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 slip-lamp biomicroscopy revealed a full thickness macular hole (FTMH) with no PVD or VMT. OCT confirmed the presence of a FTHM 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.[1]

Lecleire-Collet *et al*. have reported a patient with diabetic maculopathy who developed a FTMH after repeated

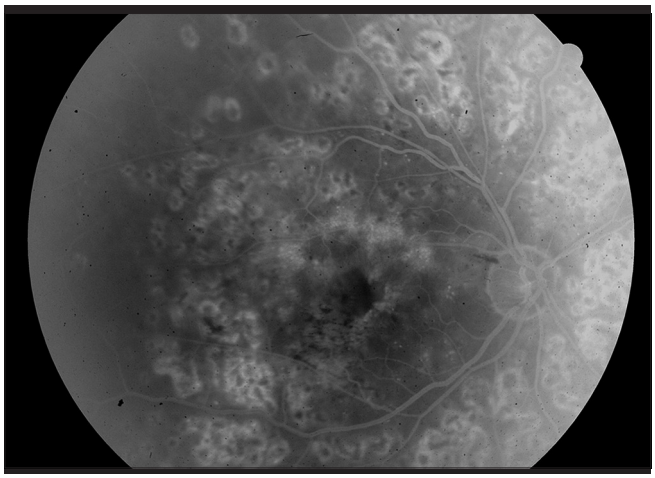

Figure 1: Fluorescein angiography of the eye showing late hyperfluorescence in the macular area

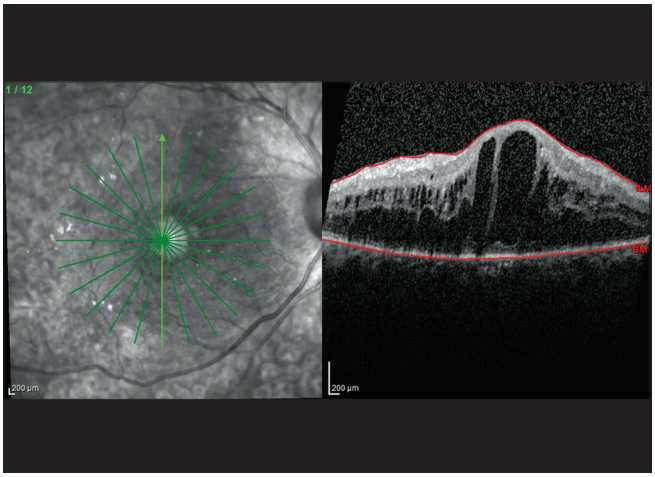

Figure 2: Patient optical coherence tomography scan depicting cystoid macular edema without vitreoretinal traction

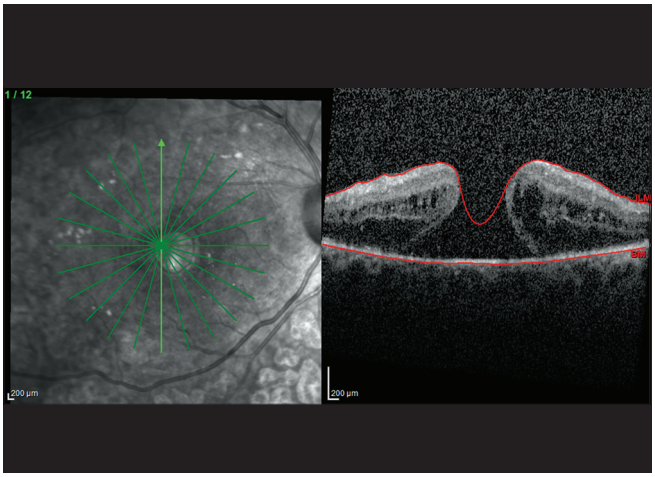

Figure 3: Patient optical coherence tomography scan depicting cystoid macular edema and full-thickness macular hole 1-month after intravitreal injection

intravitreal triamcinolone injections.[2] The authors postulated that repeated intravitreal injections might had 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.[4] Hussain *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.[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.

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