Bilateral Regression of Choroidal Neovascularization Associated with Pathologic Myopia following Unilateral Intravitreal Bevacizumab Injection

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ABSTRACT
We report a case of bilateral regression of choroidal neovascular membrane (CNVM) in a patient following intravitreal Bevacizumab injection. A middle aged myopic patient with fluorescein angiography (FFA) proven bilateral subfoveal CNVM received monthly injections of intravitreal Bevacizumab in one eye. After 3 injections bilateral regression of CNVM was noted in FFA. Possible systemic absorption of intravitreal Bevacizumab resulting in bilateral effect and its clinical implications are highlighted in this case report.

Keywords: Choroidal neovascular membrane, Pathologic myopia, Bevacizumab.

INTRODUCTION
We report an interesting case of bilateral regression of choroidal neovascular membrane (CNVM) in a patient with pathologic myopia following unilateral intravitreal injection of Bevacizumab. A 54-year-old male with history of myopia from childhood presented with defective vision in both eyes. Clinical examination and fundus fluorescein angiography (FFA) confirmed the presence of bilateral CNVM (Figs 1A to F). He received three monthly injections of intravitreal Bevacizumab in the right eye (RE). Ocular examination and FFA performed at the end of three months showed bilateral complete regression of the CNVM (Figs 2A to F).

CNVM, secondary to pathologic myopia, is an important cause of significant visual impairment in young and middle-aged patients. Different therapeutic approaches have been attempted to treat myopic CNVM, including argon laser photocoagulation,1 surgical removal and macular translocation,2 photodynamic therapy with verteporfin3 and intravitreal antiVEGF agents.4-6 The purpose of this report is to document bilateral regression of CNVM in a patient with pathologic myopia following unilateral intravitreal injection of Bevacizumab.

CASE REPORT
A 54-year-old male patient wearing corrective spectacles from childhood for high myopia presented with defective vision in both eyes for the past three months. The onset of symptoms was more recent in the RE. The patient underwent cataract surgery with intraocular lens implantation in the RE 5 years ago. On examination, his best corrected visual acuity (BCVA) was 2/60 N36 in the RE and 2/60 N18 in the left eye (LE). The myopic correction in the RE was –3.0 D spherical and in the LE –13.0 D spherical. The myopic correction in the RE was less as it was partially corrected by the intraocular lens. Anterior segment examination revealed a paracentral macular corneal opacity and pseudophakia in the RE and an immature cataract in the LE. The intraocular pressure was 14 mm Hg in both the eyes. Biomicroscopic examination of the retina showed bilateral peripapillary atrophy. The macula in both the eyes showed a grayish white membrane measuring around one-fifth of a disk diameter (see Figs 1A and D). There was a small streak of subretinal hemorrhage adjacent to the membrane in the right macula. FFA of the right macula showed a linear area of hyperfluorescence in the subfoveal region, which increased in intensity in the late phases of the angiogram suggestive of a CNVM (see Figs 1B and C). FFA of the left macula showed an area of hyperfluorescence above and nasal to the fovea, which increased in size and intensity in the late phases of the angiogram (see Figs 1E and F) confirming the diagnosis of a CNVM. He was advised intravitreal Bevacizumab—three monthly injections to RE as a loading dose. Intravitreal injection of 2.5 mg Bevacizumab in 0.1 ml was carried out in outpatient setting under strict aseptic precautions, using a 30 G needle, 3.5 mm posterior to the limbus. A follow-up examination was performed a day after each injection and at the end of every month. FFA was performed at the end of three months. A detailed ocular examination done at the end of three months revealed that the BCVA had improved to 6/24 N12 in both the eyes. The untreated LE also surprisingly showed improvement in visual acuity.
Color photography (see Figs 2A and D) of the macula showed significant reduction of the grayish membrane in both maculae. FFA (see Figs 2B, C, E and F) showed disappearance of the hyperfluorescence that was noted in the pretreatment FFA, thereby confirming the regression of the CNVM in both the eyes. Follow-up examination performed three months later, showed maintenance of visual acuity and a repeat FFA demonstrated no change in the picture.

**DISCUSSION**

Bevacizumab is a full length humanized monoclonal antibody that inhibits all isoforms of vascular endothelial growth factor-A and was initially developed for treating metastatic cancer. First used in ophthalmology to treat wet age-related macular degeneration, various reports document its safety and efficacy for the treatment of CNVM in patients with pathologic...
myopia. Although previous studies have demonstrated the effect of intravitreal Bevacizumab injection on reducing proliferative diabetic retinopathy, uveitic cystoid macular edema and diabetic macular edema in the contralateral eye, there has been no report till date to demonstrate a similar effect with CNVM in pathologic myopia. We have demonstrated in this case report the complete regression of CNVM in the contralateral eye after three injections of 2.5 mg of Bevacizumab at monthly intervals. This crossover effect can be explained by the presence of Bevacizumab in the contralateral eye as demonstrated in animal studies. Following an injection of 1.25 mg of Bevacizumab in one eye, Bakri et al reported a concentration of 0.35 ng/ml on day 1 and 11.7 ng/ml at four weeks in the vitreous humor of the contralateral eye. Low concentrations of Bevacizumab were also reported in the serum ranging from 3.3 μg/ml eight days after the injection to 1 μg/ml 29 days after.

Figs 2A to F: (A) RE showing significant regression of the grayish-white subfoveal lesion with a patch of atrophy. (B and C) Early and late phases of FFA showing complete regression of CNVM with absence of leakage. (D) Color photograph of LE showing significant regression of the grayish subfoveal lesion. (E and F) Early and late phases of FFA showing complete regression with no leakage.
the injection. Considering the larger vitreous volume in pathologic myopia and the expected greater dilution of the drug, we used 2.5 mg of Bevacizumab. In view of the higher dose used in our case, the likelihood of greater amounts of the drug finding its way into the contralateral eye exist.

Our case illustrates that small quantities of Bevacizumab are sufficient to cause regression of CNVM in pathologic myopia. It can be argued that the CNVM in the fellow eye regressed spontaneously and was not related to the injection of intravitreal Bevacizumab. The available literature on the natural history of myopic CNVM is conflicting.\(^4\)\(^,\)\(^11\) Avila MP et al,\(^11\) in their study on the natural history of Choroidal Neovascularization in degenerative myopia, have reported spontaneous regression or stabilization of myopic CNVM in a fellow eye. But this even occurred over a 40.9-month period.\(^11\) In our patient, there was complete regression of the CNVM in the fellow eye simultaneously with the treated eye, thus establishing the cause and affect relationship.

To conclude, to our knowledge, this is the first report of bilateral regression of CNVM in pathologic myopia following intravitreal injection of Bevacizumab in one eye.

REFERENCES