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Foveal Serous Retinal Detachment with Inferior Staphyloma: Long-Term Treatment Response to Anti-VEGF and Photodynamic Therapy

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Purpose: To evaluate the treatment response and long-term prognosis of foveal serous retinal detachment (SRD) associated with inferior staphyloma to anti-vascular endothelial growth factor (anti-VEGF) treatment and photodynamic therapy (PDT).
Materials and Methods: Treatment-naïve patients who underwent >24 months of follow-up were included. We analyzed inter-visit changes in the foveal subretinal fluid (SRF) height after anti-VEGF treatment or PDT compared to no treatment and long-term prognosis of best-corrected visual acuity in choroidal neovascularization (CNV)-free patients.
Results: Nineteen patients were enrolled, and the mean follow-up duration was 4.81 years. In 14 CNV-free patients, 11 received anti-VEGF injections, three patients underwent PDT, and two patients had both treatments. During the follow-up period, there were a total of 243 inter-visit events (88 injections and 155 observations without treatment). At the last visit of patients who received the treatment, complete resolution was more significantly achieved in the CNV group than in the CNV-free group (p=0.028). In CNV-free patients, visual acuity improved when complete resolution was achieved; otherwise, it generally decreased. After adjusting for confounding factors, analyses showed no statistically significant differences in inter-visit changes of foveal SRF height between the anti-VEGF treatment and no treatment cases (absolute value, rate, subgroup categorized as ±20% of change; p=0.733, p=0.916, p=0.277; respectively). All patients who underwent PDT did not show complete resolution or maintained improvement of SRF.
Conclusion: Treatment with anti-VEGF and PDT do not seem to be effective for foveal SRD of CNV-free inferior staphyloma.

Key Words: Anti-VEGF, choroidal neovascularization, inferior staphyloma, photodynamic therapy, subretinal fluid

INTRODUCTION

Inferior staphyloma is a type of primary posterior staphyloma associated with myopia and classified as a type V staphyloma.[1] In rare cases of patients with inferior staphyloma, macular serous retinal detachment (SRD) can occur and deteriorate visual function.[2-5] However, little is known about the long-term prognosis or effective treatment strategies for macular SRD associated with inferior staphyloma.

Intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection was established as the standard treatment for choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD)[6,7] and pathologic myopia,[8,9] and further has been applied in various medical situations involving subretinal or intraretinal fluids.[10-15] Recently, four case series about anti-VEGF trials for the treatment of SRD associated

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with inferior staphyloma were reported, and the results were contradictory.[16-19] These reports enrolled only one, two, one, and six patients, respectively, making it difficult to draw a definitive conclusion. Besides, low fluence photodynamic therapy (PDT) did not show effective results in two patients.[17]

Herein, we evaluated whether anti-VEGF treatment and PDT were effective for foveal SRD associated with CNV-free inferior staphyloma and determine the long-term prognosis of the disease in a relatively large number of patients.

MATERIALS AND METHODS

Patients

A retrospective study was conducted on patients newly diagnosed with foveal SRD associated with inferior staphyloma in the Department of Ophthalmology at Yonsei Medical Center (Severance Hospital and Gangnam Severance Hospital) between July 2009 and June 2021. Patients were selected for medical record review from a clinical database containing patients' ophthalmologic examinations and ocular history.

Only patients diagnosed with foveal SRD associated with inferior staphyloma and who underwent more than 24 months of follow-up were included in this study. Anti-VEGF therapy (ranibizumab, bevacizumab) and/or half-dose PDT with verteporfin was applied for the purpose of reducing SRD. Patients were presented for follow-up at 1- to 6-month intervals, depending on the disease activity and the clinician's decision.

All included patients had undergone a comprehensive ophthalmological examination at the initial presentation, which included measurement of the best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, indirect fundoscopy, color fundus photography, fluorescein angiography (FA), indocyanine green angiography (ICGA) using the Heidelberg retinal angiography device (HRA-II; Heidelberg Engineering, Dossenheim, Germany), and spectral domain optical coherence tomography (SD-OCT; Spectralis; Heidelberg Engineering, Heidelberg, Germany). SD-OCT consisted of 6-mm horizontal raster scans with 30–60-μm spacing that covered a 1500-μm diameter centered on the fovea. We also included high resolution images of 9-mm horizontal and vertical scans. At every follow-up, all examinations except angiography were performed. When the occurrence of neovascularization was suspected, FA and ICGA were performed. The CNV was determined with the consent of the two examiners based on hyperfluorescence and leakage from the suspected lesion.

The patients were excluded if any of the eyes exhibited the following signs: CNV secondary to AMD; media opacities significant enough to limit the quality of imaging; and a history of ocular inflammation, retinal detachment, retinal vascular occlusive diseases, epiretinal membrane, macular holes, ocular trauma, and previous vitreoretinal surgery and/or laser photocoagulation. There were a total of five patients with CNV who were not diagnosed with AMD. The age range of the five patients was between their 60s and 80s. None of the patients exhibited typical features of AMD, such as soft drusen, subretinal drusenoid deposits (reticular pseudodrusen), pachychoroid, or polypoidal structures. Two patients showed shallow pigment epithelial detachment associated with abnormal curvature, while three patients exhibited type 2 CNV characteristics. Two patients who underwent cataract surgery during the follow-up period were excluded from the analysis of visual acuity.

Treatment protocols

In CNV-free inferior staphyloma with foveal SRD, there is currently no established standard treatment. As a result, the decision to initiate treatment varied among physicians.

In the administration of the anti-VEGF injection, bevacizumab (Avastin) 1.25 mg or ranibizumab (Lucentis) 0.5 mg was injected 3.0 mm or 3.5 mm posterior to the limbus through the pars plana using a 30-gauge needle in the operating room, using an aseptic technique.

PDT was performed using half-dose verteporfin (Visudyne; Novartis, Basel, Switzerland). For this, 3 mg/m^2 of verteporfin was infused over 10 minutes, and the laser treatment began 15 minutes after the infusion started. Laser treatment with standard fluency of 50 J/cm^2 and a wavelength of 689 nm was applied to the affected area for 83 seconds.

In the case of CNV-free inferior staphyloma, the use of anti-VEGF and PDT treatments was off-label.

Imaging analysis

All OCT images, color fundus photographs, and FA and ICGA findings were reviewed by two independent examiners (J.L., J.W.J.) to determine the presence of accompanying CNV and the height of foveal SRD. The agreement between the two examiners was good. Discrepancies between examiners for categorical values and differences over 20% between the quantitatively measured values were resolved by open adjudication. If no consensus was reached, a final decision was made by the other senior examiner (S.H.B.) and the two closest values were averaged.

The height of the subretinal fluid (SRF) was manually measured at the subfoveal point using the OCT system's built-in calipers, specifically from the distance between the lower interface of the detached retina and the upper interface of the retinal pigment epithelium (RPE).

Outcomes and statistical analysis

The changes in BCVA between the initial and final visits were evaluated based on whether complete SRF resolution occurred and whether CNV was present. The Wilcoxon signed-rank test was used to assess the difference in BCVA between the initial and last visits. Fisher's exact test was used to compare the proportions of complete SRF resolution at the last visit according to the presence of CNV. The anti-VEGF agents administered

were bevacizumab (119) and ranibizumab (7); the two medications were not analyzed separately.

The main question of this study was whether anti-VEGF treatment was effective in foveal SRD of patients with CNV-free inferior staphyloma. We determined the inter-visit changes of SRF at every visit according to anti-VEGF treatment and observation without any treatment as the main variable, and it was analyzed under the assumption that every inter-visit change was independent. To minimize the influence of inter-treatment effects, cases of anti-VEGF therapy conducted within 12 months after PDT were excluded from the inter-visit analysis. Due to the retrospective nature of this study, the initial amount of foveal SRF, follow-up duration, inter-visit intervals, and the number of visits and anti-VEGF injections varied among subjects. Therefore, the patients, follow-up duration between the former and latter visits, and the amount of foveal SRF at the former visit were statistically adjusted. To improve the validity of the conclusion, inter-visit changes in foveal SRF height were converted into various variables and analyzed. Absolute value change and rate of change in foveal SRF between the anti-VEGF treatment group and the no treatment (observation) group were analyzed by a linear mixed model with an unstructured covariance matrix. The criteria classified changes into categorical groups, defining significant changes as ±20% or more, and changes of less than ±20% as stable. The chi-squared test and a generalized linear mixed model, adjusted for confounding factors, were used to analyze the differences in the categorical classification of ±20%. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA). A p-value <0.05 was considered statistically significant.

This retrospective study was approved by the Institutional Review Board (IRB) at Yonsei University Medical Center before the review of data began, and the requirement to obtain informed consent from the patients was waived by the IRB (3-2021-0460). All study protocols adhered to the tenets of the Declaration of Helsinki.

RESULTS

The study included 19 eyes from 19 enrolled patients (5 males, 14 females). The mean±standard deviation (SD) patient age was 62.47±13.48 years, and the mean±SD follow-up period was 4.81±2.71 years. During the follow-up period, a total number of 126 anti-VEGF injections were administered (bevacizumab, 119; ranibizumab, 7).

Patients' detailed diagnoses and received treatment are summarized in Fig. 1. Among the patients enrolled in the study, five patients were diagnosed with accompanying CNV and all patients were treated with anti-VEGF injection. Among the 14 patients without CNV, 11 patients received an anti-VEGF injection treatment and three patients also received PDT treatment. The remaining two CNV-free patients were followed up without any treatment. Among the 14 CNV-free patients, there were a total of 243 inter-visits. Of these, 88 (bevacizumab, 81; ranibizumab, 7) received intravitreal anti-VEGF injections, and 155 were observed without treatment.

Complete SRF resolution

Whether complete SRF resolution was obtained at the last visit according to the presence or absence of CNV and treatment was analyzed (Table 1). In two CNV-free patients without any treatment, one patient achieved spontaneous complete SRF resolution at the last visit. Among the patients treated, complete resolution was observed in four patients in the CNV group (4/5, 80.0%) and in only two patients in the CNV-free group

Table 1. Number of Patients Who Achieved Complete SRF Resolution at the Last Visit

	Complete SRF resolution	SRF remained	*p*
CNV free, untreated (n=2)	1 (50.0)	1 (50.0)	
CNV free, treated (n=12)	2 (16.7)	10 (83.3)	0.028*
CNV, treated (n=5)	4 (80.0)	1 (20.0)	

SRF, subretinal fluid; CNV, choroidal neovascularization.
Values are presented as n (%). Fisher's exact test.
*Statistically significant.

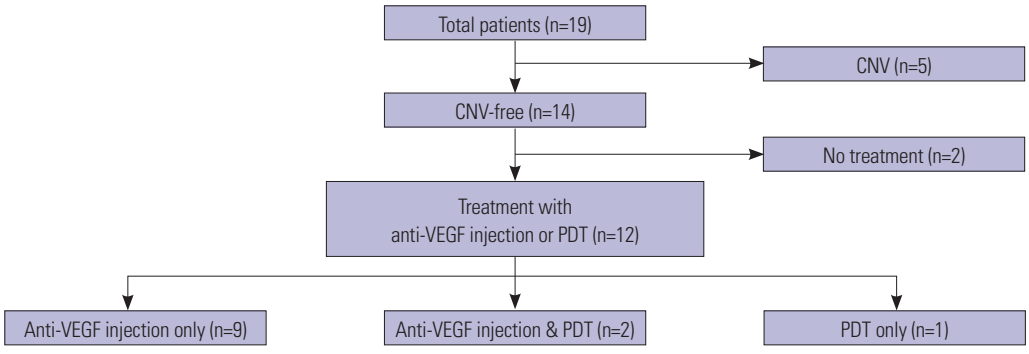

Fig. 1. Summary of detailed diagnosis and treatment of enrolled patients. CNV, choroidal neovascularization; VEGF, vascular endothelial growth factor; PDT, photodynamic therapy.

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(2/12, 16.7%), with the difference being statistically significant (p=0.028, Fisher's exact test).

Visual prognosis

In the CNV-free group, visual acuities were improved in patients with complete resolution, while visual acuities showed decreased tendency in the patients without complete resolution (mean±SD, LogMAR, 0.48±0.35 to 0.62±0.28; p=0.092, Wilcoxon signed-rank test) (Fig. 2A).

In the CNV group, despite treatment efforts, visual acuities decreased at the final visit compared to those at the first visit, showing marginal significance (mean±SD, LogMAR, 0.32±0.13 to 0.67±0.27; p=0.068, Wilcoxon signed-rank test) (Fig. 2B).

Effectiveness of anti-VEGF treatment

When the inter-visit change patterns of foveal SRF were divided into increase, stable (within ±20%), and decrease, the patterns were evaluated as 47 (30.3%), 67 (43.2%), 41 (26.5%) cases in cases of observation, and 19 (21.6%), 33 (37.5%), 36 (40.9%) cases in cases of anti-VEGF administration, respectively, with no significant differences (p=0.243, chi-squared test) (Table 2).

After correction for confounding factors, there was no difference in inter-visit SRF change between the observation cases and anti-VEGF cases for all variable types (Fig. 3, Tables 3 and 4). The estimated mean (95% confidence interval, CI) of the absolute value of inter-visit SRF change was +0.252 (-43.864, 44.368) μm in the observation cases and -11.845 (-71.003, 47.314) μm in the anti-VEGF cases, and there was no significant difference between the two groups (p=0.733, linear-mixed model with unstructured covariance matrix) (Fig. 3 and Table 3). The estimated mean (95% CI) of the rate of inter-visit SRF change was +13.738 (-73.363, 100.839) % in the observation cases and +6.270 (-111.628, 124.167) % in the anti-VEGF cases, and there was no significant difference between the two groups (p=0.916, linear-mixed model with unstructured covariance matrix) (Table 3). The adjusted proportions of increase, stable (within ±20%), and decrease cases of inter-visit SRF were 46.0%, 40.5%, and 13.3% in the observation cases and 47.2%, 33.6%, and 19.3% in the anti-VEGF injection cases, respectively, which were statistically not significant between the two groups (p=0.277, generalized linear-mixed model) (Table 4).

As a result, the anti-VEGF injection did not significantly reduce SRF compared to observation (no treatment). In fact, in many cases, the SRF was increased despite anti-VEGF injection, and the SRF was decreased despite just observation. A representative case is shown in Fig. 4.

Effectiveness of PDT

A total of three patients underwent half-dose PDT, and all patients underwent a single PDT session. After the PDT treatment, in three consecutive follow-up visits at 3-month intervals, complete resolution could not be reached at any time, and the decreased SRF was not maintained (Supplementary Fig. 1, only online).

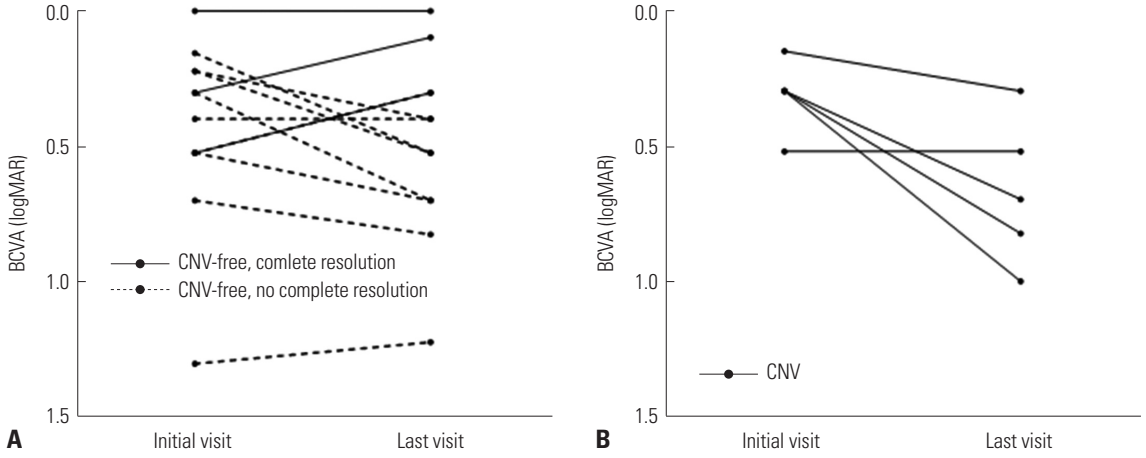

Fig. 2. Changes in BCVA at the initial and last visit. (A) In the CNV-free group, visual acuities were improved in patients with complete resolution, while visual acuities showed decreased tendency in patients without complete resolution (mean±standard deviation, LogMAR, 0.48±0.35 to 0.62±0.28; p=0.092, Wilcoxon signed-rank test). (B) In the CNV group, despite treatment efforts, visual acuities decreased at the final visit compared to that at the first visit, showing marginal significance (mean±standard deviation, LogMAR, 0.32±0.13 to 0.67±0.27; p=0.068, Wilcoxon signed-rank test). BCVA, best-corrected visual acuity; CNV, choroidal neovascularization.

Table 2. Number of Inter-Visit Changes in Foveal SRF Categorized as Increase, Stable, and Decrease in Patients with CNV-Free Inferior Staphyloma

CNV-free (n=14)	More than 20% increase	Stable	More than 20% decrease	Total	p
Observation	47 (30.3)	67 (43.2)	41 (26.5)	155	0.243
Anti-VEGF injection	19 (21.6)	33 (37.5)	36 (40.9)	88	

SRF, subretinal fluid; CNV, choroidal neovascularization; VEGF, vascular endothelial growth factor.
Values are presented as n (%). Chi-squared test.

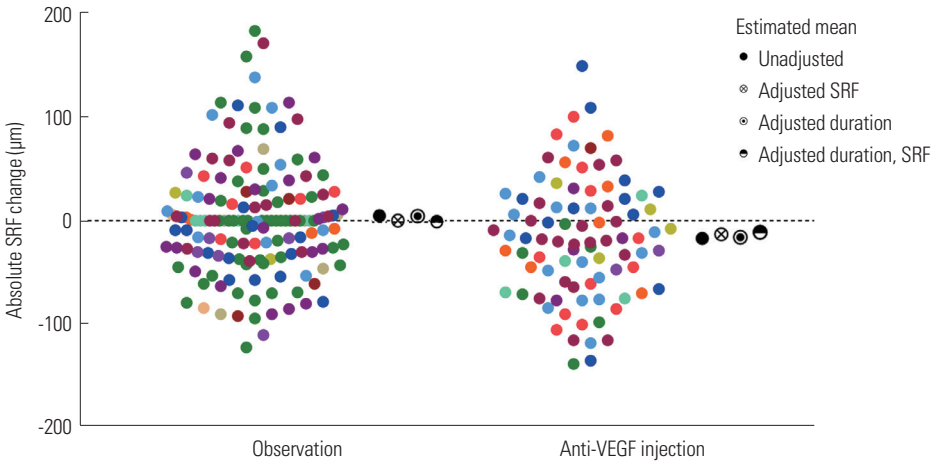

Fig. 3. Comparison of absolute value of inter-visit SRF change between the observation cases and the anti-VEGF cases. All change values are displayed with different colored dots according to the patients. The estimated means after correction for confounding factors, such as the foveal SRF height at the former visit and/or inter-visit duration, are indicated in different types of black circles. After adjusting for confounding factors, there was no difference in inter-visit SRF change between the two groups (p=0.733, linear-mixed model). SRF, subretinal fluid; VEGF, vascular endothelial growth factor.

Table 3. Comparison of Foveal SRF Changes between Observation and Anti-VEGF Cases in CNV-Free Inferior Staphyloma Patients (Absolute Value, Rate of Inter-Visit Foveal SRF Changes)

Variable	Absolute value change (μm)			Rate of change (%)		
	Observation (no treatment)	Anti-VEGF injection	p	Observation (no treatment)	Anti-VEGF injection	p
Unadjusted	+4.494 (-81.685, 90.673)	-15.738 (-130.546, 99.070)	0.766	+15.574 (-71.078, 102.226)	-0.336 (-115.315, 114.642)	0.816
Adjusted SRF	+1.072 (-42.869, 45.012)	-12.597 (-71.197, 46.002)	0.696	+13.661 (-73.227, 100.548)	+6.279 (-110.669, 123.228)	0.916
Adjusted duration	+4.072 (-82.521, 90.665)	-15.308 (-131.097, 100.480)	0.778	+15.337 (-71.720, 102.394)	-0.194 (-116.154, 115.766)	0.822
Adjusted SRF, duration	+0.252 (-43.864, 44.368)	-11.845 (-71.003, 47.314)	0.733	+13.738 (-73.363, 100.839)	+6.270 (-111.628, 124.167)	0.916

SRF, subretinal fluid; CNV, choroidal neovascularization; VEGF, vascular endothelial growth factor; CI, confidence interval.
Values are presented as estimated mean (95% CI). Linear mixed model with unstructured covariance matrix.

Table 4. Comparison of Inter-Visit Foveal SRF Changes between Observation and Anti-VEGF Cases in CNV-Free Inferior Staphyloma Patients

Variable	Observation (no treatment)	Anti-VEGF injection	p
Unadjusted			0.062
Increase	0.303 (0.037)	0.216 (0.044)	
Stable	0.431 (0.043)	0.375 (0.054)	
Decrease	0.265 (0.035)	0.409 (0.052)	
Adjusted SRF			0.290
Increase	0.525 (0.069)	0.508 (0.098)	
Stable	0.344 (0.062)	0.300 (0.078)	
Decrease	0.133 (0.038)	0.191 (0.061)	
Adjusted duration			0.073
Increase	0.259 (0.044)	0.198 (0.043)	
Stable	0.486 (0.060)	0.403 (0.062)	
Decrease	0.259 (0.042)	0.403 (0.055)	
Adjusted SRF, duration			0.277
Increase	0.460 (0.078)	0.472 (0.100)	
Stable	0.405 (0.078)	0.336 (0.088)	
Decrease	0.133 (0.041)	0.193 (0.062)	

SRF, subretinal fluid; CNV, choroidal neovascularization; VEGF, vascular endothelial growth factor; SE, standard error.
Values are presented as estimated proportion (SE). Generalized linear mixed model. Proportion Categorized as ±20%.

DISCUSSION

Inferior staphyloma with foveal SRD is a rare medical condition. Therefore, there have only been a limited number of case reports or case series studies, often with a small number of patients and short follow-up durations. The amount of SRD, especially in cases without CNV, may generally fluctuate and can spontaneously resolve without any treatment. Previously, a spontaneous resolution case was reported in a patient with inferior staphyloma with foveal SRD, and one patient was also observed in our cohort. Therefore, when SRF decreases after treatment, it is difficult to determine whether it is caused by the treatment effect or is just a spontaneous decrease. In addition, it is difficult to construct a prospective study for these rare medical conditions, and the clinical data of a retrospective study are usually unrefined and heterogenous. Given these limitations, only conclusions based on a relatively sufficient number of cases and sophisticated statistical methods would be reliable. We believe that our study could draw confirmative conclusions about the treatment effect of anti-VEGF, based on enrolling a relatively large number of patients and the anti-VEGF injections with a long-term follow-up duration of more than 2 years and a mean of 4.81 years.

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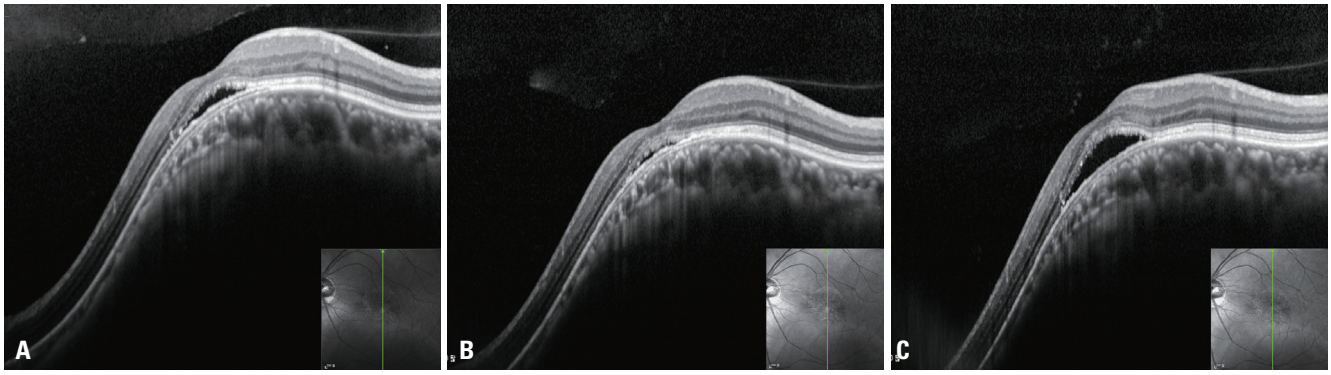

Fig. 4. Representative case of serial changes in one patient receiving anti-vascular endothelial growth factor treatment. A 63-year-old male patient with foveal serous retinal detachment associated with CNV-free inferior staphyloma in his right eye. (A) At his first visit, foveal SRF was observed; however, no treatment was given. (B) At 3 months after the initial presentation, the foveal SRF decreased. To reduce residual SRF, intravitreal bevacizumab was administered. (C) At 3 months after the injection, rather, the foveal SRF increased. CNV, choroidal neovascularization; SRF, subretinal fluid.

Longstanding SRD can cause permanent damage to photoreceptors and visual deterioration.[20-22] In our cohort of CNV-free patients, visual acuity improved when complete resolution was achieved; otherwise, visual acuity generally decreased. Therefore, any treatment which leads to complete resolution of SRF would be needed for the prevention of permanent photoreceptor damage and to improve visual prognosis.

In this study, anti-VEGF did not seem to be effective on foveal SRD of the patients with CNV-free inferior staphyloma. The inter-visit changes of foveal SRF height in CNV-free patients were investigated between 88 anti-VEGF treatment cases and 155 observation cases, and the absolute value, rate, and subgroup categorized as ±20% of inter-visit foveal SRF changes were analyzed. After adjusting for confounding factors, such as SRF height at the former visit and inter-visit duration, analyses showed no statistical differences in inter-visit change of foveal SRF between the anti-VEGF treatment cases and the observation cases (p=0.733, p=0.916, p=0.277; respectively).

Bevacizumab (anti-VEGF) has been shown to be effective in reducing neurosensory detachment by reducing the vascular permeability in various ocular diseases, such as choroidretinal vascular diseases[10-12] and choroidal tumors.[13-15] Since intravitreal anti-VEGF injections have proven their effectiveness on SRF, there have been attempts to treat anti-VEGF intravitreal injections in such refractory SRD. Previously, four case series on anti-VEGF trials for the treatment of foveal SRD associated with inferior staphyloma were reported, and the results were contradictory.[16-19] Milani, et al.[16] reported that one patient did not benefit from two consecutive monthly injections of bevacizumab. Similarly, Donati, et al.[17] described two patients, one of whom was treated using three injections of bevacizumab monotherapy, while the other was treated using combined bevacizumab and PDT. Treatment was unsuccessful in both patients. In comparison, Hirano, et al.[18] reported one case of SRD in inferior staphyloma that was refractory to ranibizumab treatment, yet exudative changes resolved after two injections of aflibercept. Lee and Yu[19] conducted a study on six patients with foveal SRD associated with CNV-free inferior staphyloma, noting a reduction of foveal SRF and choroidal thickness and complete resolution of SRF in 50% of patients treated with anti-VEGF. However, as these studies only enrolled one, two, one, and six patients, respectively, it seems difficult to draw a confirmative conclusion. In our study, the inter-visit change patterns of foveal SRF were 20% more decreased in 41 (26.5%) cases without any treatment. The decrease in SRF after anti-VEGF treatment in the preceding case series is thought to be likely due to chance. Additionally, a recent study by Ravenstijn, et al.[23] involving 26 eyes with staphyloma-induced serous maculopathy found that 31% of the untreated eyes showed spontaneous resolution. Furthermore, treatments such as anti-VEGF, PDT, and topical steroids did not affect the final BCVA. These findings significantly align with our conclusions.

In our study, the majority of anti-VEGF injections were bevacizumab (81 cases), and only seven cases were ranibizumab in 14 CNV-free patients. When comparing bevacizumab and ranibizumab, there was no statistically significant difference, indicating that both injections were ineffective. In our cases, we did not use aflibercept or brolucizumab, which are known to be superior in removing fluid in cases such as neovascular AMD. Therefore, we could not draw conclusions about the effectiveness of these anti-VEGFs.

Half-dose PDT has been established as the first-line of treatment for chronic central serous chorioretinopathy (CSC).[24] As a concept similar to reducing SRF in the CSC, half-dose PDT has been performed on SRF of CNV-free inferior staphyloma. In all three of our cases, complete resolution was not achieved, and reduced SRF was not maintained, which was similar to the results of previous studies.[17] PDT is effective in diseases showing thick choroid, so-called pachychoroid spectrum diseases such as CSC or polypoidal choroidal vasculopathy,[24,25] however, SRF accompanying inferior staphyloma is a clinical manifestation with thin choroid and high myopia, which is thought to have a different pathophysiology from that of pachychoroid-related diseases manifesting SRF.

The reason for choosing half-dose PDT in our study was due to verteporfin's does-dependent chorioretinal damage.[26] Full-dose PDT can lead to chorioretinal atrophy, and highly myopic eyes, which have thinner choroid and choriocapillaris, may be more susceptible to damage. Since half-dose PDT may reduce the risk, we chose half-dose PDT for treatment. In our half-dose PDT cases, complications such as chorioretinal atrophy were not noted during the follow-up period. However, due to the limited sample size and follow-up duration, the possibility of half-dose PDT causing chorioretinal atrophy cannot be ruled out.

Although rare, intravitreal injections can potentially cause serious complications such as endophthalmitis, and PDT, as previously stated, may cause outer chorioretinal atrophy. By not administering unproven, unnecessary treatments, ineffective medical expenses and possible complications can be reduced. Furthermore, given that spontaneous resolution can occur in a significant proportion of cases, a watchful waiting approach may be the most appropriate strategy. This approach involves regular follow-up to monitor for any visual changes or the development of complications that may necessitate further intervention. When discussing prognosis with patients, it is essential to inform them that while interventions may not always result in improved outcomes, spontaneous resolution of SRF is possible. Clear communication with patients about the likely course of their condition, the potential for improvement without intervention, and the need for ongoing monitoring can help manage expectations and ensure that patients are well-informed.

The disease entity of foveal SRD associated with inferior staphyloma appears to be similar to that of SRD with a dome-shaped macula. Both diseases are accompanied by high myopia and posterior staphyloma, and no effective treatment has been determined. Dome-shaped macula is characterized by a convex anterior protrusion (bowing towards the vitreous cavity) or posterior protrusion on both sides of the macula, whereas inferior staphyloma has a posterior protrusion only in the inferior part of the macula. The pathophysiology of both diseases remains controversial; however, both diseases are thought to accumulate foveal SRF through a similar mechanism related to anatomical changes, specifically focal scleral thickening and abrupt changes in choroidal thickness.[27,28] Firstly, it has been suggested that localized scleral thickening exerts pressure, which blocks the outflow of choroidal fluid, leading to changes in the RPE and the formation of SRF.[29-31] Secondly, the abrupt change of choroidal thickness of the margin of inferior staphyloma or dome-shaped macula could damage overlying RPE and/or choriocapillaris, resulting in dysfunction.[32] We believe that this RPE dysfunction leads to RPE atrophy, which damages the blood-retinal barrier, subsequently causing fluid accumulation. Furthermore, the marked choroidal thinning at the staphyloma margin may impair the choroid's absorptive function for SRF, thereby exacerbating SRF accumulation.[29]

This study has several limitations. First, although foveal SRF with inferior staphyloma is a very rare pathological condition, a larger number of patients would have strengthened the credibility of the conclusion. Additionally, due to the retrospective study design, there is an inherent risk of selection bias. Since the treatment and observation groups were not randomized, it is possible that patients in the treatment group had a higher necessity for intervention, which may have introduced bias. Furthermore, the amount of SRF at the time of visits and the interval between prior and current visits could have influenced treatment responses. To minimize potential biases, we made statistical adjustments to account for these confounding factors. However, despite such efforts, we acknowledge that these biases may still have impacted our findings. These limitations should be addressed in future research. Lastly, since all of the patients enrolled in this study were of East Asian descent (Korean), the study only focused on a single ethnic group. The results for diverse ethnicities should be considered in future studies.

In conclusion, in the case of foveal SRD in CNV-free inferior staphyloma, treatment with anti-VEGF and PDT does not appear to be effective. Since complete resolution of SRF can prevent potentially permanent damage to photoreceptors and lead to a better visual prognosis, novel therapies would be needed.

AVAILABILITY OF DATA AND MATERIAL

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

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