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ORIGINAL PAPER

Spectral domain optical coherence tomography findings of patients with pars planitis and risk factors affecting visual acuity

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Abstract

Purpose To evaluate spectral domain optical coherence tomography (SD-OCT) findings of 42 eyes with pars planitis and to identify risk factors affecting visual acuity.

Methods Medical records and SD-OCT findings were retrospectively reviewed.

Results Mean best-corrected visual acuity (BCVA) was 0.248 ± 0.3 on the logMAR scale at baseline. SD-OCT findings included epiretinal membrane (ERM) in 16 (38.1%) eyes, loss of normal foveal contour appearance in 8 (19.0%), ellipsoid zone (EZ) damage in 5 (11.9%), external limiting membrane (ELM) damage in 3 (7.1%), disruption of retinal pigment epithelium (RPE) in 2 (4.8%), and macular atrophy in 1 (2.4%). There was macular edema in 10 (23.8%) eyes [cystoid macular edema (CME) in 8 (19.0%), diffuse macular edema (DME) in 6 (14.3%), and serous retinal detachment in 2 (4.8%)]. The mean central macular thickness (CMT) was 272.1 ± 319.5 μm. Patients were followed up for a mean of 50.6 ± 36.7 months. Mean BCVA was 0.210 ± 0.3 at the final evaluation. SD-OCT findings included ERM in 28 (66.7%) eyes, EZ damage in 6 (14.3%), ELM damage in 3 (7.1%), disruption of RPE in 4 (9.5%), loss of normal foveal contour appearance in 12 (28.6%), and macular atrophy in 2 (4.8%). There was CME and/or DME in 6 (14.3%) eyes. The mean CMT was 238 ± 220.9 μm and was significantly lower than the baseline ($p < 0.001$). According to multivariate linear regression analysis, the presence of DME, and loss of normal foveal contour appearance at baseline were the independent factors associated with BCVA at the final examination ($B = 0.726$, $p < 0.001$; $B = 0.766$, $p < 0.001$, respectively).

Conclusions DME and loss of normal foveal contour appearance were more likely to have adverse effects on visual acuity.

Keywords Cystoid macular edema · Diffuse macular edema · Pars planitis · Spectral domain optical coherence tomography · Uveitis

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Introduction

According to the Standardization of Uveitis Nomenclature Working Group, the term ‘pars planitis’ must

be used only to refer to intermediate uveitis with snow banking or snowball formation in the absence of infection or an associated systemic disease [1]. Although this disease predominantly affects children, it can also have a late onset in adults. The estimated prevalence of pars planitis in uveitis clinics among patients of all ages ranges between 2.4 and 15.4%, while the reported prevalence of pars planitis in children with uveitis ranges from 15.3 to 26.7% [2–6].

The common presenting symptoms are floaters, blurred vision, pain, and photophobia. It may also be asymptomatic and diagnosed incidentally during the routine ophthalmologic examination [7, 8]. The most common clinical findings of pars planitis include anterior segment inflammation, diffuse vitreous cells, vitreous haze, snowballs, and snowbanks [9].

Intraocular inflammation can cause a number of ocular complications if not treated. Cataract, macular edema, epiretinal membrane (ERM) formation, neovascularizations, vitreous hemorrhage, and retinal detachment are well-known complications of pars planitis [10–12].

Spectral-domain optical coherence tomography (SD-OCT) has become a standard diagnostic technique for the evaluation of uveitic macular edema as well as other inflammatory macular pathologies including ERM formation, vitreomacular traction, and foveal atrophy. It provides important information about the fluid distribution in eyes with uveitic macular edema. Moreover, this imaging method advantageous for monitoring the response to treatment and retinal layers that are visualized using SD-OCT plays an important role in predicting visual prognosis.

Previous studies using SD-OCT focused on uveitis patients with manifest secondary changes of the retina, primarily macular edema [13–15]. Roesel et al. [16] evaluated uveitic macular edema using SD-OCT and concluded that loss of the EZ on SD-OCT in eyes with uveitic macular edema was associated with poor visual acuity. It was reported that the presence of ERM in uveitic macular edema was associated with poorer visual acuity following treatment [17].

The purpose of this retrospective study was to evaluate SD-OCT findings of patients with pars planitis and to identify risk factors affecting visual acuity.

Materials and methods

We evaluated retrospectively the clinical records of 42 eyes of 21 patients with pars planitis who were followed up between 2008 and 2019 at the Uveitis Clinic of Ankara University Faculty of Medicine. We included in this series only patients who underwent treatment. Our study was performed in adherence to the tenets of the Declaration of Helsinki. No institutional review board approval is required for chart review studies.

All the patients included in this study had been diagnosed as pars planitis based on the diagnostic criteria defined by The Standardization of Uveitis Nomenclature Working Group in 2005 [1]. The patients lost to follow-up or incompatible to regular visits, as well as the ones with systemic or infectious diseases, were excluded from the study.

The baseline is defined as the initial examination at our institution. Data from baseline, 1, 3, 6, 9, 12, 18, 24, and 36 months follow-up visits and last examination were evaluated. The data include demographic features, symptoms, laterality, best-corrected visual acuity (BCVA) on the logMAR scale, fundoscopic findings, laser flare photometry (LFP) values, intraocular pressure, SD-OCT, and fluorescein angiography (FA) findings, treatment strategies, and ocular complications.

All patients who did not use any medication earlier were given systemic immunosuppressive therapy (conventional immunosuppressives and/or TNF-alpha inhibitors). In addition, we started topical corticosteroid therapy in patients with anterior chamber cells and high LFP values. The topical prednisolone acetate 1% dose was determined by the individual course of anterior chamber cells and LFP values.

Structural SD-OCT (Optovue Inc., Fremont, CA, USA) findings that we evaluated were the presence of macular edema, RPE damage, EZ damage (Fig. 1), ELM damage, presence of ERM, loss of normal foveal contour appearance, and central macular thickness (CMT). Cases with macular edema were also classified as cystoid macular edema (CME), diffuse macular edema (DME), and serous retinal detachment. CME is characterized by the formation of clearly defined intraretinal cystoid spaces (Fig. 2). DME is characterized by disturbance of the layered retinal structure, or spongelike low reflective areas and increased retinal thickness. Serous retinal detachment is characterized

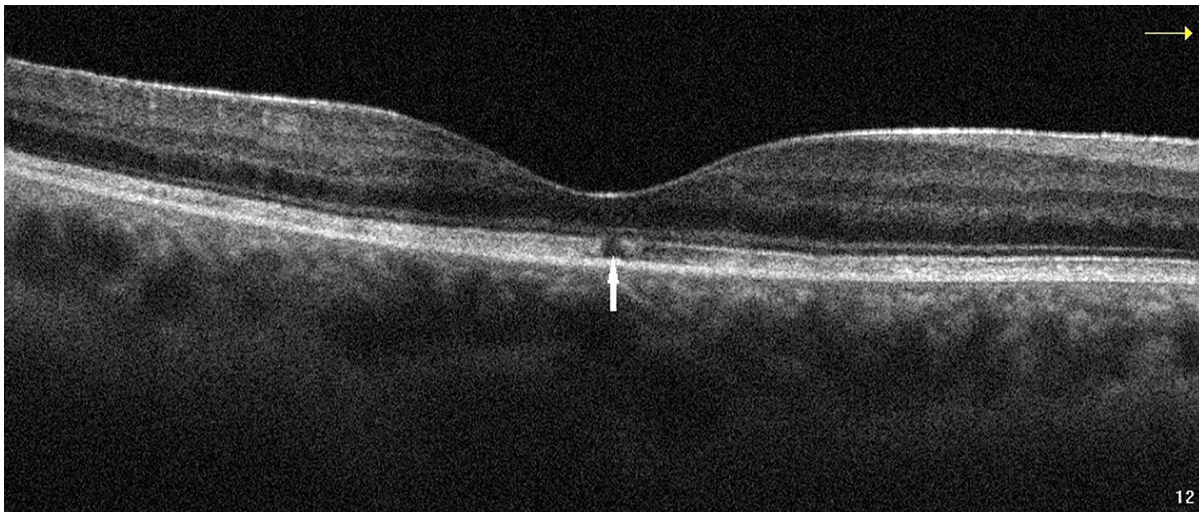

Fig. 1 Vertical arrow indicates ellipsoid zone damage

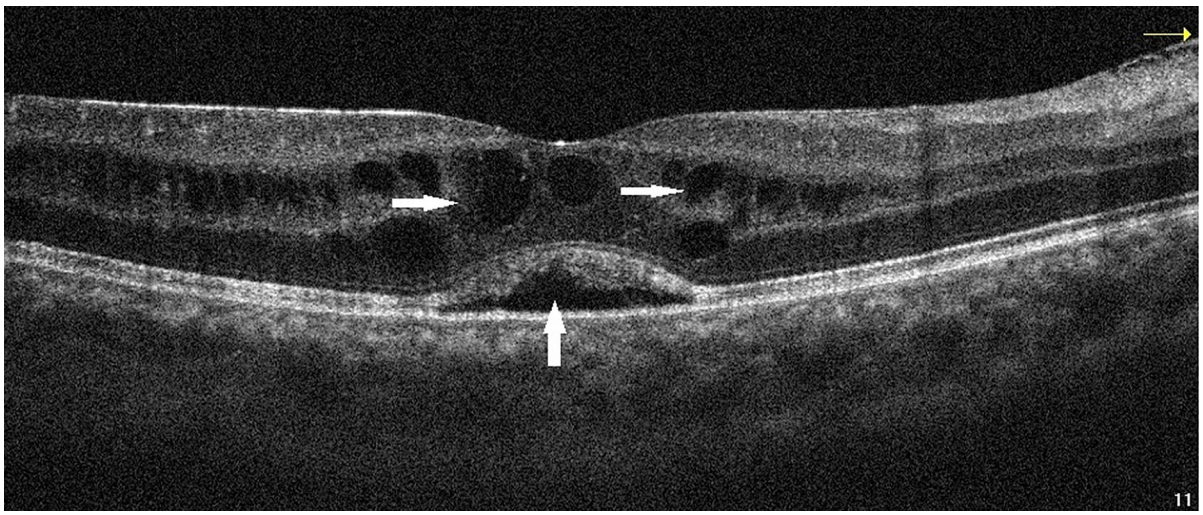

Fig. 2 Vertical arrow indicates subretinal fluid and horizontal arrows indicate intraretinal cystic cavities

by a separation of the neurosensory retina from the underlying RPE.

The EZ was identified as a distinct band just above the RPE-choriocapillaris line, and the line corresponding to the ELM was detected just above the EZ line. EZ and ELM integrity were also examined. ERM was identified as the hyper-reflective signal at the inner retinal surface. CMT was obtained by measuring the distance from the surface of the fovea to the RPE-choriocapillaris complex.

LFP measurements were performed by technicians as a routine ophthalmological examination at every visit on all patients. Flare values were measured using a Kowa FM-600 laser flare photometry (Kowa Acculas, San Jose, CA, USA). This device uses a diode laser; scattered laser beam in a 0.3 × 0.5 mm sampling window measures aqueous flare, and this value is expressed as photon counts per millisecond (ph/ms).

The data were analyzed using SPSS 11.5 for Windows (SPSS Inc., Chicago, IL, USA). Compatibility with normal distribution was evaluated with the Kolmogorov–Smirnov Test. Numerical variables with normal distribution are given as mean ± standard deviation, numerical variables without normal

distribution are given as median (min–max), and categorical variables are given as frequency (percentages). The difference between the two groups was determined by the Mann–Whitney *U*-test for numerical variables that did not have a normal distribution. The difference between more than two groups was determined with the Kruskal–Wallis test for numerical variables that did not have a normal distribution, and the relationships between categorical variables were determined by Pearson's Chi-square and Fischer's exact test. In addition, risk factors affecting the dependent variable were determined by logistic regression analysis. In the selection of candidate variables for logistic regression, $p < 0.20$ was considered statistically sufficient for significance. In general, statistical significance was set at a value of $p < 0.05$.

Table 1 Demographic and clinical characteristics of patients

Sex *n** (%)	
Female	10 (47.6)
Male	11 (52.4)
The mean age at presentation	
Years ± SD (range)	14.3 ± 10.5 (5–48)
The mean age at the onset of uveitis	
Years ± SD (range)	12.1 ± 10.3 (5–48)
The mean disease duration	
Months ± SD (range)	82.2 ± 71.0 (6–288)
Presenting symptoms *n** (%)	
Decreased visual acuity	13 (61.9)
Eye redness	1 (4.8)
Floaters	1 (4.8)
Squint	1 (4.8)
Asymptomatic	5 (23.8)

SD standard deviation

*The number of patients

Results

Forty-two eyes of 21 patients with pars planitis were included in this study. There were 10 (47.6%) female and 11 (52.4%) male. The mean age of uveitis onset was 12.1 ± 10.3 (range: 5–48) years. The mean age at our first visit was 14.3 ± 10.5 (range: 5–48) years. The mean disease duration was 82.2 ± 71.0 (range: 6–288) months. All patients were affected bilaterally. The most common presenting symptom was decreased visual acuity found in 13 patients (61.9%), followed by eye redness in 1 (4.8%), floaters in 1 (4.8%), and squint in 1 (4.8%). Five (23.8%) patients were asymptomatic. The demographic and clinical characteristics of patients are shown in Table 1.

Mean BCVA was 0.248 ± 0.3 (range: 0–1) on the logMAR scale at baseline. The mean LFP value was 9.2 ± 6.6 (range 2.8–27.4) ph/ms at baseline. Of the 42 eyes, 6 (14.3.%) had ≥ 1+ cells and 6 (14.3%) had 0.5+ cells in the anterior chamber at baseline. Complications at baseline included ERM in 16 (38.1%) eyes, macular edema in 10 (19.0%), cataract in 4 (9.5%), and glaucoma in 2 (4.8%). A statistically positive correlation was found between baseline LFP values and the presence of baseline complications ($r = 0.498$, $p = 0.017$). On FA performed at baseline evaluation, retinal vasculitis was detected in 20 (47.6%) eyes.

SD-OCT findings at baseline included ERM in 16 (38.1%) eyes, loss of normal foveal contour appearance in 8 (19.0%), EZ damage in 5 (11.9%), ELM damage in 3 (7.1%), disruption of RPE in 2 (4.8%), and macular atrophy in 1 (2.4%). There was macular edema in 10 (23.8%) eyes at baseline (CME in 8 (19.0%), DME in 6 (14.3%), serous retinal detachment in 2 (4.8%)). Mean CMT at baseline examination was 272.1 ± 114.63 (range: 96–720) μm.

At the time of presentation, 9 (42.8%) patients were treatment-naive, 7 (33.3%) were on methotrexate, 3 (14.3%) were on azathioprine, and 2 (9.5%) were on oral prednisolone. We started methotrexate in 7 patients and azathioprine in 2 patients who did not use any medication earlier. Seven (33.3%) patients were initiated topical corticosteroids. Four (19%) patients received posterior subtenon injection of triamcinolone acetonide.

Patients were followed up for a mean of 50.6 ± 36.7 (range 3–156) months. Mean BCVA was 0.210 ± 0.3 (range: 0–1) on the logMAR scale at the final examination. The difference between baseline and final BCVA (logMAR) was not statistically significant ($p = 0.441$). Mean LFP values at the final examination were 6.7 ± 4.3 (range 2.9–20.8) ph/ms. LFP values at the final visit were significantly lower than baseline LFP values ($p < 0.001$). Complications at final examination included ERM in 28 (66.7%)

eyes, cataract in 6 (14.3%), macular edema in 3 (7.1%), glaucoma in 3 (7.1%), band keratopathy in 1 (2.4%), and posterior synechiae in 1 (2.4%). There was a positive correlation between the level of baseline flare values and complication rates at the final visit ($r = 0.526$, $p = 0.012$). One of 6 eyes that develop cataract underwent cataract extraction and intraocular lens implantation during the follow-up. Glaucoma was successfully managed by topical antiglaucomatous agents. Fluorescein angiography performed at the last examination revealed retinal vasculitis in 9 (21.4%) eyes.

SD-OCT findings at final examination included ERM in 28 (66.7%) eyes, EZ damage in 6 (14.3%), ELM damage in 3 (7.1%), disruption of RPE in 4 (9.5%), loss of normal foveal contour appearance in 12 (28.6%), and macular atrophy in 2 (4.8%). There was CME and/or DME in 6 (14.3%) eyes at the final examination (CME in 4 (9.5%), DME in 4 (9.5%)). A comparison of SD-OCT findings at baseline and final examination is given in Table 2. The mean CMT at the final examination was 238 ± 102.6 (range: 96–680) μm and was significantly lower than the initial examination ($p < 0.001$). Mean BCVA values according to the SD-OCT findings at baseline and final examination are given in Table 3.

During the follow-up, methotrexate had to be discontinued in 2 patients due to side effects. Adalimumab treatment was initiated in one of these patients and mycophenolate mofetil in the other. One patient underwent pars plana vitrectomy and internal limiting membrane peeling due to vitreous hemorrhage and the presence of ERM resulting in contraction. Regarding the drugs used at the last examination, 3 (14.3%) patients were on methotrexate + adalimumab, 3 (14.3%) were on adalimumab, 1 (4.8%) was on methotrexate, 1 (4.8%) was on azatioprine + infliximab, and 1 (4.8%) was on cyclosporine + infliximab. Twelve patients have discontinued systemic treatment as their uveitis had been well controlled. Seven of these patients had used methotrexate during the follow-up period, 4 had used azathioprine, and 1 had used methotrexate + cyclosporine. All patients discontinued topical corticosteroids.

Table 2 Comparison of SD-OCT findings at baseline and final examination

	Baseline *n* (%)	Final examination *n* (%)	*p*-value
ERM	16 (38.1)	28(66.7)	0.003*
EZ damage	5 (11.9)	6 (14.3)	1.000
ELM damage	3 (7.1)	3 (7.1)	1.000
Disruption of RPE	2 (4.8)	4 (9.5)	0.500
Macular atrophy	1 (2.4)	2 (4.8)	1.000
Loss of normal foveal contour appearance	8 (19.0)	12 (28.6)	0,125

SD-OCT spectral domain optical coherence tomography, *ERM* epiretinal membrane, *EZ* ellipsoid zone, *EML* external limiting membrane, *RPE* retinal pigment epithelium

*Statistically significant *p*-value

We could not find a difference in final BCVA in patients who required more than one immunosuppressive agent ($p > 0.005$). Also, we could not find a difference in presence of macular edema, disruption of RPE, EZ damage, ELM damage, ERM, macular atrophy, loss of normal foveal contour appearance in OCT at the final examination in patients who required more than one immunosuppressive agent ($p > 0.005$, for all).

DME, CME, EZ damage, ELM damage and loss of normal foveal contour appearance at baseline examination have been identified as risk factors associated with BCVA at the final visit, and univariate linear regression analysis for that factors is given in Table 4. However, the contribution of DME and loss of normal foveal contour appearance variables to the model were found statistically significant and the final model was established with these two variables. The final predictive model was that final BCVA (logMAR) = −109 + 0.726 * DME + 0.766 * loss of normal foveal contour appearance. According to multivariate linear regression analysis, the presence of DME and loss of normal foveal contour appearance at baseline were the independent factors associated with final BCVA ($B = 0.726$, $p < 0.001$; $B = 0.766$, $p < 0.001$, respectively). Multivariate linear regression analysis for factors that may affect final BCVA is given in Table 5.

Discussion

SD-OCT is a very useful diagnostic technique for the evaluation of retinal layers and macular pathologies related to intraocular inflammation. It provides reproducible and consistent results and most importantly

Table 3 BCVA according to the SD-OCT findings at baseline and final examination

	Mean BCVA at baseline (range)	Mean BCVA at final examination (range)
ERM	0.59 ± 0.34 (0.15–1)	0.66 ± 0.33 (0.1–1)
EZ damage	0.27 ± 0.09 (0.15–0.4)	0.3 ± 0.21 (0.15–0.7)
ELM damage	0.28 ± 0.12 (0.15–0.4)	0.35 ± 0.30 (0.15–0.7)
Disruption of RPE	0.27 ± 0.17 (0.15–0.4)	0.36 ± 0.24 (0.15–0.7)
Macular atrophy	0.4	0.42 ± 0.38 (0.15–0.7)
Loss of normal foveal contour appearance	0.35 ± 0.25 (0.15–0.8)	0.47 ± 0.31 (0.15–1)

BCVA best-corrected visual acuity, *SD-OCT* spectral domain optical coherence tomography, *ERM* epiretinal membrane, *EZ* ellipsoid zone, *EML* external limiting membrane, *RPE* retinal pigment epithelium

Table 4 Univariate linear regression analysis for factors predicted to associated with BCVA (logMAR) at the final visit

Variable	Beta	%95 Confidence interval		*p*-value
		Lower bound	Upper bound	
DME	0.331	0.079	0.583	0.011*
CME	0.414	0.209	0.618	< 0.001*
EZ damage	0.282	0.001	0.563	0.049*
ELM damage	0.375	0.029	0.727	0.037*
Loss of normal foveal contour appearance	0.402	0.208	0.597	< 0.001*

BCVA best-corrected visual acuity, *DME* diffuse macular edema, *CME* cystoid macular edema, *EZ* ellipsoid zone, *ELM* external limiting membrane

*Variables with a *p*-value below 0.20 were included in the multivariate linear regression analysis

Table 5 Multivariate linear regression analysis for independent factors associated with BCVA (logMAR) at the final visit

Variable	Beta	%95 Confidence interval for Beta		*p*-value
		Lower bound	Upper bound	
DME	0.726	0.354	1.097	< 0.001*
Loss of normal foveal contour appearance	0.766	0.376	1.156	< 0.001*

BCVA best-corrected visual acuity, *DME* diffuse macular edema

*Statistically significant *p*-value

provides quantitative measurements of retinal thickness that are useful for follow-up of patients with uveitis [18]. Structural changes such as CME, DME, vitreomacular interface diseases, the integrity of the outer retinal structures, the photoreceptor layer, and RPE can be evaluated with this imaging method [19]. Besides its diagnostic value in uveitis, SD-OCT has enabled assessment of treatment response and provided predictive value for visual recovery and prognosis. In this study, we were interested to analyze the macular structural changes in patients with pars planitis, using SD-OCT. To our knowledge, this is the first study analyzing structural macular changes and factors that affect visual acuity solely in patients with pars planitis.

Macular edema is common and potentially sight-threatening complication in eyes with pars planitis. Therefore, detecting and monitoring macular edema are of particular importance [2, 20]. A retrospective review of patients with pars planitis found that the most common complication of pars planitis was CME (47.7%), followed by vitreous opacities (38.6%), optic disc edema (38.6%) and vasculitis (36.4%) [21]. Another study showed that the most common complications were CME (63.4%) and cataract (47.5%) in children with pars planitis [22]. Sancho et al. also analyzed ocular complications in pediatric and adult patients with intermediate uveitis and showed that

CME occurred in 36% of the eyes [23]. Navarrette et al. included 58 eyes of 33 children with pars planitis and reported that 31% of these eyes developed CME [24]. Unlike these studies, in the study by Jain et al. [25] the rate of CME was found to be lower (17%) in children with pars planitis. Eser-Ozturk and Sullu [26] analyzed the demographic characteristics, clinical features, ocular complications, and visual outcomes of 93 pediatric patients with uveitis. According to their results, anterior uveitis was the most common anatomic type followed by panuveitis, intermediate uveitis, and posterior uveitis [26]. Macular edema was developed as a complication in 2 of 17 (11.8%) patients with intermediate uveitis during the follow-up period [26]. In our study, there were 10 (19.0%) eyes with macular edema at baseline. CME was detected in 8 (19.0%) of these eyes and DME in 6 (14.3%).

The most common complication was ERM in 28 (66.7%) eyes in our study. Donaldson et al. observed ERM in 36.9% of subjects as the most common complication of pars planitis in their study [10]. Malinowski et al. reported that twenty-nine eyes (23.1%) of 19 patients demonstrated either mild or moderate ERM formation, whereas an additional seven eyes (6.5%) of five patients demonstrated severe ERM formation [27].

Reiff retrospectively reviewed a cohort of 75 children and adolescents with idiopathic pars planitis, panuveitis, and Vogt–Koyanagi–Harada disease. According to the results of that study, long-term sequelae included various degrees of vision loss associated with anterior or posterior synechiae, cataracts, glaucoma, vitreous membranes, retinal detachment, band keratopathy, retinal fibrosis, retinal neovascularization, and persistent CME [28]. Similarly, in our study, macular edema, cataract, glaucoma, band keratopathy, and posterior synechia were observed as complications during the follow-up period.

It is also important that retinal layers that are visualized using SD-OCT play an important role in predicting visual prognosis in uveitic eyes. Roesel et al. evaluated uveitic macular edema using SD-OCT and concluded that loss of the EZ on SD-OCT in eyes with uveitic macular edema was associated with poor visual acuity [16]. Markomichelakis et al. included anterior, intermediate, posterior, and panuveitis cases with macular edema in their studies and showed that visual acuity was negatively correlated with increased macular thickness and the presence of CME [29]. Iannetti et al. reported that morphological and functional analysis of the inflammatory ERM showed that EZ disruption and central retinal thickness were correlated with poor vision in patients with uveitis [30]. Massamba et al. reported that there was a correlation between EZ disruption and decreased visual acuity probably resulting from the loss or alteration of the photoreceptors in patients with posterior uveitis [31].

We performed both univariate and multivariate regression analyses to determine the factors affecting the final visual acuity of patients diagnosed with pars planitis. According to univariate linear regression analysis, the presence of DME, CME, EZ damage, ELM damage, and loss of normal foveal contour appearance were found statistically significant for worse final visual acuity. When these variables were included in the model and multivariate regression analysis was applied, the presence of DME and loss of normal foveal contour appearance were determined as factors associated with final visual acuity. Therefore, our findings support that macular edema is an important complication that is related to poor final visual acuity in patients with pars planitis.

Relationships between LFP values and complications of uveitis in children have been reported by several authors [32, 33]. Davis et al. investigated possible relationships between baseline LFP values, complications of uveitis, and outcomes in children with various forms of chronic uveitis and reported that elevated flare was associated with any complication of uveitis [33]. In our study, there was a positive correlation between the level of baseline flare values and complication rates at baseline. In addition, we found a positive correlation between the level of baseline flare values and complication rates at the last visit. Therefore, our findings also support that higher flare values in the presence of intraocular inflammation correlate with a higher prevalence of uveitic complications.

Early and aggressive management of intraocular inflammation is very important, as pars planitis can lead to serious ocular complications and threaten vision. In our current clinical practice, the use of corticosteroids is limited and mostly used concomitantly until the preferred conventional immunosuppressive agent is expected to take action. We prefer to start conventional immunosuppressive agents early

and also monoclonal TNF-alpha inhibitors infliximab and adalimumab in patients not responding to conventional immunosuppressives. Eiger-Moscovich et al. investigated the clinical course and visual outcome of macular edema in pediatric patients with chronic noninfectious uveitis [34]. In that study, the most common diagnosis was intermediate uveitis, in 14 children [34]. Their treatment regimens included corticosteroids (systemically and/or locally), immunosuppressive agents (methotrexate, azathioprine, mycophenolate mofetil), and anti-tumor necrosis factor-alpha agents (infliximab and adalimumab) [34]. Their findings suggest that early and intensive treatment of noninfectious uveitis-related macular edema can lead to a favorable outcome in terms of macular edema resolution and visual acuity [34]. This finding is compatible with the results of our study.

Despite the small sample size of the present study, the results are encouraging and demonstrate the potential of SD-OCT for the identification of prognostic factors that may lead to more proper therapeutic decision making in patients with pars planitis. Future studies involving a larger sample size will be helpful to further explore the risk factors associated with final visual acuity in patients with pars planitis.

In conclusion, SD-OCT is a very useful diagnostic technique for the evaluation of macular pathologies related to intraocular inflammation in patients with pars planitis. Visual potential and prognostic factors can also be determined by this imaging method. Our findings demonstrate that macular edema in patients with pars planitis takes the form of DME or CME with or without serous retinal detachment. Patients with DME and loss of normal foveal contour appearance were more likely to have adverse effects on visual acuity.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval Our study was performed in adherence to the tenets of the Declaration of Helsinki. No institutional review board approval is required for chart review studies.

Informed consent Informed consent was obtained from all individual participants included in the study.

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