Long-term efficacy and recurrence of anti-vascular endothelial growth factor therapy for idiopathic choroidal neovascularization

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Research article

Abstract

Background Choroidal neovascularization (CNV) is a common cause of visual impairment. Intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs has previously shown to be effective in the treatment of ICNV. However, the prognostic factors and incidence of recurrence has not been fully demonstrated. The follow-up period in previous studies has also been relatively short. This study aimed to evaluate the long-term efficacy and recurrence of intravitreal anti-vascular endothelial growth factor (VEGF) therapy for idiopathic choroidal neovascularization (ICNV).

Methods This retrospective study included 35 patients (35 eyes) with ICNV from Peking University Third Hospital from July 2012 to October 2017. All patients received "treat and extend" treatment regimen. Intravitreal bevacizumab or ranibizumab were administered for each injection. To evaluate CNV recurrence, we continued to follow-up 27 of the 35 patients for at least 2 years after the initial diagnosis, and the longest period was 5 years. Best corrected visual acuity (BCVA) and central retinal thickness (CRT) were recorded. Parameters that affect prognosis and recurrence were analyzed.

Results The mean follow-up period after diagnosis was 168.0±34.82 months. BCVA improved from 56.20 ± 14.13 to 73.31±12.57 (P <0.01) and CRT decreased from 353.6±98.70μm to 273.1±53.56μm (P <0.001) one month after the last injection during the initial follow-up period. Better baseline BCVA indicated a better morphological improvement (P =0.026) in OCT. Those with high baseline BCVA (more than 60 letters) showed significant resolution of CNV lesions (P =0.036). 6 patients (22.2%) relapsed. The mean recurrence period was 90.83±49.02 weeks after diagnosis. Patients with recurrence underwent 3.67±0.816 injections, which was significantly higher than that without recurrence. The morphological improvement was compared between the two groups, and there was no statistical difference.

Conclusions Intravitreal anti-VEGF therapy was effective on ICNV, which could improve BCVA and make CNV lesions subsided. High baseline BCVA indicated a better prognosis. Re-treatment with anti-VEGF could effectively lead to resolution of recurrent ICNV. Disease recurrence had no significant effect on the long-term prognosis and had no correlation with the morphological improvement during treatment, suggesting that long-term follow-up should be performed in all ICNV patients.

Background

Choroidal neovascularization (CNV) is a proliferative disease and a common cause of visual impairment. Originated from choroidal blood vessels, this disease is usually associated with other fundus pathology(1). It has been suggested that when abnormal blood vessels originated from the choriocapillaris break through Bruch membrane and grow in the retinal pigment epithelium (RPE), or infiltrates into the subretinal pigment epithelium or subretinal space(2, 3), can result in CNV. CNV can occur in more than 30 ocular diseases, and it is most commonly associated with age-related macular degeneration (AMD)(4). CNV developed in younger patients who are less than 50 years old is usually attributed to pathologic myopia, angioid streaks, trauma, cytomycosis, central serous chorioretinopathy

(CSC) and other hereditary ocular diseases(5, 6). However, the cause of CNV still remains unclear in a large number of younger patients. In this subset of disease, no apparent primary ocular or systemic pathology can be detected, and such cases are defined as idiopathic choroidal neovascularization (ICNV) (7, 8).

Currently, there are several treatment options for ICNV at our fingertips, intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs such as ranibizumab, aflibercept and off-label use of bevacizumab has previously shown to be effective in the treatment of choroidal neovascularization in age-related macular degeneration or myopic CNV(9–11). The anti-VEGF therapies has also been reported to be effective in idiopathic CNV(12). Since majority of ICNV patients are under the age of 50, it is necessary to study long term efficiency of this treatment. The follow-up period in previous studies had been relatively short, usually within 1 or 2 years. Therefore, the long-term prognosis of this therapy as well as the possibility of disease recurrence have not been fully investigated.

Fundus fluorescein angiography (FFA) has been regarded as the gold standard for CNV diagnosis and monitoring, however, it is invasive and has risks such as nausea or even anaphylactic shock(13). Optical coherence tomography (OCT), on the other hand, is widely used to evaluate the prognosis and monitor recurrence of the disease because of its minimum side effect. Besides, retinal morphological change from OCT, which represent the retinal fluid, is convenient for clinicians to monitor the progression of disease. However, few studies have taken morphological parameters of OCT into account when evaluating the prognosis of the disease. The aim of our study is to evaluate long-term efficacy for intravitreal anti-VEGF therapy and the incidence of CNV recurrence in ICNV patients with focus on morphological changes in OCT.

Methods

This retrospective study was performed at Peking University Third Hospital, Beijing, China. 35 patients (35 eyes) with ICNV from July 2012 to October 2017 were enrolled. All procedures conformed to the tenets of the Declaration of Helsinki and the study was approved by the Medical Science Research Ethics Committee. Informed consent was obtained. Among the patients, 14 were male (14 eyes) and 21 were female (21 eyes). All patients were less than 50 years of age, and the average age was 35.94±9.471 years (ranged:17–50yr). Patients received "treat and extend" treatment regimen(11), including 1–4 initial monthly intravitreal ranibizumab (1.25 mg/0.05ml, Genentech, USA) or bevacizumab (1.25 mg/0.05ml, Genentech, USA) until there was no signs of CNV activity by the following criteria: presence of subretinal/intraretinal fluid, persistent/recurrent retinal hemorrhage or drop in visual acuity of 5 letters(14). The follow-up visits were scheduled every four weeks during this period. Subsequently, when there was no CNV activity, the follow-up interval was extended to a maximum of 12 weeks to evaluated recurrence. When recurrent exudation is detected, additional intravitreal anti-VEGF was provided and the treatment interval was reduced to the prior interval. The total follow-up period ranged from 3 months to 5 years. During the initial follow-up period, the shortest follow-up time was 12 weeks and the longest was

83.9 weeks. Then, eight patients failed to complete the follow-up period. The subsequent follow-up period was at least 2 years and the longest was 5 years.

All subjects undergone a comprehensive pre-operative examination which included a best-corrected visual acuity (BCVA) using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, intraocular pressure measured by Goldman method, slit-lamp biomicroscopy, color fundus photography, spectral-domain OCT (SD-OCT; Spectralis-OCT, Heidelberg Engineering, Heidelberg, Germany), and fluorescein angiography (ff450, Carl Zeiss GmbH, Oberkochen, Germany). With SD-OCT images, the quantitative and morphologic measurements of the fovea was evaluated. Central retinal thickness (CRT) was recorded as the central 1-mm radius of the macular map, which represented the distance between the vitreoretinal interface and the retinal pigment epithelial-Bruch's membrane complex(15) and the presence of macular edema and intraretinal/subretinal fluid was evaluated. All patients were under 50 years of age, diagnosed ICNV according to fluorescein angiography and optical coherence tomography, which showed CNV lesions in the foveal area and the thickness of the retina increased. No other ocular diseases was found during the follow-up period. Patients who had CNV caused by pathological myopia (refractive index> 6D), uveitis, angioid streaks, trauma, cytomycosis, central serous chorioretinopathy (CSC) or other hereditary ocular diseases were exclude. Patients who had received other treatments before injections of anti-VEGF, such as laser, glucocorticoid, and ocular surgery were also exclude from the study.

All patients were prescribed levofloxacin antibiotic eye drops for 3 days before and after the injection. Eyes were anesthetized with 0.4% orbucaine hydrochloride eye drops preoperatively. After sterilization, intravitreal injections of bevacizumab or ranibizumab was performed with 30-gauge needle 3.5 mm posterior to the limbus. After each intravitreal injection, follow-up visits were performed monthly and ophthalmological examinations including BCVA testing, intraocular pressure testing, fundus photography, and SD-OCT were performed to evaluate the effects of injection. Additional injections of the same anti-VEGF drug were performed when remained or recurred CNV lesions were detected by OCT. Data collected included age, gender, type of anti-VEGF therapy, number of injections, ICNV duration, baseline BCVA, baseline CRT and the resolution of BCVA and CRT after the initial follow-up period. The main observation indicators were the changes of BCVA and CRT of the first and last injections. Patients were classified into two groups according to the morphological changes based on OCT results after the initial period of treatment: patients with morphological improvement and patients without morphological improvement. After the ICNV lesion completely subsided or remained unchanged, BCVA and OCT were performed every six months to observe the recurrence of the disease. Recurrence criteria included appearance of intraretinal or subretinal fluid or heme on clinical examination and/or on SD-OCT. Recurrent ICNV lesions were retreated again using additional intravitreal anti-VEGF therapy. After receiving the same kind of anti-VEGF therapy as before, the patients were followed up every 4 weeks until there was no signs of CNV activity. Then patients were divided into two groups on the basis of the ICNV recurrence: patients with recurrence and patients without recurrence.

Statistical analysis was performed using SPSS 23.0 (SPSS Inc., USA). Data were expressed as means ± standard deviation. Follow-up and baseline data were compared using the paired t-test. Comparisons of

age, gender, type of anti-VEGF therapy, number of injections, ICNV duration, baseline BCVA, baseline CRT and the resolution of BCVA and CRT, BCVA after treatment between the two groups were performed using the Chi-square test for categorical variables and independent sample t-test for continuous variables. Univariate analysis was performed using a logistic regression model. A P value of <0.05 was considered statistically significant.

Results

Thirty-five eyes (35 patients; 14 males and 21 females) with ICNV were included in this study. Mean age was 35.94±9.471 years old. Duration of the first follow-up period was 24.25±15.97 weeks (ranged:12 to 83.9). The average number of injections was 2.40±0.78 times (ranged:1 to 4).

Visual outcomes and changes in OCT

Table 1 shows the changes after anti-VEGF treatment in patients. BCVA improved from 56.20 ± 14.13 to 73.31 ± 12.57 letters (P <0.001) one month after the last injection of the first follow-up period. CRT of patients decreased from 353.6 ± 98.70μm to 273.1 ± 53.56μm (P <0.001) one month after the last injection of the first follow-up period. Among them, 19 eyes (54.3%) increased 15 letters or more in BCVA after the treatment. 12 eyes (34.3%) increased less than 15 letters in BCVA. And 4 eyes (11.4%) decreased in BCVA.

Table 1. Changes in visual acuity and OCT after intravitreal anti-VEGF treatments in patients

Times	Eyes	BCVA	CRT（μm）
Baseline	35	56.20±14.13	353.6±98.70
1 month after the last treatment	35	73.31±12.57	273.1±53.56
t-value		5.85	5.65
P		<0.001	<0.001

Comparison between subgroups according to the morphological change

Patients were classified into two groups on the basis of the morphological improvement according to OCT reports at the last follow-up in the first period: patients with morphological improvement and

patients without morphological improvement. In addition, factors which affected the prognosis were analyzed. Among them, eyes with morphological improvement were defined as: compared to the baseline, CNV lesions in the macular region was resolved or only scar remained (Fig. 1). The remaining eyes whose intraretinal/subretinal fluid remained or no recovery of foveal contour were defined as the group without morphological improvement (Fig. 2). As shown in Table 2, there was no statistical difference in age, gender, eyes, duration of disease, number of injections, and baseline CRT between the two groups (P>0.05). Among eyes with morphological improvement, 3 eyes (23.1%) were treated with intravitreal bevacizumab, and 10 eyes (76.9%) were treated with intravitreal ranibizumab. Among eyes without morphological improvement, 7 eyes (31.8%) received intravitreal bevacizumab treatment, and 15 eyes (68.2%) received intravitreal ranibizumab treatment. There was no significant statistical difference between the two groups (P=0.709). The baseline BCVA (63.00 ± 14.24) of patients with morphological improvement was significantly better than patients without morphological change (52.18 ± 12.73; P=0.026). After intravitreal anti-VEGF treatment, BCVA and CRT improvement were observed in both groups compared with baseline, but the differences were not statistical significant (P> 0.05).

Table 2. Comparison of parameters between patients with and without morphological improvement

Characteristics	Patients with morphological improvement（n=13）	Patients without morphological improvement（n=22）	P
Age(a)	34.46±9.404	36.82±9.620	0.544
Gender(M/F)	7/6	7/15	0.288
Eye(right/left)	3/10	10/12	0.282
Anti-VEGF(bevacizumab ranibizumab)	3/10	7/15	0.709
Duration of disease(wk)	21.53±11.85	25.86±18.04	0.446
Number of injections	2.23±0.725	2.50±0.802	0.328
Baseline BCVA	63.00±14.24	52.18±12.73	0.026*
Baseline CRT	347.9±104.1	357.0±97.73	0.795
BCVA improvement	14.69±13.51	18.55±19.35	0.532
CRT decrease	99.77±89.55	69.18±80.89	0.306

Univariate logistic analysis of morphological improvement

Number of injections, baseline BCVA, age, baseline CRT, duration of disease were included in a univariate analysis using morphological improvement after the last injection in the first follow-up period as the

dependent variable. Factors affecting the efficacy of intravitreal anti-VEGF injections were analyzed. Univariate analysis showed that the baseline BCVA had the strongest correlation with the morphological alterations after treatments (OR=1.063,P=0.04) (Table 3).

Table 3. Univariate analysis of morphological improvement

Characteristics	OR	95%CI	P
Number of injections	0.629	0.253-1.566	0.319
Baseline BCVA	1.063	1.004-1.126	0.036*
Age	0.973	0.904-1.048	0.473
Baseline CRT	0.999	0.992-1.006	0.788
Duration of disease(wk)	0.980	0.931-1.032	0.444

Comparison between subgroups according to the baseline BCVA

Patients were divided into 2 groups on the basis of the baseline BCVA: less than 60 letters (21 eyes) and better than 60 letters (14 eyes). CRT of the patients whose baseline BCVA were less than 60 letters reduced by 66.71μm at the end of the first follow-up period. CRT of the patients whose baseline BCVA were better than 60 letters reduced by 101.3μm at the end of the first follow-up period. There was no significant difference between the two groups (P=0.240). And there was no significant difference in baseline CRT between the two groups (P=0.877). Although there were no statistical different in CRT reduction between the two groups, CRT was lower in the group with better baseline BCVA than in the group with poor baseline BCVA (P=0.028) after intravitreal anti-VEGF therapy (Table 4).

Table 4. Comparison of parameters between patients with different baseline BCVA

Characteristics	Baseline BCVA⊠60 letters	Baseline BCVA≥60 letters	P
Number of injections	2.43±0.746	2.36±0.842	0.794
Baseline CRT	355.8±102.4	350.4±96.50	0.877
CRT change	66.71±89.04	101.3±74.79	0.240
Final CRT	289.1±56.04	249.1±40.47	0.028*

Recurrence

After the end of the first follow-up period, there was no evidence of CNV activity. We continued to follow up and observe the ICNV patients, who were scheduled to visit the doctor every 12 weeks, and 8 patients lost to follow-up. The longest follow-up period was 259.7 weeks after diagnosis, and the shortest follow-up period was 111.5 weeks. The mean follow-up period was 168.0 ± 34.82 weeks. During this follow-up period, CNV recurrence was found after the last anti-VEGF therapy. In the CNV recurrent cases, the vision of patients decreased again and new OCT scan showed recurred intraretinal/subretinal fluid exudate or hemorrhages, and the increased retina thickness (Fig. 3, Fig. 4). In this study, CNV recurred in 6 cases, with a recurrence rate of 22.22%. Recurrence was observed at a mean of 90.83 ± 49.20 weeks (ranged from 33 weeks to 177 weeks) after diagnosis. After receiving repeated anti-VEGF therapy, CNV lesions subsided. Interval to the next follow-up shortened to 4 weeks after the injection until there was no evidence of CNV activity. BCVA of the last follow-up was recorded. Patients with recurrence had received an average of 3.67±0.816 injections, which was significantly higher than that of patients without recurrence. There was no significant difference in age, type of the anti-VEGF drugs, baseline BCVA, baseline CRT and final BCVA between the two groups (Table 5, Table 6). Patients were divided into groups according to the morphological improvement after the last intravitreal treatments and recurrence of ICNV during follow-up period. Among patients with recurrence, there were 1 case (16.7%) which showed morphological improvement and 5 cases (83.3%) who didn't show morphological improvement. Among patients without recurrence, there were 7 cases (33.3%) with morphological improvement and 14 cases (66.6%) without morphological improvement. There was no significant difference between the two groups (χ^2=0.622,P⟩0.05; Table 6).

Table 5. Comparison between patients with and without recurrence

Characteristics	Patients with recurrence（n=6）	Patients without recurrence（n=21）	P
Age	37.50±11.98	35.38±8.755	0.634
Number of injections	3.67±0.816	2.24±0.768	0.001*
Baseline BCVA	49.67±15.14	57.43±15.15	0.279
Baseline CRT	298.8±63.87	349.6±93.55	0.227
Final BCVA	65.33±16.68	75.95±9.687	0.056
Duration of follow-up	168.5±53.43	167.9±29.37	0.973

Table 6. Comparison of anti-VEGF therapy and morphological changes between patients with and without recurrence

	Eyes	Anti-VEGF therapy				Morphological changes			
		bevacizumab		ranibizumab		Patients with morphological improvement		Patients without morphological improvement	
		Eyes	n	Eyes	n	Eyes	n	Eyes	n
Patients with recurrence	6	3	50.0%	3	50.0%	1	16.7%	5	83.3%
Patients without recurrence	21	5	23.8%	16	76.2%	7	33.3%	14	66.6%
χ^2		1.535				0.622			
P		0.319				0.633			

Discussion

Comparative studies have shown promising outcomes of anti-VEGF therapy for ICNV, but few have demonstrated the long-term efficacy. The aim of the present study was to investigate the prognostic factors and long-term outcomes related to retinal morphological changes of ICNV and the timing and incidence of CNV recurrence.

There are numerous treatment options for ICNV including laser photocoagulation, radiation therapy, verteporfin photodynamic therapy (vPDT), and transpupillary thermotherapy (TTT), etc., but most of them have poor long-term prognosis and many complications(16). At present, PDT and intravitreal anti-VEGF therapy are widely used for ICNV treatment. Because of the high cost of PDT therapy, possible repeated treatment requirements, and potential retinopathy secondary to pigment epithelial dysfunction(17), this treatment option limited its clinical application. Vascular endothelial growth factor (VEGF) plays an important role in the pathogenesis of CNV(18). VEGF is a neovascular stimulating factor that specifically binds to vascular endothelium to stimulate angiogenesis(19). Anti-VEGF agents can specifically bind to VEGF, regulate neovascularization, reduce permeability, and protect the internal retina(20, 21). In this study, a "treat and extend" intravitreal anti-VEGF therapy was used to treat ICNV. Patients were treated with ranibizumab or bevacizumab. A number of studies have found that, ranibizumab and bevacizumab seem equally effective in treating ICNV, recovery of visual acuity and CRT reduction(22–24). In our study, during the initial period, patients were scheduled to visit hospital 1 month after each injection. At the end of the initial follow-up period, BCVA increased by an average of 17 letters, and CRT decreased by 80μm on average, suggesting that both intravitreal anti-VEGF agents had beneficial effect in the treatment of ICNV. In addition, no cases of complications, such as endophthalmitis, retinal detachment were observed after injections. Lai TYY et al(3) reported that after 12 months of intravitreal bevacizumab, BCVA increased by an average of 11 letters, CRT decreased by an average of 77μm, suggesting the efficacy of this therapy. These results were confirmed by Inoue M et al(25), who reported that through intravitreal bevacizumab for subfoveal ICNV, patient's BCVA increased from 0.31 to 0.15 LogMAR, the CRT decreased by 71 μm on

average, and after one year of follow-up, patients' visual acuity remained stable and no visual loss was observed. Our study also showed similar results to these studies. By comparison, our study had demonstrated that both bevacizumab and ranibizumab were efficient in curing ICNV. And we decided to follow up the patients for a longer period.

Since the introduction of SD-OCT, it has become a major element in both initial diagnosis and management of patients with fundus disease, especially exudative AMD(13). Because OCT scan is safe, quick and non-invasive, it is regarded as a routine follow-up examination and retreatment indication. Morphological improvement represents recovery of foveal contour and indicates a good prognosis and retinal function(26), so nowadays, we often diagnose the CNV recurrence and decide whether to continue the anti-VEGF treatment according to the best corrected visual acuity and the morphological changes in OCT scans(27). In this study, we used morphological changes of OCT as an important parameter. Therefore, in the current study, patients were regrouped to investigate the predictors for outcomes related to the OCT morphological changes at the end of the initial follow-up period. Further analysis indicated that a better baseline BCVA was associated with morphological improvement, however other parameters such as the number of injections, age, duration of disease, and baseline CRT had little correlation with prognosis. Then the patients were further divided into two groups according to their baseline BCVA to confirm this finding. We found that the better the baseline BCVA (more than 60 letters) was, lower the CRT value was after injections, and more significant the resolution of foveal CNV was. It suggested that a timely treatment for ICNV when BCVA remained good might result in better resolution of CNV lesions, recovery of foveal contour and better visual outcome. This was consistent with the study by Sudhalkar A et al(22) that patients with higher baseline BCVA had better prognosis. High permeability of neovascular could cause bleeding and exudation(6). The levels of IL−17, IL−2, IL−10, GM-CSF and other inflammatory factors in the aqueous humor of ICNV patients increased significantly(6, 28), which induced inflammatory reactions and retinal damage. ICNV patients with good baseline BCVA might not suffer from those irreversible cytotoxic effects and retinal damage mentioned above yet, therefore, our results suggest that timely anti-VEGF treatment can effectively reduce the inflammatory response and make CNV lesions subsided, in turn leads to better prognosis.

Subsequently, we continued to observe the recurrence of the disease after the end of treatment. After multiple anti-VEGF injections, there were 6 patients whose CRT was reduced and the subretinal effusion subsided with recovery of foveal contour after the initial follow-up period, underwent recurrence of ICNV. The longest recurrence period was 177 weeks after diagnosis, suggesting that although ICNV lesions subsided after anti-VEGF treatments, long-term follow-up was still needed to prevent recurrence of the disease and irreversible visual damage. Kim JH et al(29) reported a long-term follow-up of 26 patients with ICNV after intravitreal anti-VEGF treatment, in which the mean follow-up period was 33.9 months. The recurrence rate was 30.8% and the recurrence of the disease was not related to age, baseline BCVA or CRT. But visual prognosis of patients with recurrence was not significantly different from that without recurrence. In our study, CNV lesions in the 6 patients with recurrence had subsided after additional intravitreal anti-VEGF treatment. The recurrence rate was 22.22%. Compared with the non-recurrence group, final BCVA of the recurrence group were not statistical different, suggesting that recurrent ICNV

could be treated with additional anti-VEGF treatment and recurrence had no significant effect on long-term prognosis of the disease, which was consistent with the results of Kim JH's study(29). In our study, patients did not change the type of anti-VEGF agent. Compared with the non-recurrence group, type of anti-VEGF agent was not statistical different, suggesting that additional anti-VEGF treatment was effective for ICNV lesions. At present, indicator for diagnosing ICNV recurrence remains unclear. Fluorescein angiography can clearly show leakage of fluorescein which indicates disease occurrence(30). However, fluorescein angiography is an invasive examination and is not suitable for frequent examination during long-term follow-up(31). Therefore, OCT scan was scheduled every time when patients came to hospital during the long-term follow-up in the current study. We analyzed the relationship between ICNV recurrence and the morphological improvement in OCT at the end of the first follow-up period. We found that there was no correlation between the morphological changes of OCT and recurrence. In our study, patients with good morphological improvement after treatments also relapsed during long-term follow-up, suggesting that improvement in foveal morphology might not effectively predict the long-term prognosis. This may attribute to the formation of scar and decreased retinal function due to ICNV disease, which can lead to poor visual prognosis(32). Our study suggests that although patients with morphological improvement and recovery of foveal contour seems to have good prognosis, long-term follow-up should also be performed to avoid ICNV recurrence.

There were limitations to this study. The study was retrospective, the sample size was relatively small, the follow-up time was too long which resulted in loss of some follow-up patients. The results need to be validated by prospective, large sample size long-term follow-up studies.

Conclusion

In conclusion, anti-VEGF therapy was effective on ICNV, which could improve BCVA and make CNV lesions subsided. Patients with good baseline BCVA had better prognosis. The morphological improvement during follow-up period had no significant correlation with recurrence, suggesting that long-term follow-up should be performed in all ICNV patients. Re-treatment with anti-VEGF could effectively lead to resolution of recurrent ICNV but might not significantly influence long-term prognosis of the disease. Further clinical research with larger sample size and long-term follow-up are necessary to explore predictors and outcomes for ICNV prognosis and recurrence.

Abbreviations

CNV: Choroidal neovascularization

VEGF: Vascular endothelial growth factor

ICNV: Idiopathic choroidal neovascularization

BCVA: Best corrected visual acuity

CRT: Central retinal thickness

RPE: Retinal pigment epithelium

AMD: Age-related macular degeneration

CSC: Central serous chorioretinopathy

FFA: Fundus fluorescein angiography

OCT: Optical coherence tomography

SD-OCT: Spectral-domain optical coherence tomography

vPDT: Verteporfin photodynamic therapy

PDT: Photodynamic therapy

TTT: Transpupillary thermotherapy

Declarations

Ethics approval and consent to participate

The study followed the tenets of the Declaration of Helsinki and was approved by the Peking University Third Hospital Medical Science Research Ethics Committee. All patients provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

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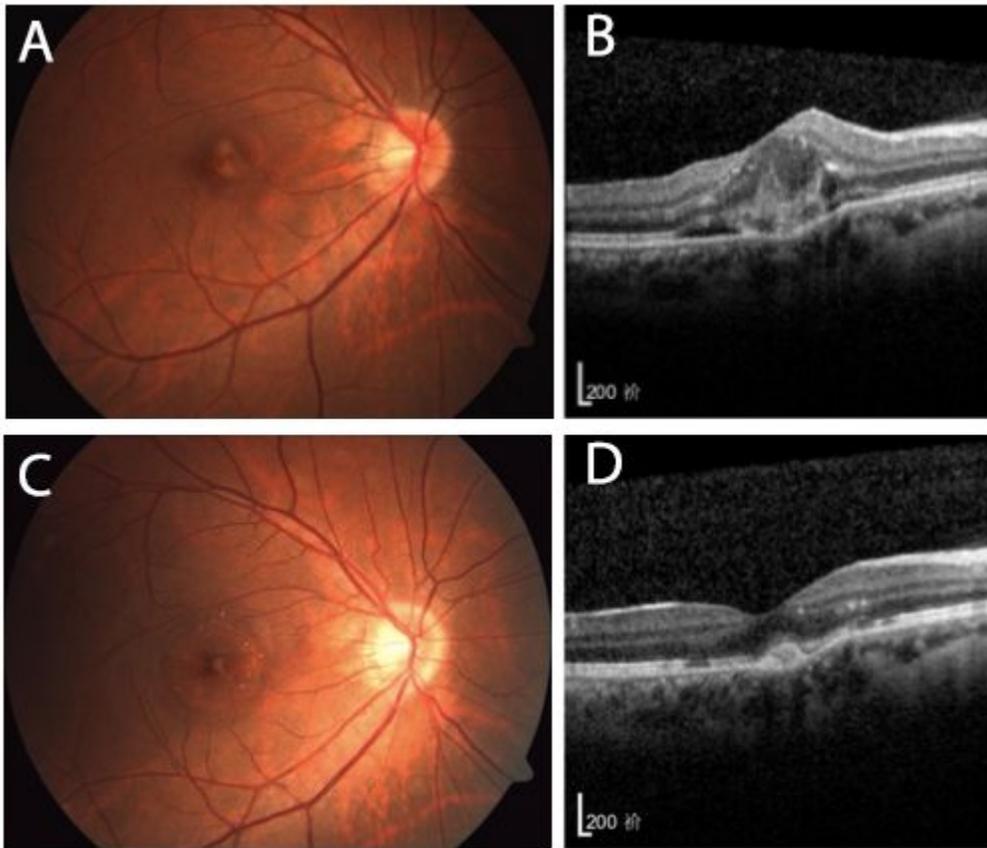
Figures

Figure 1

Left eye of a patient with morphological improvement after the first follow-up period. At baseline, BCVA was 54 letters, color fundus photo (A) showed a pigmentation disorder of the macular center. SD-OCT (B) showed ICNV lesion and intraretinal fluid, with significant increased CRT. After two intravitreal anti-VEGF injections, BCVA increased to 75 letters. Fundus color photo (C) and SD-OCT (D) showed that the fluid had subsided and scar with recovery of foveal contour.
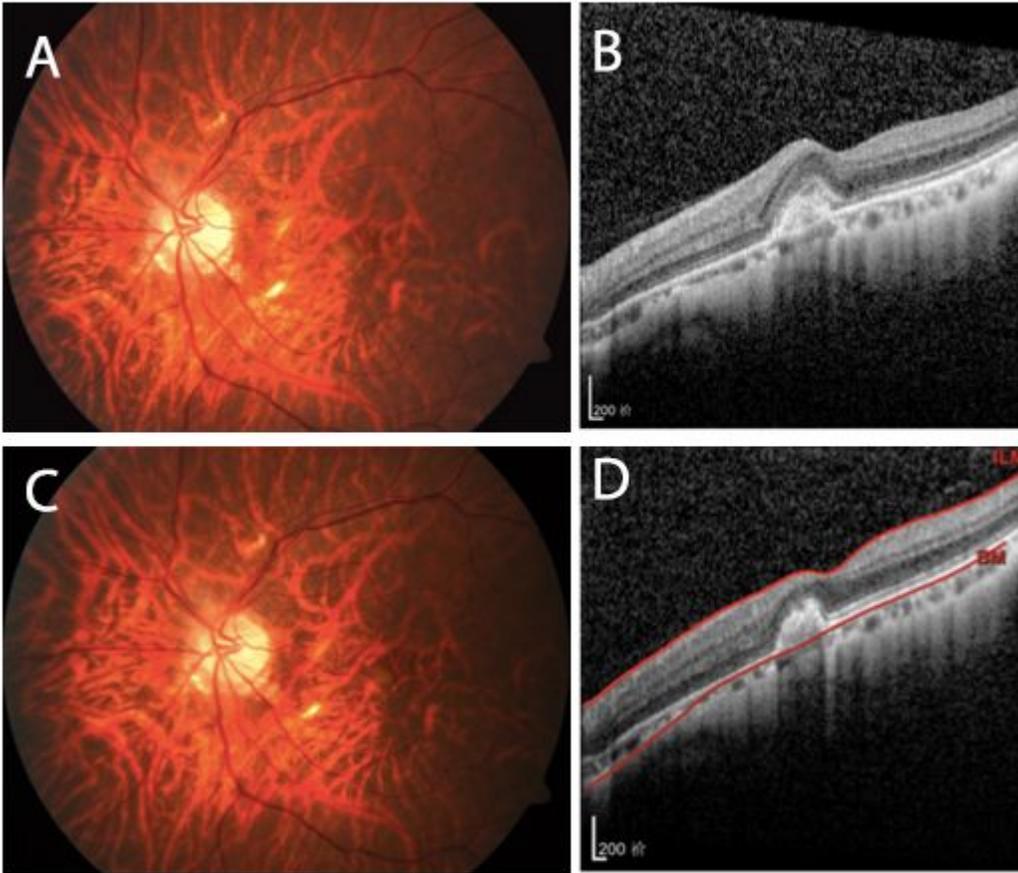
Figure 2

Left eye of a patient without morphological improvement after the first follow-up period. At baseline, BCVA was 53 letters, color fundus photo (A) showed a pigmentation disorder of the macular center. SD-OCT (B) showed the CNV lesion at the center of the macula, with subretinal fluid and CRT increased. After two intravitreal anti-VEGF injections, BCVA increased to 75 letters. Fundus color photo (C) and SD-OCT (D) showed the ICNV lesion remained.
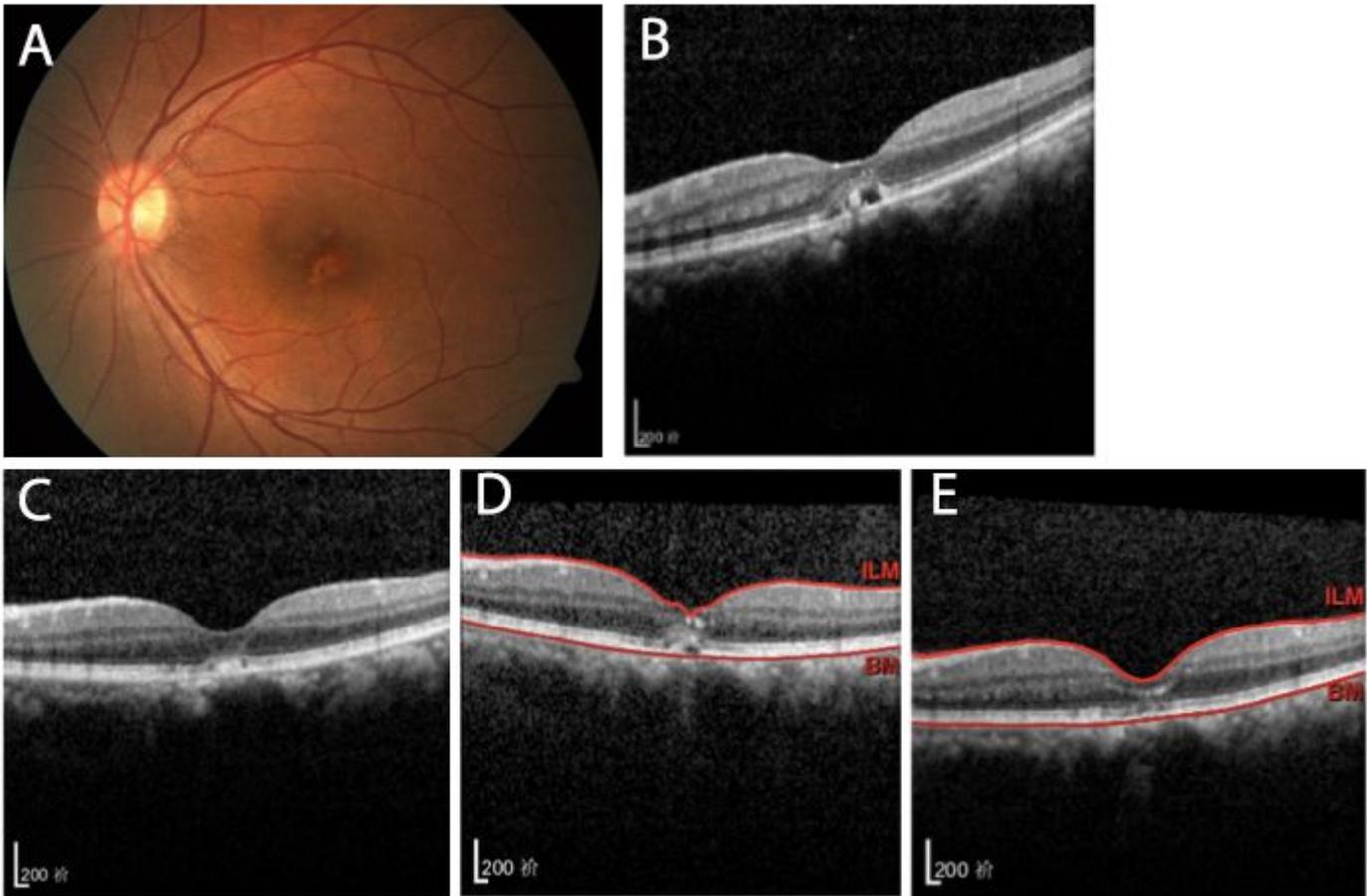
Figure 3

Left eye of a patient with morphological improvement after first follow-up period and ICNV recurred. At baseline, BCVA was 65 letters, color fundus photo (A) showed a pigmentation disorder of the macular center. SD-OCT (B) showed CNV lesions with intraretinal fluid, and the structure of each layer of the retina was unclear. 5 months later, after the second intravitreal injection, BCVA improved to 75 letters, OCT (C) showed that CNV lesions had subsided with recovery of foveal contour. 18 months after initial diagnosis, OCT (D) showed recurred intraretinal fluid and the thickness of fovea increased significantly. One month after an additional intravitreal anti-VEGF therapy (E), fovea returned to normal with the CNV lesions had completely subsided.
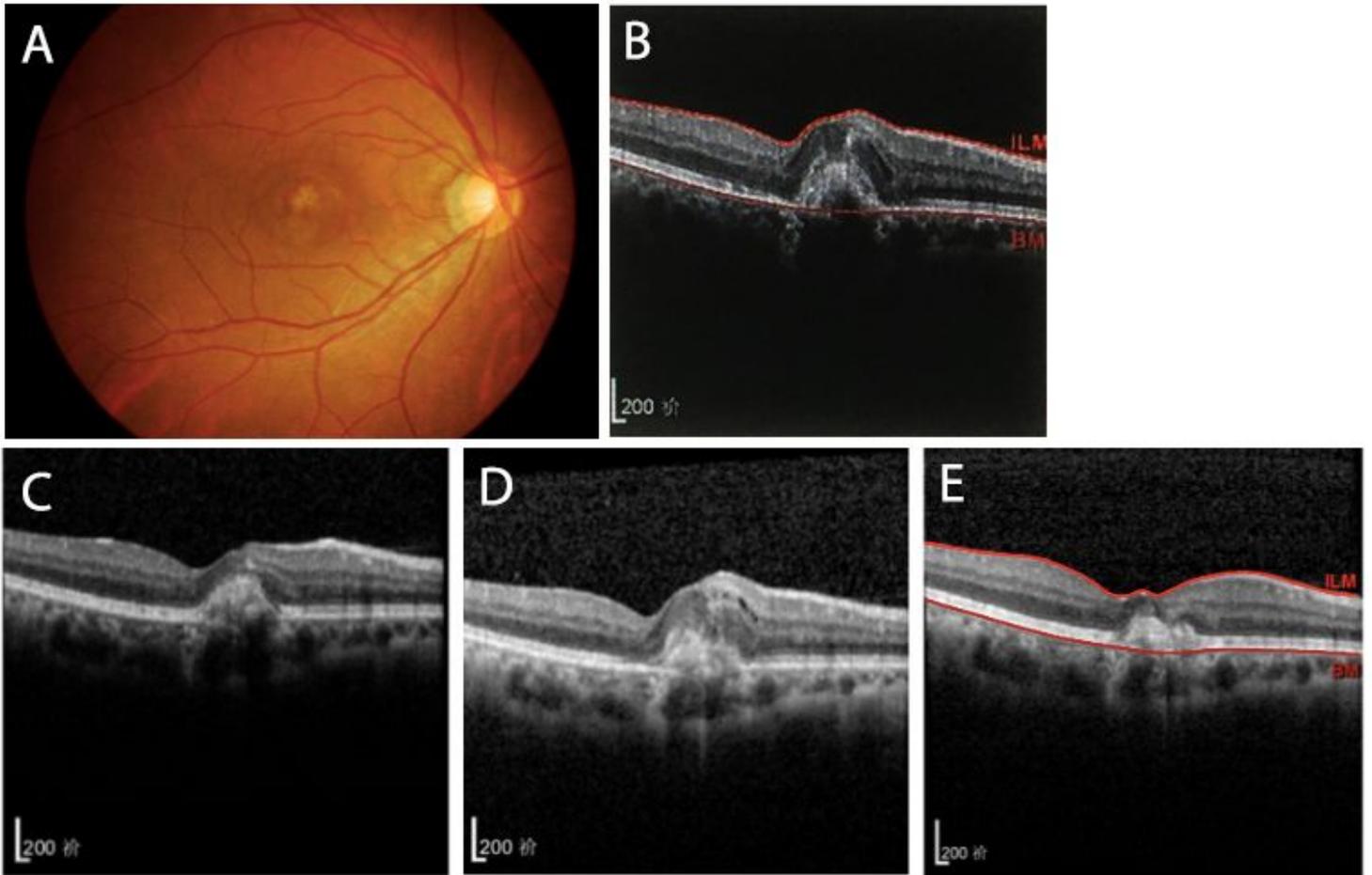
Figure 4

Right eye of a patient without morphological improvement after first follow-up period and ICNV recurred. At baseline, BCVA was 50 letters, color fundus photo (A) showed a pigmentation disorder of the macular center. SD-OCT (B) showed CNV lesions with subretinal fluid, and the structure of each layer of the retina was unclear. 11 months later, after the second intravitreal injection, BCVA improved to 69 letters, OCT (C) showed scar. 15 months after initial diagnosis, BCVA decreased to 44 letters, and OCT (D) showed recurred subretinal fluid and the thickness of fovea increased significantly. One month after an additional intravitreal anti-VEGF therapy (E), subretinal fluid had subsided and scar remained.