Original article

Clinical characteristics and antivascular endothelial growth factor effect of choroidal neovascularization in younger patients in Taiwan

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ARTICLE INFO

ABSTRACT

Background/Purpose: The purpose of this study is to share experiences diagnosing and treating choroidal neovascularization (CNV) in young patients (age $\leq$ 50 years) at our hospital.
Methods: The study reviewed retrospective data of patients ($\leq$ 50 years old) with CNV who received antivascular endothelial growth factor treatment (anti-VEGF) between January 2007 and August 2012 at Shin Kong Wu Ho-Su Memorial Hospital. We recorded the total number of injections, types of drugs, preoperative and final best-corrected visual acuity (BCVA), central retinal thickness (CRT) in optical coherence tomography (OCT), and total follow-up times, and then used two-tailed paired t tests to compare mean changes in BCVA and CRT on OCT.
Results: The study enrolled 59 patients $\leq$ 50 years of age with CNV diagnosed in 67 eyes. The mean age was 36.9 $\pm$ 10.0 years (range, 8—50 years). Twenty-one patients were male and 38 patients were female. Forty-two CNV lesions were subfoveal, 19 were juxtafoveal, and five were extrafoveal. The mean total follow-up time was 18.5 $\pm$ 19.9 months (range, 0.5—71 months). Pathologic myopia was the most common cause of CNV in this study (47.8%), followed by punctate inner choroidopathy (17.9%), idiopathic CNV (16.4%), polypoidal choroidal vasculopathy (13.4%), angioid streaks (3.0%), and choroidal rupture (1.5%). After anti-VEGF treatment, the mean BCVA improved from 0.69 $\pm$ 0.61 to 0.42 $\pm$ 0.59 ($p < 0.05$). CRT decreased from 257.5 $\pm$ 48.2 to 210.3 $\pm$ 35.7 ($p < 0.05$). The mean number of injections was 1.9 $\pm$ 1.6 (range, 1—9).
Conclusion: In this study we found that pathologic myopia, punctate inner choroidopathy, and idiopathic and polypoidal choroidal vasculopathy comprised the four most common causes of CNV in patients $\leq$ 50 years of age in Taiwan. We also revealed that anti-VEGF treatment is highly effective in the treatment of CNV in this age group.

1. Introduction

Choroidal neovascularization (CNV) is a common cause of visual impairment in older adults in developed countries.[1–3] CNV is characterized by new, abnormal blood vessels growing from the choroid via breakage in Bruch's membrane or the basement membrane of the retinal pigment epithelium (RPE). These vessels can leak blood and fluid, and are accompanied by fibrous tissue, which often leads to damage of the retinal tissues and vision loss.[4–6] CNV develops as a consequence of processes related to wound healing and tissue repair.[4] CNV may cause vision loss from the exudation of intraretinal or subretinal fluid, hemorrhage, or fibrosis.[5] CNV is most commonly seen in patients with exudative age-related macular degeneration (AMD), which occurs at ages > 50 years.[2,7]

CNV can also occur in younger patients ($\leq$ 50 years), who usually do not have conspicuous drusen or pigmentary abnormalities. The biomicroscopic findings of CNV in younger patients are generally better defined when compared with CNV in older patients with AMD. The CNV is usually visible as a grayish green subretinal membrane, surrounded by a halo of pigmentation, sometimes with clearly visible subretinal blood, fluid, or lipids.[5] In

this age group, there are several causes of CNV, such as pathological myopia (PM), angioid streaks, inflammatory or infectious conditions [histoplasmosis, sarcoidosis, multifocal choroiditis, punctate inner choroidopathy (PIC)], choroidal tumors (nevi, melanoma, hemangioma, osteoma), trauma (choroidal rupture, laser photocoagulation), or idiopathic cause.[5,6,8] Regardless of the cause, the vision loss as a result of untreated CNV may have a major impact on the daily lives of patients, especially if both eyes are affected. The initial stimulus that activates the processes leading to the development of CNV can arise from several sources, such as lacquer cracks in pathologic myopia, disruption of the elastic layer of Bruch's membrane in angioid streaks, or inflammatory conditions in PIC or multifocal choroiditis.[4—6]

In the past decade, studies have found that antivascular endothelial growth factor (anti-VEGF), such as bevacizumab, ranibizumab, and aflibercept, is highly effective in treating CNV in AMD.[9—14] However, there are not as many studies of anti-VEGF treatment of CNV in younger patients compared with patients > 50 years of age. The purpose of this study is to reveal the clinical characteristics and the result of anti-VEGF treatment of CNV in young patients (age ≤ 50 years) at our hospital.

2. Materials and methods

This study reviewed a retrospective chart of CNV patients from January 2007 to August 2012 at Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan. The study was approved by the institute review board of Shin Kong Wu Ho-Su Memorial Hospital and conformed to the tenet of the Declaration of Helsinki. The study included patients who were ≤ 50 years of age and who were diagnosed with CNV. All patients had evidence of dye leakage that represented occult or classic CNV over subfoveal or juxtafoveal areas in fluorescein angiography (FA) and/or indocyanine angiography at baseline. Optical coherence tomography (OCT; Stratus III; Carl Zeiss, Dublin, CA, USA) also revealed evidence of CNV such as subretinal fluid, macular edema, RPE detachment (RPED), subretinal or sub-RPE hyperreflectivity lesion, derangement of retina-RPE tissue density, or various combinations of the above findings.[15] Exclusion criteria were as follows: (1) patients with any retinal vasculopathies (including diabetic retinopathy, retinal vein occlusions, retinal vasculitis, etc.); (2) patients with previous subfoveal or juxtafoveal laser treatment; (3) patients with advanced glaucoma or intraocular pressure in the study eye > 22 mmHg in spite of adequate treatment; and (4) patients with acute ocular or periocular infection. We recorded the patients' sex, age, lesion side (subfoveal, juxtafoveal, or extrafoveal), total follow-up time, and initial best-corrected visual acuity (BCVA) using Snellen charts in logMAR and Early Treatment Diabetic Retinopathy Study (ETDRS) charts. Funduscopic examination, OCT, FA, and, if needed, indocyanine angiography were performed on the initial visit for every patient. In the follow-up period, funduscopic examination and OCT were performed on every visit, whereas FA and/or indocyanine

green angiography were performed at the discretion of attending physician.

The study employed intravitreal anti-VEGF injection including bevacizumab and ranibizumab for most patients, except for some patients with extrafoveal CNV. For those patients who received anti-VEGF treatment, the following data were recorded: total number of injections, types of drugs (bevacizumab or ranibizumab) used, preoperative and final BCVA, EDTRS, and central retinal thickness (CRT). The study also documented other treatment such as pars plana vitrectomy, photodynamic therapy (PDT), and photocoagulation therapy.

The study performed statistical analysis using SPSS version 17.0 (SPSS, Chicago, IL, USA). We used two-tailed paired t tests to compare mean changes in BCVA and CRT on OCT. A value of $p < 0.05$ was considered statistically significant. Values in the text are represented by mean ± standard deviation.

3. Results

The study enrolled 59 patients (67 eyes) ≤ 50 years of age diagnosed with CNV. We identified six types of CNV in young patients, the definition of which is depicted in Table 1 and includes CNV associated with PM, PIC, idiopathic cause, polypoidal choroidal vasculopathy (PCV), angioid streak, and traumatic choroidal rupture.

Table 2 summarizes all demographic data including mean age, sex, cause of CNV, lesion site, and follow-up time. The mean age was 36.9 ± 10.0 years (range, 8—50). Twenty-one patients were male (35.6%) and 38 patients were female (64.4%). The diagnoses of 32 eyes (47.8%) exhibited PM, 12 eyes (17.9%) exhibited PIC, 11 eyes (16.4%) exhibited idiopathic CNV (ICNV), nine eyes (13.4%) exhibited PCV, two eyes (3.0%) exhibited angioid streaks, and one eye (1.5%) exhibited choroidal rupture. The CNV lesions were subfoveal in 42 (63.6%) eyes, juxtafoveal in 19 (28.8%) eyes, and extrafoveal in five (7.6%) eyes. In one case of PCV, the lesions were ruptured with vitreous hemorrhage, and therefore the lesion site could not be classified.

We administered anti-VEGF drugs, including bevacizumab and ranibizumab, to treat 63 eyes (32 PM, 9 PIC, 11 idiopathic CNV, 8 PCV, 2 angioid streaks, and 1 choroidal rupture). All lesion eyes in the category of PM, idiopathic CNV, angioid streaks, and choroidal rupture received anti-VEGF injection; one eye in PCV received vitrectomy without anti-VEGF owing to vitreous hemorrhage; one eye of PIC was lost in follow up before receiving treatment, and two eyes in PIC received oral steroid therapy instead of anti-VEGF. The mean total follow-up time was 18.5 ± 19.9 months (range, 0.5—71). The mean number of intravitreal injections was 1.9 ± 1.6 (range, 1—9) with 1.7 ± 1.3 in PM, 2.7 ± 2.5 in PIC, 1.6 ± 1.2 in idiopathic CNV, 2.2 ± 1.1 in PCV, 1.0 ± 0.0 in angioid streaks, and 1.0 in choroidal rupture (Table 3). We administered two injections of ranibizumab in PIC and idiopathic CNV, respectively, and others were given bevacizumab injections. In addition to anti-VEGF

Table 1
Definition of CNV types in young patients.

Type of CNV	Definition
PM	Myopia > 6 diopter and with characteristic fundus features of PM such as lacquer cracks, patch atrophy, peripapillary atrophy or posterior staphyloma
PIC	Characteristic fundus features of PIC such as multiple small yellow-white nodular lesions or atrophic scars
PCV	Typical finding of polypoidal lesion in ICG
Angioid streaks	Characteristic feature of irregular narrow streaks radiated from optic nerve head
Traumatic choroidal rupture	Trauma history and linear tear in choroid, Bruch membrane, and RPE layer
Idiopathic	Absence of any other ophthalmic abnormality

CNV = choroidal neovascularization; ICG = indocyanine angiography; PCV = polypoidal choroidal vasculopathy; PIC = punctate inner choroidopathy; PM = pathological myopia; RPE = retinal pigment epithelium.

Table 2
Demographic data of patients.

	All	PM	PIC	ICNV	PCV	Angioid streaks	Choroidal rupture
No. of patients (%)	59	30 (50.8%)	9 (15.3%)	11 (18.6%)	7 (11.9%)	1 (1.7%)	1 (1.7%)
Sex:							
Male	21 (35.6%)	9 (30%)	2 (22.2%)	3 (27.3%)	6 (85.7%)	0	1 (100%)
Female	38 (64.4%)	21 (70%)	7 (77.8%)	8 (72.7%)	1 (14.3%)	1 (100%)	0
Mean age (y)	36.9 ± 10.0	36.2 ± 7.2	25.1 ± 10.6	35.5 ± 8.0	48.0 ± 1.3	50.0 ± 0.0	28.0
No. of eyes (%)	67	32 (47.8%)	12 (17.9%)	11 (16.4%)	9 (13.4%)	2 (3.0%)	1 (1.5%)
Lesion site:[a]							
Subfoveal	42 (63.6%)	20 (62.5%)	6 (50.0%)	10 (90.9%)	3 (37.5%)	2 (100%)	1 (100%)
Juxtafoveal	19 (28.8%)	9 (28.1%)	5 (41.7%)	1 (9.1%)	4 (50.0%)	0	0
Extrafoveal	5 (7.6%)	3 (9.4%)	1 (8.3%)	0	1 (12.5%)	0	0
Follow up time (mo)	18.5 ± 19.9	18.8 ± 20.1	22.8 ± 19.9	23.3 ± 20.9	9.9 ± 20.8	4.0 ± 0.0	4.5

ICNV = idiopathic choroidal neovascularization; PCV = polypoidal choroidal vasculopathy; PIC = punctate inner choroidopathy; PM = pathological myopia.
[a] One eye was diagnosed as ruptured choroidal neovascularization (CNV) in PCV and therefore was not classified as a subfoveal or juxtafoveal lesion.

Table 3
Number of intravitreal injections.

	All	PM	PIC	ICNV	PCV	Angioid streaks	Choroidal rupture
Number of eye injected	63	32	9	11	8	2	1
Total number of injections	117	55[a]	24[b]	18[b]	17[c]	2	1
Mean number of injections	1.9 ± 1.6	1.7 ± 1.3	2.7 ± 2.5	1.6 ± 1.2	2.2 ± 1.1	1.0 ± 0.0	1.0
Duration between injections	11.3 ± 1.2	10.9 ± 2.1	10.9 ± 1.3	13.4 ± 1.5	12.1 ± 2.2	1.0 ± 0.0	4.5
Follow-up time (mo)	18.5 ± 19.9	18.8 ± 20.1	22.8 ± 19.9	23.3 ± 20.9	22.9 ± 20.8	1.0 ± 0.0	4.5

ICNV = idiopathic choroidal neovascularization; PCV = polypoidal choroidal vasculopathy; PDT = photodynamic therapy; PIC = punctate inner choroidopathy; PM = pathological myopia.
[a] One patient of PM received PDT.
[b] One injection of ranibizumab in PIC and idiopathic CNV, others were bevacizumab.
[c] One patient of PCV received focal laser treatment, and 2 received vitrectomy for vitreous hemorrhage; one patient of PM received PDT.

treatment, two PCV eyes received pars plana vitrectomy owing to vitreous hemorrhage, one PCV eye received laser photocoagulation for juxtafoveal polyp, and one PM eye received PDT. Figs. 1–6 show the baseline and post-treatment FA and OCT of the cases in each group.

Tables 4 and 5 summarize the initial and final mean BCVA in logMAR and CRT, and compare the differences using paired t test. The mean BCVA improved from 0.69 ± 0.61 to 0.42 ± 0.59 after intravitreal anti-VEGF treatment ($p < 0.05$) (PM: 0.57 ± 0.46 to 0.36 ± 0.53, $p < 0.05$; ICNV: 0.69 ± 0.71 to 0.33 ± 0.57, $p < 0.05$; PCV: 1.25 ± 0.84 to 0.81 ± 0.69, $p < 0.05$; Table 4). Our study also found improvement trends for BCVA in PIC (0.43 ± 0.51 to 0.27 ± 0.39, $p = 0.12$). The overall mean CRT showed a parallel finding, which decreased from 257.5 ± 48.2 µm to 210.3 ± 35.7 µm ($p < 0.05$) (PM: 253.6 ± 40.8 to 207.2 ± 31.2, $p < 0.05$; ICNV: 272.2 ± 33.9 to 208.2 ± 43.5, $p < 0.05$; PCV: 286.3 ± 67.7 to 220.9 ± 62.7, $p = 0.05$; Table 5). We also discovered trends for decreased CRT in PIC (229.4 ± 38.0 to 202.9 ± 17.1, $p = 0.12$),
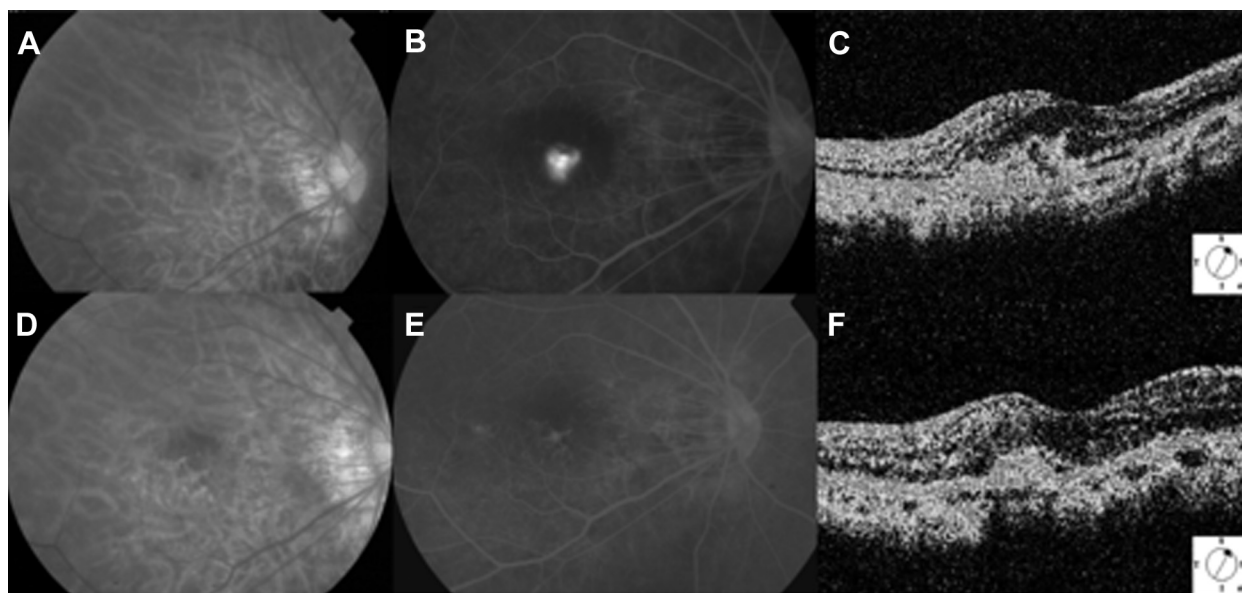
Fig. 1. A 44-year-old female with pathological myopia (PM) in her right eye. Color fundus (A) before treatment and (D) post-treatment. Before treatment, (B) fluorescein angiography (FA) showed obvious dye leakage, and there was (C) a hyperreflective lesion with elevation on optical coherence tomography (OCT). Regression of choroidal neovascularization was noted then on (E) FA without dye leakage and (F) OCT after intravitreal injection of bevacizumab.
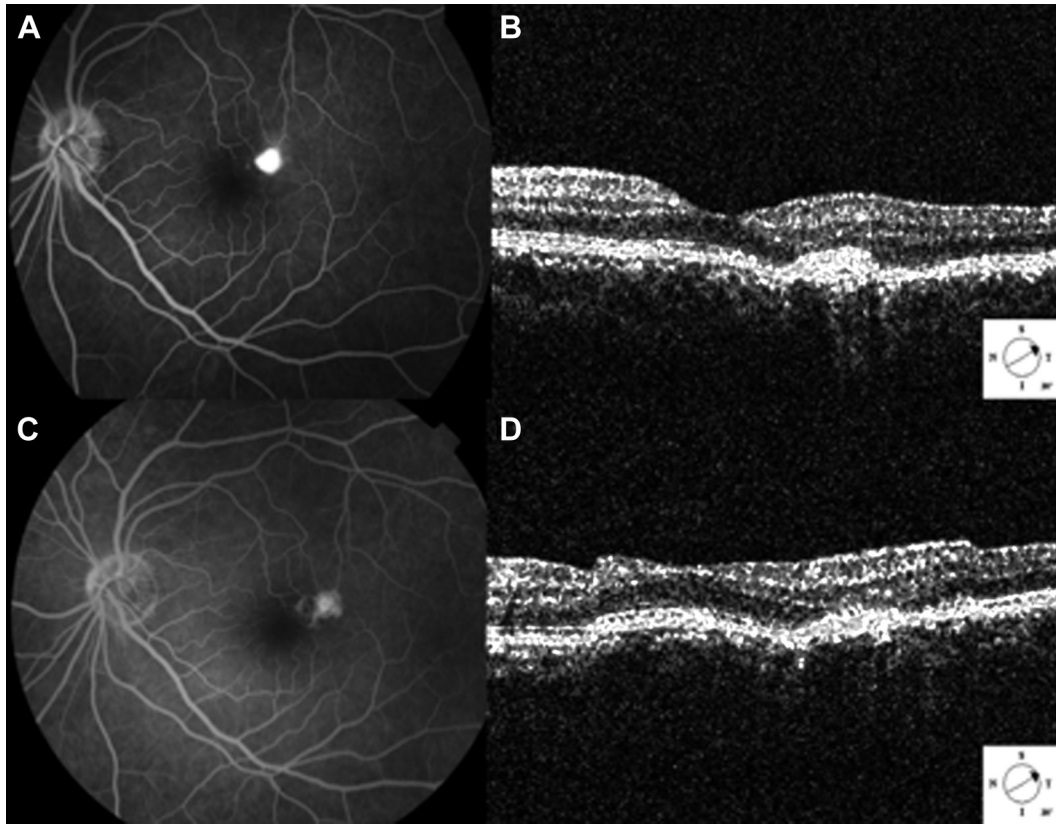
Fig. 2. A 29-year-old female with idiopathic choroidal neovascularization (CNV) in the left eye. Fluorescein angiography (FA) revealed (A) obvious dye leakage and (B) hyper-reflective lesion with thickening of retinal pigment epithelium (RPE) and Bruch's membrane. After one injection of bevacizumab, (C) no dye leakage occurred, but staining occurred on FA and (D) regression of CNV lesion on optical coherence tomography.

angioid streaks (282.5 ± 44.5 to 258.5 ± 27.5; 2 eyes only) and choroidal rupture (216 to 203; 1 eye only). Currently, the study has registered no serious adverse effects, such as endophthalmitis, uveitis, retinal detachment, vitreous hemorrhage, lens damage, stroke, myocardial infarction, exacerbated hypertension, or gastrointestinal upset.

4. Discussion

Our study revealed that PM (47.8%) is the most common cause of CNV in our cohort of 67 eyes of 59 young patients in Taiwan. PM was followed by PIC (17.9%), ICNV (16.4%), PCV (13.4%), angioid streaks (3%), and choroidal rupture (1.5%). Cohen et al[8] in 1996
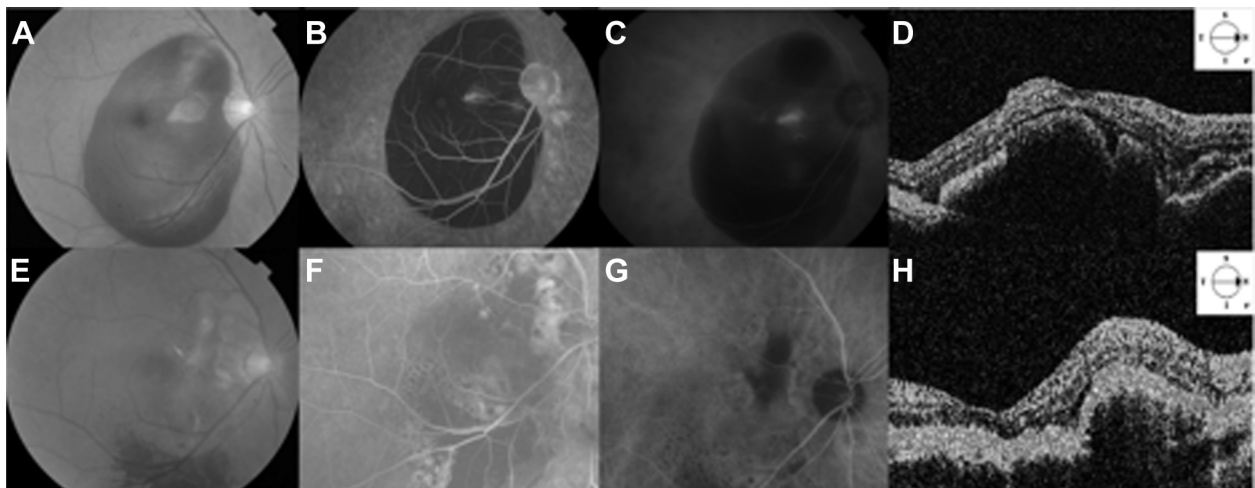
Fig. 3. A 45-year-old man with polypoidal choroidal vasculopathy (PCV) of the right eye. The first row shows the picture before treatment and the second row represents the images after intravitreal injection of bevacizumab. The initial presentation was ruptured PCV with (A) subretinal hemorrhage, (B) fluorescein angiography (FA) disclosed a point of dye leakage, and (C) indocyanine angiography (ICGA) demonstrated the hot spot. (D) Optical coherence tomography (OCT) showed subretinal hemorrhage and subretinal fluid. (E) Subretinal hemorrhage was absorbed and retinal pigment epithelium (RPE) change was left over. (F) Only a window defect was found in FA and (G) the previous hot spot also disappeared in ICGA. (H) OCT revealed absorption of subretinal fluid.
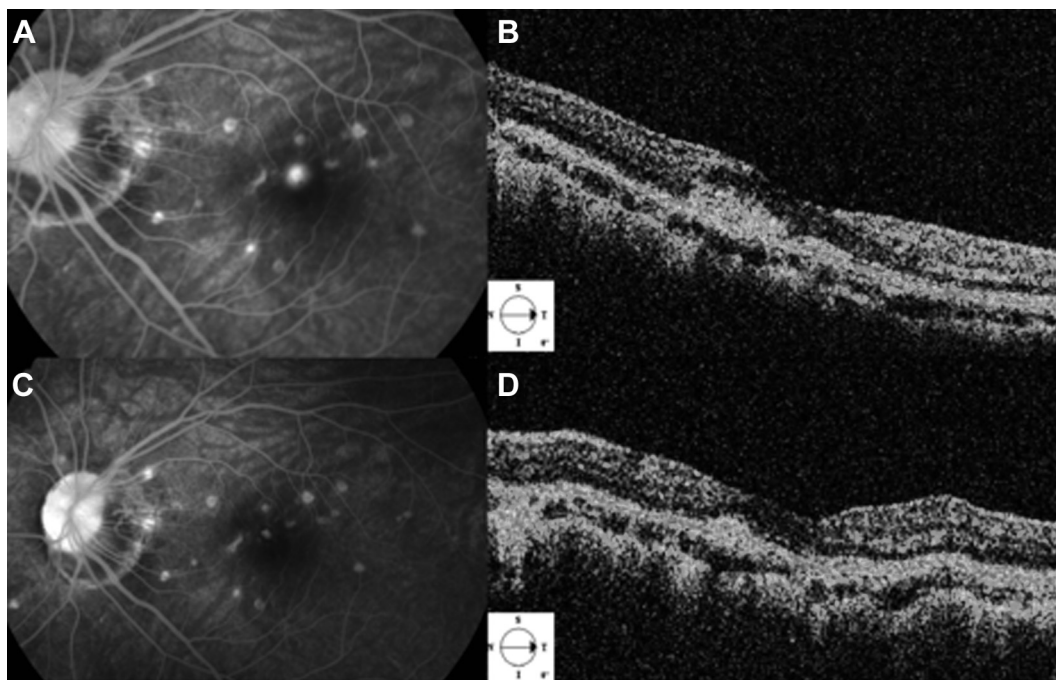
Fig. 4. A 22-year-old women was diagnosed as having punctate inner choroidopathy (PIC) in her left eye. (A) Multiple hyperfluorescence lesions were noted on fluorescein angiography (FA) with one obvious leaking point. (B) The corresponding lesion of choroidal neovascularization (CNV) on optical coherence tomography (OCT). Shrinkage of the CNV was documented from (C) FA and (D) OCT following antivascular endothelial growth factor (anti-VEGF) injection.

reported that the etiologies of CNV in 363 young patients in Western Europe were PM in 62% of the cases, ICNV in 17%, PIC in 12%, angioid streaks in 5%, and miscellaneous hereditary or traumatic or inflammatory disorders in 4%. Compared with the study of Cohen et al,[8] similar components of the common etiologies were found in our study aside from PCV, which accounted for the fourth common etiology in our study. This difference is not surprising, because the incidence of PCV is higher in Asian populations compared with Caucasian populations, and the onset age of PCV in Asian populations is known to be generally younger than typical AMD.[16—20] By contrast, pathologic myopia is the major cause of CNV in young patients in both Taiwan (47.3%) and Western Europe (62%). This common result is interesting because the prevalence of high myopia (< −6 diopters) is very different between these two areas. High myopia is much more common in Taiwanese (21%)[21] and Asian populations (6.8—21.6%)[22—26] than in European and Caucasian populations (1.4—2.5%).[27—29] The predominant prevalence of high myopia as a risk factor for the development of CNV in young patients in such different ethnic groups highlights the rarity of other factors as the cause of development of CNV in patients ≤ 50 years of age.

In addition, our study revealed that anti-VEGF is highly effective in treating CNV with various causes in young patients (≤ 50 years old). The effects of anti-VEGF are significant not only in overall BCVA improvement (from logMAR 0.69 ± 0.61 to 0.42 ± 0.59, $p < 0.05$), but also in three major categories of etiologies (PM: 0.57 ± 0.46 to 0.36 ± 0.53, $p < 0.05$; ICNV: 0.69 ± 0.71 to 0.33 ± 0.57, $p < 0.05$; and PCV: 1.25 ± 0.84 to 0.81 ± 0.69, $p < 0.05$; Table 4). Our study also found trends for improvement in PIC (0.43 ± 0.51 to 0.27 ± 0.39, $p = 0.12$), angioid streaks (1.35 ± 0.25 to 1.24 ± 0.54; 2 eyes only), and choroidal rupture (0.52 to 0.0; 1 eye only) (Table 4). We also found parallel improvement of macular edema in each category and in the overall results (Table 5). For CNV associated with AMD, frequent injection of anti-VEGF is necessary for maintaining the initial gain in the improvement of vision[9,11]; whereas in

our study for younger patients with CNV, lower injection rates of a mean injection of 1.9 ± 1.6 shots of anti-VEGF in a mean follow-up time of 18.5 ± 19.9 months (mean interval between two injections is 11.3 ± 1.2 months) could be effective in achieving the beneficial goal. Chang et al[30] also reported the results of intravitreal injection of bevacizumab for subfoveal CNV in non-AMD patients, with 3.4 mean injections/eye during a mean follow-up time of 58.8 weeks to achieve a median visual acuity of 20/40 (logMAR, 0.30). The mean number of injections and the mean duration between two injections had no significant difference among PM, idiopathic CNV, PIC, and PCV in our study ($p = 0.21$), which implies that the frequency of anti-VEGF injection is similar among younger CNV patients regardless of the etiology.

Other treatment modalities have been proposed for CNV treatment. For example, thermal laser photocoagulation is very effective in ablating the CNV lesions. However, laser photocoagulation can only be applied to extrafoveal or juxtafoveal lesions in order not to damage the retinal fovea tissue. Even in juxtafoveal lesions, the long-term results on visual acuity maintenance are limited, due to the late extension of photocoagulation scars.[31—33] In our series, the majority of lesions in most categories (except PCV) were subfoveal (Table 2), in which laser photocoagulation might not be suitable for treatment.

For subfoveal and juxtafoveal CNV, excluding AMD, verteporfin PDT has been shown to be effective in stabilizing vision in many types of CNV listed in our study, including PM,[34,35] PIC,[36,37] idiopathic CNV,[38] and PCV.[39,40] However, subsequent studies have documented limited long-term visual outcome.[41—44] Furthermore, recent studies have shown that anti-VEGF treatment seems to be more effective than PDT in improving vision in these categories.[45—49] In a prospective, multicenter study comparing the effectiveness of ranibizumab monotherapy with verteporfin PDT (the RADIANCE study) in subfoveal CNV in PM patients, Wolf et al[45] revealed that ranibizumab was significantly superior to PDT in improving the visual outcome (10.5—10.6 ETDRS letters in
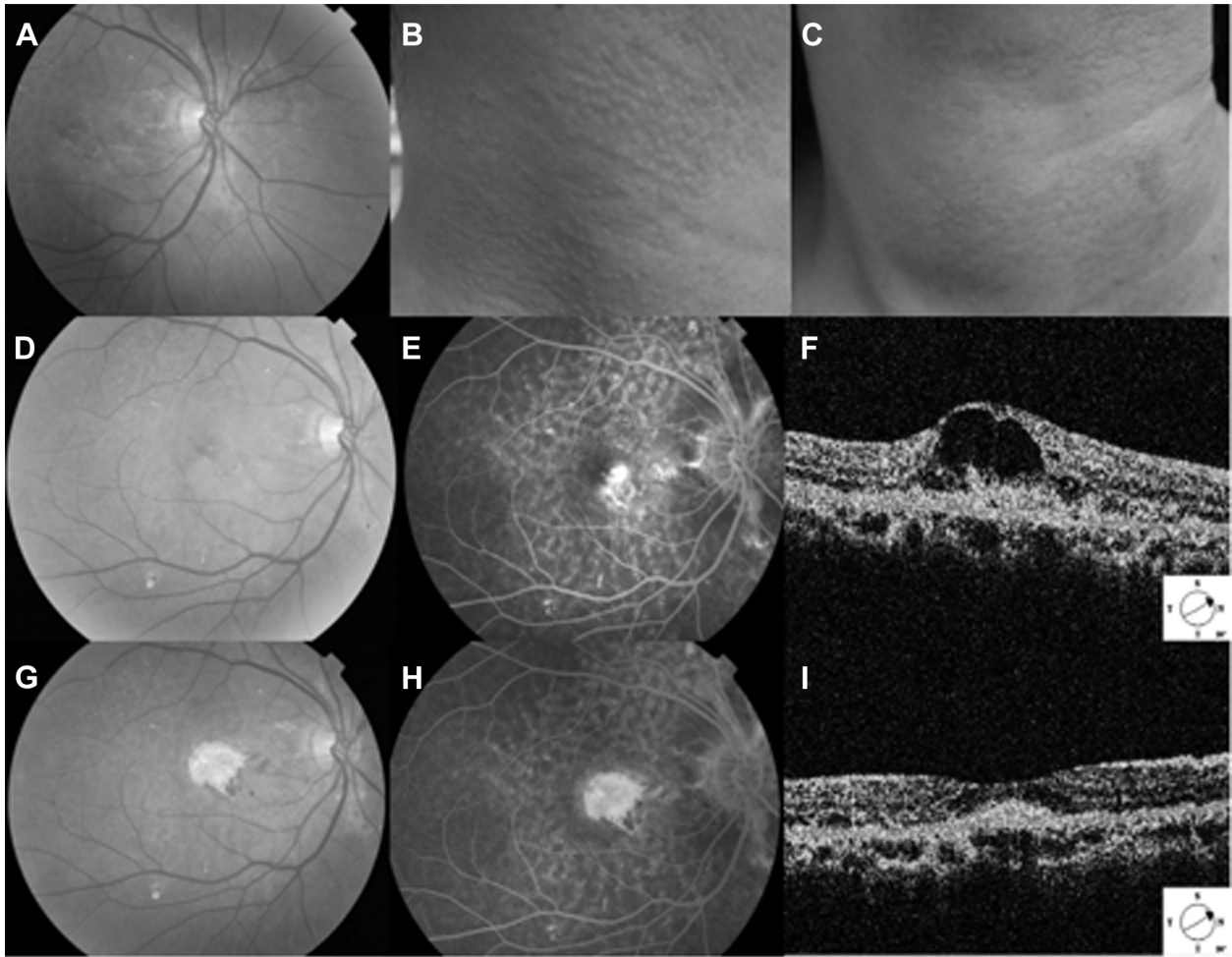
Fig. 5. A 50-year-old women with angioid streaks in both eyes. For the right eye, (A) color fundus shows the linear radial streaks over the peripapillary area, (B) and (C) show the pseudoxanthoma elasticum of her lateral and anterior neck, (D) a patch of macular retinal pigment epithelium (RPE) change, (E) dye leakage from subfoveal lesion in fluorescein angiography (FA), and (F) cystoid macular edema with elevated lesion from RPE. After one injection of bevacizumab, (G) previous RPE change turned out to be a macular scar with (H) FA staining and total regression of macular edema on optical coherence tomography (OCT) (I).
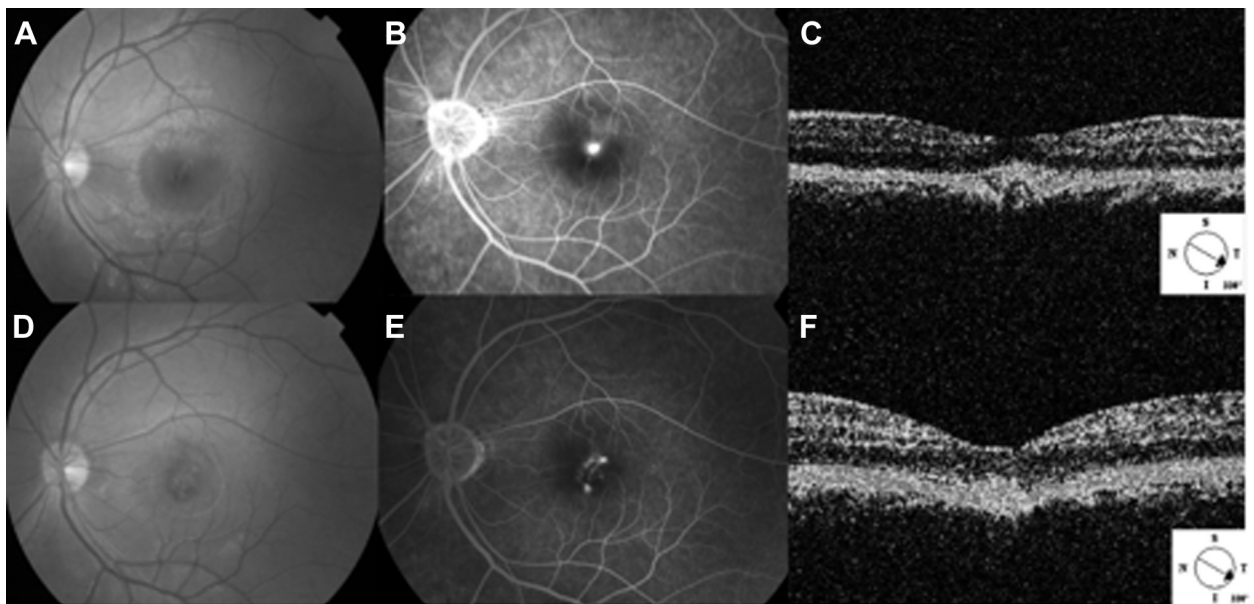
Fig. 6. A 28-year-old man with choroidal rupture in the left eye. (A) A linear lesion of retinal pigment epithelium (RPE) change on the fundus. (B) Fluorescein angiography (FA) revealed dye leakage from choroidal neovascularization (CNV) and (C) optical coherence tomography (OCT) revealed the presence of the break in the RPE and Bruch's membrane with choroidal neovascular membrane. After one intravitreal injection of bevacizumab, (D) a patch lesion of RPE changed. (E) Dye staining along the site of choroidal rupture occurred and (F) the choroidal neovascular membrane on OCT exhibited shrinkage.

Table 4

Initial and final mean best-corrected visual acuity (BCVA) in logMAR of young choroidal neovascularization (CNV) patients after antivascular endothelial growth factor (anti-VEGF) treatment.

	All	PM	PIC	ICNV	PCV	Angioid streaks	Choroidal rupture
Number of eye injections	63	32	9	11	8	2	1
Initial	0.69 ± 0.61	0.57 ± 0.46	0.43 ± 0.51	0.69 ± 0.71	1.25 ± 0.84	1.35 ± 0.25	0.52
Final	0.42 ± 0.59	0.36 ± 0.53	0.27 ± 0.39	0.33 ± 0.57	0.81 ± 0.69	1.24 ± 0.54	0.0
p	< 0.05	< 0.05	0.12	< 0.05	< 0.05		

ICNV = idiopathic choroidal neovascularization; PCV = polypoidal choroidal vasculopathy; PIC = punctate inner choroidopathy; PM = pathological myopia.

ranibizumab group vs. 2.2 letters in PDT alone group, $p < 0.00001$). In another study comparing the visual outcomes after anti-VEGF injection or PDT for ICNV, Kang and Koh[47] found that the anti-VEGF group showed significantly better mean BCVA than the PDT group at each follow-up visit for up to 24 months.

PIC comprised the second category in our series. It is a relatively uncommon inflammatory multifocal chorioretinopathy with a higher prevalence in young women according to our results (Table 2). PIC may be regarded as a subtype of multifocal choroiditis with little or no vitreous inflammation.[50,51] Although most cases of PIC had a self-limited disease course, severe visual loss could develop as a result of CNV formation. Macular CNV was a well known complication of PIC. In a recent report of complications of 31 eyes with PIC, 64.5% of the investigated eyes were found to have either past history or active presentation of macular CNV.[52] In another recent report of 112 eyes with PIC in Chinese patients, Zhang et al[53] also found that 64% of investigated eyes had macular CNV. VEGF was found to be associated with CNV secondary to PIC. Using immunohistochemical stain, Shimada et al[54] found that VEGF was expressed in all samples of surgically excised CNV in 14 patients with PIC or multifocal choroiditis. Recently, anti-VEGF has been found to be very effective in the treatment of CNV associated PIC. In a prospective study following 12 eyes for 12 months, Zhang et al[46] found that a mean of only 1.9 (1—4) injections were necessary to improve or maintain vision. In another study following eight eyes for 24 months, Arevalo et al[55] revealed that a mean of only 1.5 (1—3) injections were necessary for the as-needed treatment of CNV in PIC. These results are very similar to ours, in which a mean of only 2.7 injections were necessary to maintain the BCVA in PIC associated CNV in a mean follow-up period of 22.8 months.

Idiopathic CNV comprised the third category in young CNV patients in our series. Although the definition of ICNV is usually by exclusion of other types of CNV, ICNV still has several unique findings. For example, the morphology of ICNV is usually of classic type CNV, and the occurrence of CNV is usually solitary and unilateral.[56] According to Ho et al,[56] the natural history of ICNV is usually self-limited. However, severe visual loss might develop in some patients without treatment, particularly in those with lesions no smaller than one disc area.[56] As with other types of CNV, anti-VEGF was also found to be very effective in treating ICNV.[57,58] In a prospective study of 40 eyes of ICNV in Chinese patients for 12 months, Zhang et al[58] was able to achieve a mean improvement of 2.4 lines with a mean of only two injections of bevacizumab. Similar results were also noted in our series that, with a mean of 1.6 injections of anti-VEGF, significant improvement of BCVA (approximately 3 lines, from 20/81 to 20/40, $p < 0.05$) was achieved after a mean follow-up time of 23.3 months.

In the current study, CNV in young patients was more common in women (64.4%) than in men. This is also noted in Cohen et al's[8] report of Western European patients (female 58%). The tendency of female predominance was detected in different etiologies including PM, ICNV, and PIC or inflammatory causes. This may suggest the role of estrogen in the development of CNV in younger patients.[59] By contrast, PCV has a predominant male prevalence in our current series (men: 75%), which is similar to the PCV in patients > 50 years of age; most studies reported a male predominance.[16—18] In our series, although PCV comprises the fourth prevalent cause of CNV in patients ≤ 50 years old, the mean age of PCV (48.0 ± 1.3 years) is significantly older than other major causes (PM 36.2 ± 7.2 years, PIC 25.1 ± 10.6 years, ICNV 35.5 ± 8.0 years, $p < 0.05$). This suggests that PCV is probably more like a degenerative disease similar to AMD, except that the onset age is relatively younger than the criteria for the definition of AMD (> 50 years old).

Anti-VEGF has also been found to be effective for the treatment of PCV in terms of both visual improvement and fluid absorption. In a long term study (mean follow-up time 42.58 months) for the treatment of 36 PCV patients, Kang and Koh[60] achieved a significant improvement in both BCVA and OCT with a mean of 11.45 ranibizumab injections, which corresponded to a mean interval of 3.72 months between two injections. Our previous study of the annual result of bevacizumab for treatment of PCV in an older cohort (> 50 years) had a similar frequency of 3.3 injections in 12 months follow-up (mean interval of 3.63 months between two injections).[61] By contrast, the current study revealed that younger patients with PCV have much less frequency of injections or a much longer interval between two injections in the PCV group (12.1 ± 2.2 months). This finding implies a more sustained effect of anti-VEGF injection in younger PCV patients.

Our series only included sporadic cases of CNV associated with angioid streaks and traumatic choroidal rupture, and thus, our study could not characteristically describe CNV of these two groups. Anti-VEGF treatment successfully reduced the activity of CNV in both patients and maintained or improved the visual outcome in these two patients. Recently, anti-VEGF has also been advocated as an effective treatment modality for the treatment of both angioid streak[62] and choroidal rupture.[63,64] Our case with angioid streak

Table 5

Initial and final mean central retinal thickness [CRT (μm)] of young choroidal neovascularization (CNV) patients after antivascular endothelial growth factor (anti-VEGF) treatment.

	All	PM	PIC	ICNV	PCV	Angioid streaks	Choroidal rupture
Number of eyes	63	32	9	11	8	2	1
Initial	257.5 ± 48.2	253.6 ± 40.8	229.4 ± 38.0	272.2 ± 33.9	286.3 ± 67.7	282.5 ± 44.5	216.0
Final	210.3 ± 35.7	207.2 ± 31.2	202.9 ± 17.1	208.2 ± 43.5	220.9 ± 62.7	258.5 ± 27.5	203.0
p	< 0.05	< 0.05	0.12	< 0.05	0.05		

ICNV = idiopathic choroidal neovascularization; PCV = polypoidal choroidal vasculopathy; PIC = punctate inner choroidopathy; PM = pathological myopia.

was a 50-year-old woman with bilateral CNV and pseudoxanthoma elasticum occurring on the neck. Interestingly, over the past 29 months of follow up (August 2012 to November 2014), she has asked for a regular intravitreal injection of bevacizumab every 2 months to prevent any chance of recurrence. BCVA was increased from 6/75 to 6/30 in the Snellen chart, with a gain of 25 letters in the ETDRS chart for the right eye; the left eye BCVA in the Snellen chart was maintained at 6/200 with persistent macular scar.

Our study exhibited a few notable disadvantages. The study was retrospective and the case size was minimal, especially that of angioid streaks and choroidal rupture. The follow-up duration was also short and had wide variation due to the variable compliance of the patients. A larger-scale study with each type of CNV in young adults and a longer follow-up time is needed for further evaluation of the efficacy, treatment frequency, and predictability of intra-vitreal injection of anti-VEGF.

5. Conclusion

Our study reviewed 67 eyes with CNV in younger patients in Taiwan. We described the most common etiology as PM, followed by PIC, ICNV, and PCV. We observed an effective response to anti-VEGF treatment in these subgroups. Elucidating the common etiologies of CNV and the difference in prevalence compared with Western countries may help the early diagnosis of CNV-related problems and avoid further morbidity in younger patients.

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