Full-thickness macular hole formation following antivascular endothelial growth factor injection in a case of hemicentral retinal vein occlusion

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Abstract:
A rare case reporting the occurrence of full-thickness macular hole (MH) formation following intravitreal antivascular endothelial growth factor injection in a case of hemicentral retinal vein occlusion and the subsequent management of the case. As described in few other similar case reports in the literature, there are quite a few probabilities of factors causing this pathology. An acute posterior vitreous detachment or sudden decompression of the macular edema can quite possibly lead to the above situation. This case report shares light on the evolution of a MH following intravitreal injection and the subsequent treatment process.

Keywords:
Bevacizumab, cystoid macular edema, intravitreal injections, macular hole, retinal vein occlusion

Introduction
Macular edema is being successfully and rampantly treated by intravitreal antivascular endothelial growth factor (VEGF) injections. Macular hole (MH) formation following intravitreal anti VEGF injection for the treatment of cystoid macular edema (CME) has been reported in this case. It is a rare adverse effect reported in very few cases in the literature.

Case Report
A 62-year-old female presented with chief complaints of floaters in the right eye (RE) for 3 weeks. She was a known diabetic (on OHD) since 6 years and hypertensive since 10 years (on treatment), rheumatoid arthritis (on treatment), and with no known adverse drug reactions. Her best-corrected visual acuity (BCVA) was 4/60 in RE and 6/6 in left eye (LE). On examination, her anterior segment revealed normal findings in both the eyes except for relative afferent pupillary defect in RE. Posterior segment revealed multiple intraretinal haemorrhages all over the superior quadrant, engorged tortuous blood vessels, and CME in RE while there was no abnormality in LE. A provisional diagnosis of RE hemicentral retinal vein occlusion (CRVO) with CME was made [Figure 1a]. Her blood pressure was 160/90 mm of Hg, and her blood investigations showed deranged lipid profile and raised blood sugar. Optical coherence tomography (OCT) showed a central macular thickness of 551 µ with intraretinal cystic spaces and fluid [Figure 1b]. Fundus fluorescein angiography of RE revealed capillary dropouts and nonperfusion areas corresponding to the area of vein occlusion.
along with angiographic CME. She received a single intravitreal injection bevacizumab following which her vision improved to 6/36. Her OCT of RE revealed a full thickness MH a month later! [Figure 2a and b] She was explained about requiring surgery. Over the next 18 months, she received 5 more injections of intravitreal Bevacizumab. Her RE BCVA before vitrectomy was 6/18. A 25G vitrectomy was performed and intraoperatively posterior vitreous detachment (PVD) had to be induced, conventional internal limiting membrane peeling done and a tamponade of C3F8 (perfluoropropane) was given. Four months postsurgery, her RE BCVA 6/24 with cataract formation and MH Type 1 (U-shaped) closure was seen [Figure 3a and b]. In the subsequent months, she underwent cataract extraction following which she developed CME. She underwent scatter laser (sectoral superior quadrant) in her RE along with intravitreal injection Ranibizumab three times. She has remained in regular follow-ups ever since and her BCVA has remained stable at 6/9 [Figure 4].

Discussion

Our case report remains rather unique as there have been just a handful of similar reports over the years. Muramatsu et al.[1] have reported a similar approach to MH following ranibizumab injection due to increased vitreomacular traction. The expression of transforming growth factor-β2, which is known to cause fibrosis, was reported after anti-VEGF therapy.[2] Acute regression of macular edema and increased fibrosis might have triggered a mechanical force to the damaged retina and might have been a possible cause of MH formation. Querques et al.[3] reported increasing vitreous macular traction after Ranibizumab injection, with formation of a Stage 2 MH. Recurrent intravitreal triamcinolone injections may have had an indirect role in the development of the MH, by favoring the rupture of distented Muller cells and intraretinal pseudocysts.[4] In the treatment of age-related macular degeneration, rapid reduction in the volume of choroidal neovascularization may cause MH formation as reported by Miura et al.[5] Nagpal et al.[6] reported MH formation after bevacizumab injection to a hemi-CRVO patient possibly caused by rapid PVD after injection; however, it was assumed that there was possibility of a preexisting stage 2–3 MH which was masked by the hemorrhages and edema at the fovea and the MH had progressed following the injection. In our case, PVD was induced intraoperatively which would leave us with possibilities of either injection induced anteroposterior vitreomacular traction or a preexisting MH not visualized due to hemorrhages in acute stage.

Conclusion

Since anti-VEGF injections are commonly used in many retinal conditions, the various causative factors for MH formation in each scenario should be looked into and approached differently. Careful and thorough examination and investigations should be done to avoid
overlooking such situation along with proper patient counseling regarding the possibility of MH formation following anti-VEGF injections in suspected scenarios.

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Conflicts of interest
There are no conflicts of interest.

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