Full thickness macular hole following intravitreal ranibizumab injection for diabetic macular edema; a rare complication or coincidence?

Dear Sir,

Anti-vascular endothelial growth factors (VEGFs) improved vision and macular edema in patients with diabetic macula edema and reduced the risk of further visual loss. We report a 67-year-old woman with type 2 diabetes mellitus who had panretinal photocoagulation for proliferative diabetic retinopathy presented at our department for decreased vision in her right eye (RE). On examination, best corrected visual acuity (BCVA) was 20/400 in the RE. Anterior segment examination was unremarkable and funduscopy of the RE revealed cystoid macular edema (CME). There was no posterior vitreous detachment (PVD) or clinically detectable vitreomacular traction (VMT). Fluorescein angiography of the RE showed late hyperfluorescence in the macular area due to leakage from microaneurysms and areas of increased vascular permeability [Fig. 1]. Optical coherence tomography (OCT) (The Heidelberg Spectralis OCT, Heidelberg Engineering, Inc., Heidelberg, Germany) confirmed the presence of cystoid DME without VMT [Fig. 2]. Central foveal thickness was 830 μm. An informed consent form was taken and intravitreal 0.5 mg ranibizumab injection (Lucentis; Genentech, South San Francisco, CA, USA and Novartis, Basel, Switzerland) was administered without complication.

One-month after the injection of anti-VEGF, patient complained of newly developed metamorphopsia. BCVA deteriorated to 6/200 and slit-lamp biomicroscopy revealed a full thickness macular hole (FTMH) with no PVD or VMT. OCT confirmed the presence of a FTMH and no evidence of any areas of partial vitreous separation associated with vitreoretinal adhesions or areas of vitreous traction in any OCT scan [Fig. 3]. Patient underwent pars plana vitrectomy, internal limiting membrane peeling and fluid gas exchange (SF6). One-month after the surgery there was no FTMH or CME and BCVA improved to 20/200.

Anterior-posterior traction by the vitreous on the macula causes idiopathic FTMH. Pathogenetic mechanism of FTMH associated with macular edema is unclear. A few studies were presented macular hole formation after intravitreal injections for CME. [1‑3]

Georgalas et al. postulated that retinal changes due to the massive CME, the absence of PVD in combination with the vitreous traction induced either by the mechanical globe deformation and vitreous synaeresis or by a possible vitreous incarceration at the injection site, could lead to the development of FTMH in central retinal vein occlusion. [3]

Lecleire-Collet et al. have reported a patient with diabetic maculopathy who developed a FTMH after repeated...
intravitreal triamcinolone injections.\textsuperscript{[2]} The authors postulated that repeated intravitreal injections might have an indirect role in the development of FTMH formation by favoring the rupture of distended Müller cells and intraretinal pseudocysts. During breakdown of the blood-retina barrier, Müller cells become swollen and are eventually lysed. This results in extracellular fluid accumulation in the outer plexiform and inner nuclear layers. Consequently, CME can be caused directly, due to endothelial cell damage, as it occurs in the context of diabetes mellitus may lead to macular hole development.\textsuperscript{[4]} Hussain \textit{et al.} reported a FTMH after foveal pseudocyst formation in vitrectomized eye and they hypothesised that Muller cell insult was a probable hypothesis of FTMH.\textsuperscript{[5]}

In conclusion, although development of macular hole is a rare adverse effect of the anti-VEGF injection, this possibility must be kept in mind. Further investigations are required to confirm our results.

\textit{Hasan Basri Arifoğlu, Arzu Seyhan Karatepe Hashas, Tülay Ersekerci, Mustafa Atas}

Kayseri Research and Education Hospital, Kayseri, \textsuperscript{1}Finike State Hospital, Antalya, Turkey

Correspondence to: Dr. Arzu Seyhan Karatepe Hashas, Kayseri Research and Education Hospital, Kayseri, Turkey.

E-mail: arzuskaratepe@hotmail.com

\textbf{References}

1. Georgalas I, Rouvas A, Kotsolis A, Karagiannis D, Ladas I. Full thickness macular hole formation in a patient with cystoid macular edema caused by CRVO treated with intravitreal bevacizumab. Ophthalmic Surg Lasers Imaging. 2010 Mar 9:1-4. [Epub ahead of print].

2. Lecleire-Collet A, Offret O, Gaucher D, Audren F, Haouchine B, Massin P. Full-thickness macular hole in a patient with diabetic cystoid macular oedema treated by intravitreal triamcinolone injections. Acta Ophthalmol Scand 2007;85:795-8.

3. Erdurman FC, Pellumbi A, Durukan AH. Lamellar macular hole formation in a patient with diabetic CME treated by intravitreal bevacizumab injections. Ophthalmic Surg Lasers Imaging 2012;43:e87-9.

4. Moschos MM, Gatziosfas Z, Rotsos T, Symeonidis C, Song X, Seitz B. Macular hole formation in a patient with Irvine-Gass syndrome: Coincidence or rare complication? Clin Ophthalmol 2013;7:1437-9.

5. Hussain N, Hussain A, Natarajan S. Optical coherence tomographic evaluation of foveal pseudocyst in the formation of macular hole. Indian J Ophthalmol 2003;51:353-5.
Author response: Repeat gas insufflation for successful closure of idiopathic macular hole following failed primary surgery

Dear Editor,

We appreciate the interest of Goel et al.\(^{[1]}\) and their remarks in response to our article “Repeat gas insufflation for successful closure of idiopathic macular hole following failed primary surgery.”\(^{[2]}\) We also congratulate them on their success in achieving closure in two cases of primarily failed macular hole closure as shared in their report.

They attribute our interpretation of type 2 macular hole closure in a case with residual foveal defect and cuff of subretinal fluid as incorrect. This needs some clarification. Tornambe et al. have classified macular hole surgery outcomes into three possible situations: Elevated/open, flat/open and flat/closed.\(^{[3]}\) The first two situations are recognized as type 2 closure while the third situation is considered as type 1 closure; presence/absence of residual foveal defect being the prime determinant.

We would like to reemphasize that the focus of our report was on factors related to the closure of idiopathic macular hole following failed primary surgery. Preoperative optical coherence tomography configuration of the macular hole can offer predictive clues to successful re-surgery.\(^{[4]}\)

We again thank Goel et al. for bringing up this point thus helping generate clarity on this issue.

References
1. Goel N, Prakash A, Gupta AK. Repeat fluid-gas exchange for failed primary macular hole surgery. Indian J Ophthalmol 2014;62:1104-5.
2. Rishi P, Reddy S, Rishi E. Repeat gas insufflation for successful closure of idiopathic macular hole following failed primary surgery. Indian J Ophthalmol 2014;62:363-5.
3. Tornambe PE, Poliner LS, Cohen RG. Definition of macular hole surgery end points: Elevated/open, flat/open, flat/closed. Retina 1998;18:286-7.
4. Hoerauf H. Predictive values in macular hole repair. Br J Ophthalmol 2007;91:1415-6.
