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Intravitreal Bevacizumab Injection for Choroidal Neovascularization Associated with Multifocal Choroiditis

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Purpose: To evaluate the long-term efficacy and safety of intravitreal bevacizumab injections for choroidal neovascularization (CNV) associated with multifocal choroiditis (MFC).

Methods: This is a retrospective case series study. Patients who were treated with intravitreal bevacizumab injections for CNV associated with MFC from January 2004 to August 2016 were included. The characteristics of patients, change in best corrected visual acuity, and central subfield thickness (CST) were reviewed.

Results: Among 34 MFC eyes (22 patients), 6 eyes (6 patients, 17.6%) had CNV associated with MFC. The mean age of patients was 41 (26-64) years and four of six patients (66%) were female. The mean duration of follow-up was 101.5 (36-178) months and the mean number (range) of intravitreal bevacizumab injections was 2.3 (1-6). Three of six (50%) eyes showed evident inflammation and were treated with immunosuppression agents. Visual acuity improved in five of six (83%) eyes and CST decreased in all eyes at final visit. One eye with initial poor visual acuity (2/100) continued to have poor final visual acuity (2/100) with scar changes. No adverse events were reported.

Conclusions: Intravitreal bevacizumab injections were safe and effective at improving visual acuity and decreasing CST over long-term follow-up in a small series of patients with CNV secondary to MFC.

Keywords: Bevacizumab; Choroidal neovascularization; Multifocal choroiditis

Introduction

Multifocal choroiditis (MFC) is chronic ocular inflammation commonly characterized by the presence of vitritis and mul-

tiple chorioretinal lesions in the posterior pole and/or periphery [1-5]. Although it has been reported that visual prognosis is relatively good in most patients with MFC, several complications, including macular edema, choroidal neovasculariza-

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tion (CNV), and corticosteroid-related cataract or glaucoma, can occur [6]. Among these complications, CNV has been reported as the most common cause of visual loss, developing in 27% to 32% of MFC patients [1-11]. Many treatment options for CNV associated with MFC have been suggested such as local corticosteroids [6], rapamycin [10], photodynamic therapy (PDT) [12], transpupillary thermotherapy [13], submacular surgery [14], and macular translocation [15]. In general, these treatment options do not achieve significant visual acuity improvement on follow-up. A new treatment option for CNV associated with MFC is needed.

Anti-vascular endothelial growth factors such as bevacizumab have demonstrated improvement of visual acuity in treating CNV for neovascular age-related macular degeneration [16], pathologic myopia [17], and retinal vein occlusion [18]. The development of CNV in MFC may share a final common pathway with these diseases [19]. Therefore, anti-vascular endothelial growth factor (anti-VEGF) therapies seem to be a rational treatment approach to CNV associated with MFC. Several studies have reported clinical outcomes after anti-VEGF treatment and demonstrated favorable results after short-term follow-up [20,21]. However, few reports have examined long-term results after treatment. The aim of this study was to evaluate the long-term efficacy and safety of intravitreal bevacizumab injections for naïve CNV associated with MFC after more than 3 years of follow-up.

Materials and Methods

Retrospective chart review was conducted for patients with a diagnosis of CNV associated with MFC who received intravitreal bevacizumab injection from January 2004 through August 2016. The diagnostic criteria for MFC were based on the original description [22]. CNV diagnosis was made by identification of the early hyperfluorescence, with late dye leakage on fluorescein angiography (FA). Patients were treated until the absence of intra- and subretinal fluid was observed in optical coherence tomography (OCT) and the FA showed an absence of leakage. This research followed the tenets of the Declaration of Helsinki and was approved by the institutional review boards.

Data was collected from medical records and included age at presentation, gender, best-corrected visual acuity (BCVA) on Snellen, evidence of active inflammation, location of

CNV, and central subfield thickness (CST). According to Macular Photocoagulation Study criteria, the location of CNV was defined as extrafoveal (200 μ m outside the center of the foveal avascular zone), juxtafoveal (within 1-199 μ m of the center of the foveal avascular zone), or subfoveal (under the center of the foveal avascular zone). CST was measured by a macular cube scan of OCT. Duration since CNV inactivation from treatment to the last follow-up was recorded. Use of any form of immunosuppression was recorded, as were ocular and systemic adverse events such as vitreous hemorrhage, retinal detachment, endophthalmitis, and thrombotic event.

Results

A total of 34 eyes (22 patients) diagnosed with MFC were included in this study. Among 34 eyes, 6 eyes (6 patients, 17.6%) had treatment naïve CNV associated with MFC. The mean age of the patients was 41 (26-64) years and four of six patients (66%) were female. The mean follow-up duration was 101.5 (36-178) months and the mean number of intravitreal bevacizumab injections was 2.3 (1-6). Among the 6 eyes, 3 (50%) eyes showed evident inflammation and were treated with immunosuppression agents. Among 6 CNV eyes, 3 (50%) eyes had subfoveal CNV. After treatment, 5 of 6 (83%) eyes improved to 20/40 or better at final visit. However, one eye with initial poor visual acuity (2/100) continued to have poor visual acuity (2/100) at final visit with scar changes. CST decreased in all eyes after intravitreal bevacizumab injections. Durations from CNV regression after treatment to last follow-up was 41.8 (12-84) months. After regression of CNV lesion, it did not recur and was maintained during long-term follow-up. No ocular or systemic adverse events associated with intravitreal bevacizumab injection were reported (Table 1).

A representative case is included in Fig. 1. A 31-year-old female visited our clinic with the complaint of decreased visual acuity in her right eye. On ophthalmic examination, best corrected visual acuity was 20/40 in the right eye and 20/25 in the left eye with a -1.50 spherical equivalent bilaterally. Anterior examination revealed no evidence of inflammation. However, dilated fundus examination revealed vitreous cells with multifocal chorioretinal lesion in the posterior pole of the right eye. There was juxtafoveal yellow gray membrane

Table 1. Patient characteristics and clinical outcomes of multifocal choroiditis with choroidal neovascularization

Patient	Sex	Age	Laterality	Spherical equivalent (diopters)	Duration of follow up (months)	Evident inflammation	Immunosuppression agent	Location of CNV	Number of injections	BCVA		CST		Adverse event	Durations since CNV inactivation to final visit (months)
										Initial visit	Final visit	Initial visit	Final visit		
1	F	26	L	-3.25	120	None	None	Subfoveal	1	20/30	20/20	270	229	None	12
2	F	64	R	-4.00	92	Yes	Prednisolone	Juxtafoveal	1	20/50	20/40	236	221	None	84
3	M	42	L	-0.50	144	None	None	Subfoveal	2	2/100	2/100	255	231	None	67
4	F	39	L	-0.75	36	Yes	Prednisolone, azathioprine	Subfoveal	2	20/50	20/25	503	259	None	24
5	F	31	R	-1.50	39	Yes	Prednisolone, cyclosporine	Juxtafoveal	2	20/40	20/25	291	236	None	30
6	M	44	R	-2.50	178	No	None	Juxtafoveal	6	20/25	20/25	267	242	None	34

CNV = choroidal neovascularization; BCVA = best corrected visual acuity; CST = central subfoveal thickness.

superior to fovea. Following FA and OCT examination, we confirmed the diagnosis of CNV associated with MFC (Fig. 1A-D).

The patient was treated with prednisolone and cyclosporine for control of evident inflammation and received two courses of intravitreal bevacizumab injections for the CNV lesion. BCVA of the right eye improved to 20/25 and was maintained during 30 months of follow-up. FA and OCT examination revealed decrease CNV activity (Fig. 1E-H). There was no adverse event associated with intravitreal bevacizumab injection.

Discussion

In this case series, choroidal neovascularization (CNV) associated with multifocal choroiditis (MFC) was successfully treated with intravitreal bevacizumab injections. BCVA improved to 20/40 or better in 5 of 6 eyes (83%) without adverse events. In addition, the decrease of central subfield thickness (CST) was observed in all eyes. After regression, the CNV lesion did not recur and was maintained through long-term follow-up.

Because CNV associated with MFC has been the most common cause of severe visual loss [1-11], several treatment approaches have been tried. Conventional treatment such as corticosteroid and immunosuppressant agents might be beneficial in controlling inflammation, but their safety and effectiveness in CNV continue to be debated [8-10]. Surgery for CNV may provide positive results in some selected cases but requires considerable surgical skill and has high rates of recurrence and complications [11]. Photodynamic therapy has had several positive reports, but this intervention merely stabilizes the visual function and is unable to guarantee significant improvement of visual acuity [12].

Anti-VEGF agents are a newly emerged treatment option for CNV associated with MFC. This treatment is based on the concept that vascular endothelial growth factors are important in the development of CNV. Shimada et al. [23] reported that there was overexpression of vascular endothelial growth factor in samples of active CNV from patients with MFC. Fine et al. [21] reported a case series of 6 eyes and concluded that bevacizumab and ranibizumab were effective at improving visual acuity over 6 months in patients with CNV associated with MFC. Parodi et al. [20] reported intra-

Figure 1. Representative case (Patient 5) of choroidal neovascularization (CNV) associated with multifocal choroiditis (MFC). Before intravitreal bevacizumab injection (A-D). (A) Color photograph of patient 5 showed multiple chorioretinal lesion in the posterior pole with juxtafoveal yellow gray membrane superior to fovea which is consistent with CNV secondary to MFC. (B) The late phase of fluorescein angiography (FA) of the same patient showed leakage superior to fovea consistent with CNV lesion. (C) The horizontal scan of optical coherence tomography (OCT) showed a photoreceptor layer defect corresponding to the chorioretinal lesions. (D) The vertical scan of OCT showed a hyperreflective area located above the retinal pigment epithelium (RPE) corresponding to the CNV. After intravitreal bevacizumab injection (E-H). (E) Color photograph showed decrease of juxtafoveal yellow gray membrane superior to fovea. (F) The late phase of FA showed decrease of leakage at the CNV lesion. (G) The horizontal scan of OCT showed progression of photoreceptor layer defect. (H) The vertical scan of OCT showed a decrease of hyperreflective area located above the RPE after intravitreal bevacizumab injection.

vitreal bevacizumab injection was beneficial for juxtafoveal CNV associated with MFC. In our case series, visual acuity improved to 20/40 or better at final visit and CST decreased after intravitreal bevacizumab injections, which is consistent with previous reports. One eye with initial poor visual acuity continued to show poor final visual acuity with scar changes. This patient already had atrophic changes at initial presentation and these changes might have restricted improvement of visual acuity.

On long-term follow-up (178 months), the regressed CNV lesion did not recur in our case series. The duration from CNV regression to last follow-up (41.8 months) was more than 3 years. These results were consistent with previous studies that reported the recurrence of CNV associated with MFC was rare [6]. Parodi et al [20], also reported that juxtafoveal CNV associated with MFC stabilized and did not recur after intravitreal bevacizumab injection within the first 6 months.

An inflammatory mechanism may play a role in CNV for-

mation. Patients with MFC are at risk for the development of CNV, possibly because of chronic peri-vascular, predominantly B-cell lymphocytic infiltration of the choroid, and/or disruption of Bruch's membrane [24]. In our case series, among 6 eyes with CNV, half had evidence of active inflammation and were successfully treated with anti-inflammatory agents.

In conclusion, intravitreal bevacizumab injection was effective and safe for improving visual acuity and decreasing CST after long-term follow-up in a small series of patients with CNV associated with MFC. Further studies with a larger samples size and controls are required to evaluate the clinical efficacy of bevacizumab for the management of MFC.

Conflicts of interest

There are no conflicts of interest.

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