demographic data of all patients, best corrected visual acuity (BCVA) obtained using Snellen chart, intraocular pressure (IOP) values measured by Goldmann Applanation Tonometer, anterior and posterior segment examination findings at the time of diagnosis were evaluated. All complications along with medical and surgical treatments were also analyzed.

Data collection for this study has been approved by University Local Research Ethics Committee. The study protocol adhered to the Declaration of Helsinki for research involving human participants.

Statistical analysis was conducted with SPSS v.26.0 (IBM Co. Armonk, NY, USA). All data were reported as averages  $\pm$  standard deviations. Paired t-test was used in comparison of pre- and post-treatment parameters. BCVA was converted to LogMAR for statistical analysis. P<0.05 was considered to be statistically significant.

#### Results

Among of 1106 anterior uveitis patients, 56 eyes of 56 (5.06%) patients with FUS were included in the study. FUS diagnosed was made on basis of clinical findings. These findings included low-grade anterior chamber reaction, diffusely spread fine/stellate KPs (Fig. 1), iris atrophy or heterochromia (Fig. 2), absence of posterior synechiae, and varying degrees of vitritis. A diagnostic work-up (full blood count, erythrocyte sedimentation rate, C-reactive protein, chest radiograph, serological test and radiologic imaging) were ordered in case of suspicion of other causes of infectious or noninfectious uveitis.



Fig. 1. (a) Diffusely spread stellate keratic precipitates throughout corneal endothelium were observed on the anterior segment photograph in 28 year-old, female diagnosed with Fuchs uveitis syndrome. (b) Posterior subcapsular cataract was seen in the same eye.



Fig. 2. Heterochromia in a 32 years-old, female Fuchs uveitis syndrome patient. Loss of stromal melanocytes and crypts of iris are observed in the left eye.

The mean age of 56 FUS patients (32 female and 24 male) were 40.19±9.69 (range, 20–66) years at the time of diagnosis, and the mean follow-up period was 25.91±33.86 (6–154) months. Demographic and clinical findings of the patients are shown in Table 1.

The most common presenting symptom was decreased and blurred vision (39.2%). The other frequent complaints were floaters (35.5%), pain (10.7%), stinging and lacrimation (1.7%). At the time of admission, 12.9% of the patients were asymptomatic. Before applying to our clinic, 16 (28.6%) patients were treated with topical steroids, 9 (16.1%) received topical and systemic steroids, 1 (1.8%) patient used only systemic steroid, and another one (1.8%) was on systemic immunosuppressive agent in addition to topical and systemic steroids. The mean duration of systemic immunosuppressive treatment was  $4.7\pm2.6$  (1–10) months in these 11 patients. After admission to our clinic, all systemic treatments were gradually tapered and discontinued.

The mean BCVA was  $0.43\pm0.73$  (0–3.1) LogMAR, and the mean IOP value was  $17.75\pm9.64$  (8–52) mmHg. All patients had fine, non-granulomatous KP, and anterior chamber reaction was observed in 24 (42.8%) of them. Posterior synechia was not observed in any eye. One (1.7%) eye was presented with hyphema (Amsler's Sign) height in 2 mm without sign of rubeosis iridis. The iris nodules were observed in one (1.7%) eye in that the nodules were located both at the pupillary edge (Koeppe) and iris surface (Busacca). The frequent clinical findings were cataract in 53.5%, heterochromia in 46.4% and glaucoma in 26.7% of the eyes. While 11 (19.6%) eyes were pseudophakic, 45 (80.1%) eyes were phakic at the time of admission.

Vitritis, membrane formation in the vitreous, chorioretinal scars, epiretinal membrane (ERM), and peripheral retinal

tear were detected as the posterior segment findings. Clinical findings are summarized in Table 2. Laser photocoagulation was applied to 3 (5.4%) patients with peripheral retinal tears. Pars plana vitrectomy was performed in 1 (1.7%) patient with complaints of blurred vision and floaters due to membrane formation in vitreous and his BCVA increased from 4.0 to 0.00 LogMAR in post-operative period. Cystoid macular edema (CME) was detected in 1 (1.7%) pseudophakic eye. In this patient, CME regressed within 3 months with 1 drop of ketorolac tromethamine 4 times/day. In addition,

 
 Table 1. Demographic features and clinical characteristics of the patients with FUS

Parameters	
Age (year) Mean±SD (min-max)	40.19±9.69 (20–66)
No of patients, n	25
No of eyes, n	25
Gender, n (%)	
Female	32 (57)
Male	24 (43)
Affected eye, n (%)	
Right	23 (41)
Left	33 (59)
Symptoms, n (%)	
Decreased and blurred vision	22 (39)
Floaters	20 (36)
Pain	6 (11)
Stinning, lacrimation	1 (2)
Anterior chamber reaction, n (%)	24 (43)
Keratic precipitate, n (%)	56 (100)
Iris nodules, n (%)	1 (2)
Heterochromia, n (%)	26 (46.4)
Hyphema, n (%)	1 (2)
Vitreous inflammation, n (%)	21 (37.5)
Chorioretinal scars, n (%)	4 (7.1)

FUS: Fuchs uveitis syndrome, n: Number of eyes.

Table 2.	Complications and	l treatment of e	yes with FUS
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Complications/Treatment	No of eye (%)
Cataract	30 (54)
Posterior subcapsular cataract	27 (90)
Mature cataract	3 (10)
Treatment	
ollow-up	15 (50.0)
Cataract surgery	15 (50.0)
High IOP level	15 (27)
Secondary open angle glaucoma	15 (100)
Treatment	
Topical hypotensive agent	
Monotherapy	5 (33.3)
Fixed combinations	3 (20.0)
3 or more hypotesive molecules	3 (20.0)
Surgery	
Trabeculectomy	3 (20)
Express minishunt	1 (6.7)
Vitreous membrane formation	7 (12.5)
Treatment	
Follow-up	6 (86)
Pars plana vitrectomy	1 (14)
ERM	4 (7.1)
Treatment	
Follow-up	4 (100)
Peripheral retinal tear	3 (5.3)
Treatment	
Argon laser photocoagulation	3 (100)
CME	1 (2)
Treatment	
Ketorolac tromethamine eye drop	1 (100)

IOP: Intraocular pressure; ERM: Epiretinal membrane; CME: Cystoid macular edema; FUS: Fuchs uveitis syndrome.

mild ERM that did not require surgery was detected in 4 (7.1%) eyes by optical coherence tomography (OCT).

The most common complications were cataracts (53.5%) and IOP elevation (26.7%) during follow-up. Phacoemulsification and intraocular lens implantation were performed in 15 (50%) of 30 eyes with cataracts. BCVA showed a statistically significant increment from 1.22±1.06 (0.3–3.1) to 0.07±0.08 (0–0.3) LogMAR after cataract surgery (p<0.0001, paired t-test). Amsler sign, which is characterized by mild anterior chamber hemorrhage during surgery, was a frequently observed finding. No intraoperative complications occurred in any patient except one eye in which posterior capsule rupture was developed during phacoemulsification. The intraocular lens was placed in the ciliary sulcus and mild subluxation of the intraocular lens which did not affect the visual acuity occurred postoperatively. Standard treatment protocol consisting of antibiotic and steroid drops combination was used postoperatively as 1 drop for every 2 h in the first 5 days, and then 4 times a day to the end of the 1st month. No serious post-operative complication was occurred. Only 2 patients developed posterior capsule opacification and one of them was treated with YAG capsulotomy due to significant decrease in BCVA. Pressure could be controlled with medical treatment in 11 (73.3%) of 15 eyes with high IOP. Iridocorneal angle was observed as open on gonioscopy in all patients. A stepwise treatment algorithm was used for reducing IOP medically. Monotherapy was started as initial IOP-lowering treatment, and fixed combinations were preferred in cases that pressure could not be controlled with a single agent. Dorzolamide-timolol combination was the most frequently used medication. Prostaglandin analogues were added to the treatment as the last option before surgery. Topical anti-glaucomatous agents failed to control IOP in 4 (26.7%) eyes and decision for surgery was made. Trabeculectomy was performed in 3 of these eyes and in 1 eye Express mini shunt was implanted. Visual acuity was found <2.10 logMAR in 3 eyes at the last visit. All of these eyes with permanent vision loss had IOP  $\geq$  32 mmHg at the first visit, and one patient had vision loss at admission. The mean C/D ratio increased from 0.45±0.26 (0.2-1) to 0.52±0.32 (0.2-1) and the mean retinal nerve fiber thickness decreased from 95.6 $\pm$ 20.5 (69–119)  $\mu$ to 74±25.94 (44–107) µ at the last follow-up but differences were statistically insignificant (respectively; p=0.102 and p=0.225, paired t-test).

When the relationship between systemic immunosuppressive therapy and development of complications (glaucoma/cataract) was investigated, it was found that 2 (13.3%) of the 15 patients with high IOP and 6 (20%) of 30 patients with cataract had previously received systemic therapy (respectively; p=0.803 and p=0.472, Chi-square test). There was no statistical significance between systemic therapy and eye complications.

Thirteen (23.2%) patients underwent serological examination, including a panel of Toxoplasma gondii, Toxocara canis, herpes simplex virus, herpes zoster virus, Hepatitis A, Hepatitis B, Hepatitis C and HIV because of clinical suspicion. T. gondii immunoglobulin (Ig)M and IgG positivity was detected in only one patient. Viral serology positivity was not detected in any of the patients.

### Discussion

We evaluated, clinical features, complication rates, and treatment results of patients treated in our clinic with FUS diagnosis throughout 11 years in this study. The prevalence of FUS is reported between 1% and 20% in several studies.

<sup>[14]</sup> In accordance with the literature, FUS makes up 5.06% of our anterior uveitis patients.

FUS is mostly seen between 27 and 44 years and is reported to impact both sexes equally.<sup>[2,15]</sup> Herein, a female predominance was detected with a 57%, but the difference between genders was not statistically significant. Mean age of the study patients was 40.2 years and it was similar to the literature.<sup>[15–18]</sup>

Diffuse non-granulomatous endothelial KPs, which is considered as one of the classical findings of FUS, was detected in all patients. Accorinti et al.<sup>[2]</sup> reported the prevalence of these KPs as 95.6% and in another study from Mexico, it was reported as 80%.<sup>[15]</sup> Velilla et al.<sup>[16]</sup> reported that they observed the typical KPs in 100% of the patients in their study.

The prevalence of heterochromia was 46.4% in our study. In other studies from Turkey, the prevalance of heterochromia was reported as 27.4% by Nalcacioglu et al.<sup>[17]</sup> and as 39.8% by Tuğal-Tutkun et al.<sup>[18]</sup> The prevalance of heterochromia was reported between 70% and 90% in studies from West,<sup>[16,19–23]</sup> whereas it was reported between 14% and 34% in studies from Asia and Middle East.<sup>[8,24,26]</sup>

While the iris nodules were reported between 13% and 50%<sup>[15,17,18,25,27]</sup> in various studies, they were detected in only 1.7% of our study eyes. In that one eye, the iris nodules were located in both the pupil margin (Koeppe) and on the iris surface (Busacca). Koeppe nodules are seen frequently in FUS, but Busacca nodules are rarely reported.<sup>[25]</sup>

The presence of inflammatory cells in vitreous were reported between 50% and 91% in different studies.<sup>[2,17,27,28]</sup> In this study, vitritis was observed in 37.5% of the eyes. This relatively low percentage was thought to be related with the systemic steroid treatment 19.6% of the eyes got before applying to our clinic.

Retinal scar is another finding that might be seen in FUS patients, and its prevalence is 4–11% in literature.<sup>[19]</sup> The presence of retinal scars in FUS, which is considered as an anterior uveitis, gives the idea of T. gondii infection might have a role in the etiology.<sup>[19]</sup> Parrat et al.<sup>[29]</sup> demonstrated, in their study, that anti-toxoplasma antibodies were found in aqueous humor of FUS patients with retinal scars. Similarly, Ganesh et al.<sup>[30]</sup> observed that a female patient with bilateral T. gondii retinochoroiditis developed clinical findings of FUS bilaterally after recurrent episodes and detected that anti-toxoplasma IgM and IgG antibodies were highly positive in aqueous humor. In another study, it was suggested that if anti-T. gondii antibodies are negative in a FUS patient with retinal scars, anti-T. canis antibodies might

be positive.<sup>[31]</sup> Hereby, it's suggested that FUS might occur as a result of an immune reaction, triggered by a probable T. gondii infection. In our study, retinal scar was observed in 4 (7.1%) eyes, similar to the literature. Aqueous humor antibody levels are unknown due to the retrospective design of our study, but serum antibody levels were studied and retinal scar was not observed in the eye of the only patient with positive serum anti-toxoplasma antibodies.

The percentage of cataract was 53.5% in our study. In addition to that, 19.6% of the patients were already pseudophakic when they first applied. Similar to the literature, posterior subcapsular cataract was the most common type (90%). <sup>[14,17,28]</sup> The prevalence of cataract was 69% in Arellanes et al.'s<sup>[15]</sup> study, whereas it was reported as 85.6% in another study.<sup>[27]</sup> In the one study from China, cataract was reported as 70.7% amongst 118 FUS patients.<sup>[25]</sup> Similar to our study, cataract was detected as 52% in another study from Turkey.<sup>[17]</sup> Phacoemulsification and intraocular lens implantation was performed for 50% of the eyes with cataracts and none of the eyes had any complication resulted with permanent loss of vision. This indicates that cataracts surgery is a safe procedure for FUS patients with cataracts.

Glaucoma prevalence was reported between 4% and 27% in various studies.<sup>[2,16,19,21,32]</sup> This disparity might be a result of uneasy differentiation of glaucoma from ocular hypertension in FUS patients. Lens opacities developed in time, makes the fundus examination harder and causes unreliable OCT analysis and visual field tests. Furthermore, the increased thickness of peripapillary retina and optic disc secondary to the inflammation, effects the evaluation of these tests. Glaucoma was detected in 26.7% of our study patients, in accordance with the literature. Requirement of a surgical procedure due to inadequate IOP reduction with medical treatment was seen in 26.6% of these patients, which is reported between 32–73% in other studies.<sup>[32]</sup>

CME is rare in inflammatory pathologies effecting the anterior segment such as FUS. Tandon et al.<sup>[33]</sup> reported that none of the 198 FUS patients in their study did not developed CME. Bouchenaki et al.,<sup>[34]</sup> detected CME in 9.1% of the 99 FUS eyes. In our study, CME was detected in only 1 (1.8%) patient, who had cataract surgery history as a risk factor. These findings support that CME is rare in FUS patients. ERM is a posterior segment pathology, that might be seen in FUS patients. Zarei et al.,<sup>[28]</sup> detected ERM in 19.4% of 89 eyes with FUS, in their retrospective study. ERM was detected in 7.1% of the eyes in our study. Peripheral retinal tear was observed in 2 of the eyes with ERM. This suggest that a careful peripheral retinal examination is essential when ERM is detected in eyes with anterior segment inflammatory pathologies such as FUS.

11 (19.6%) of our patients were under systemic immunosuppressive treatment (corticosteroid/ immunomodulator agents). Unable to differentiate FUS from other non-infectious uveitis etiologies with posterior segment involvement is probably the reason behind systemic immunosuppressive treatment. FUS might present with a vitreus inflammation, thus it might be neccessary to eliminate other causes of intermediate and panuveitis in some patients. In our study, we noticed that we felt the need to investigate Behçet's disease in 2 eyes and multiple sclerosis in 6 eyes, amongst the 8 eyes with vitreus inflammation and reach the FUS diagnosis during follow-up visits when the classical FUS features became evident. It's been known that topical or systemic immunosuppressive treatment does not have a positive impact for the prognosis in patients with FUS. Therefore, vitrectomy is suggested in cases with decreased visual acuity due to severe vitreous inflammation. Vitrectomy was performed to only one of the eyes in our study with decreased visual acuity caused by dense membrane formation in the vitreous.

#### Conclusion

FUS diagnosis is based on clinical features. The typical fine stellate KPs are not always present at the beginning and might become evident later. The absence of typical clinical features at the presentation makes it harder to diagnose and causes unnecessary corticosteroid exposure. Furthermore, because FUS is known as an anterior uveitis, the vitreus opacities that are not as rare as thought of before, directs the ophthalmologist to other non-infectious causes of uveitis and results with prolonged and excessive usage of corticosteroids. This increases the risk of cataract and glaucoma, which are the two most common complications in FUS.

In our study, we observed that cataract surgery with phacoemulsification is a safe and effective procedure in FUS patients. Even though glaucoma is usually treated with medical therapy and the need for surgery is less frequent, it was the most common cause of irreversible blindness in the study. Posterior synechia, CME and ERM are rarely seen in eyes with FUS and must be investigated for other etiologies when detected in these patients.

**Ethics Committee Approval:** This study was approved by Ege University Faculty of Medicine Ethics Committee (date: 15.05.2019; number 19-5.1T/63).

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