Bilateral Full-Thickness Macular Hole Formation After Single Dose of Intravitreal Conbercept Injection

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Abstract: *Aim:* To report a case of bilateral full-thickness macular hole formation after a single dose of conbercept injection.

Method: A 46-year-old high myopic female developed full-thickness macular hole in both eyes at 7 and 19 days after intravitreal injection of conbercept. The myopic foveoschisis was misdiagnosed as macular edema. The macular holes in both eyes were repaired surgically.

Results: The macular holes in both eyes were repaired successfully by surgery.

Conclusion: The full-thickness macular hole formation could occur after anti-VEGF treatment. The possible reasons for this case might be traction caused by anti-VEGF agent or progression of myopic foveoschisis and PVD.

Keywords: Myopic foveoschisis, Full-thickness macular hole, Conbercept, Anti-VEGF.

INTRODUCTION

Anti-vascular endothelial growth factor(VEGF) has become the first line treatment for choriodal neovascularization, including Neovascular Age-Related Macular Degeneration, pathological myopic maculopathy, and macular edema caused by diabetic maculopathy and retinal vein occlusion [1]. The retinal pigment epithelium(RPE) tear is one of the complications of anti-VEGF treatment in wet-AMD cases. It has been reported that different kinds of anti-VEGF agents are related to the RPE tears, including pegaptanib, bevacizumab, ranibizumab and aflibercept [2-4]. However, the macular hole formation related to anti-VEGF injection is quite rare. The mechanism of full-thickness macular hole formation is an abnormal anteroposterior and tangential vitreous traction at foveal retinal surface [5]. We report a case of bilateral full-thickness macular hole formation after intravitreal conbercept injection.

CASE PRESENTATION

A 46-year-old female presented at our clinic with chief complain of blurred vision for one month and distortion for 2 weeks in both eyes. She had no specific past history both in eyes and in general health. She had her both eyes examined 25 days ago in a prefectural hospital. At that time, her best corrected visual acuity (BCVA) in both eyes was 0.22 log MAR. She received fundus image (Figure **1**) and OCT scan (Figure **2**). Fundus image showed tessellated fundus in both eyes. OCT scan showed dark space in fovea area of both eyes. She was diagnosed by local ophthalmologists as bilateral idiopathic macular edema in both eyes. The patient received intravitreal conbercept(0.5mg, Chengdu Kanghong Biotechnologies Co. Ltd) injection for both eyes at the same day. One week later, the patient complained the decreased vision in both eyes. Fundus photo (Figure **1**) and OCT scan (Figure **2**) were repeated in local hospital and the full thickness macular hole was detected in the right eye. Nineteen days after injection, the BCVA was decreased to 0.39 log MAR in both eyes. Fluorescein angiography (FFA) and OCT were performed. FFA (Figure **3**) showed window defect in fovea of both eyes. No exudation or pooling was seen in FFA. OCT showed full thickness macular hole in both eyes. Thus, the patient was referred to our hospital. The BCVA was 0.69 log MAR in both eyes. The refraction was -7.00DS/-1.00DCX175 for the right eye and -8.00/-1.50DCX10 for the left eye. The axial length was 29.1mm and 30.2mm in the right eye and the left eye, respectively. OCT scan (Figure **2**) in our hospital confirmed the full thickness macular hole in both eyes. After discussion with the patient, a 25 guage pars plana vitrectomy + inner limiting membrane peeling + air injection was performed in the left eye and the right eye, respectively. During the surgery, a horse-shoe tear was found in the temporal-inferior retina of the left eye. The tear was treated by laser. The macular holes were closed in both eyes three days after surgery (Figure **1** and **2**). BCVA in the both eyes was improved

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to 0.22 log MAR, same as visual acuity at baseline. We followed the patient for half year after the surgery. In the last visit, her BCVA in both eyes was 0.22 log MAR and the macular holes were closed.

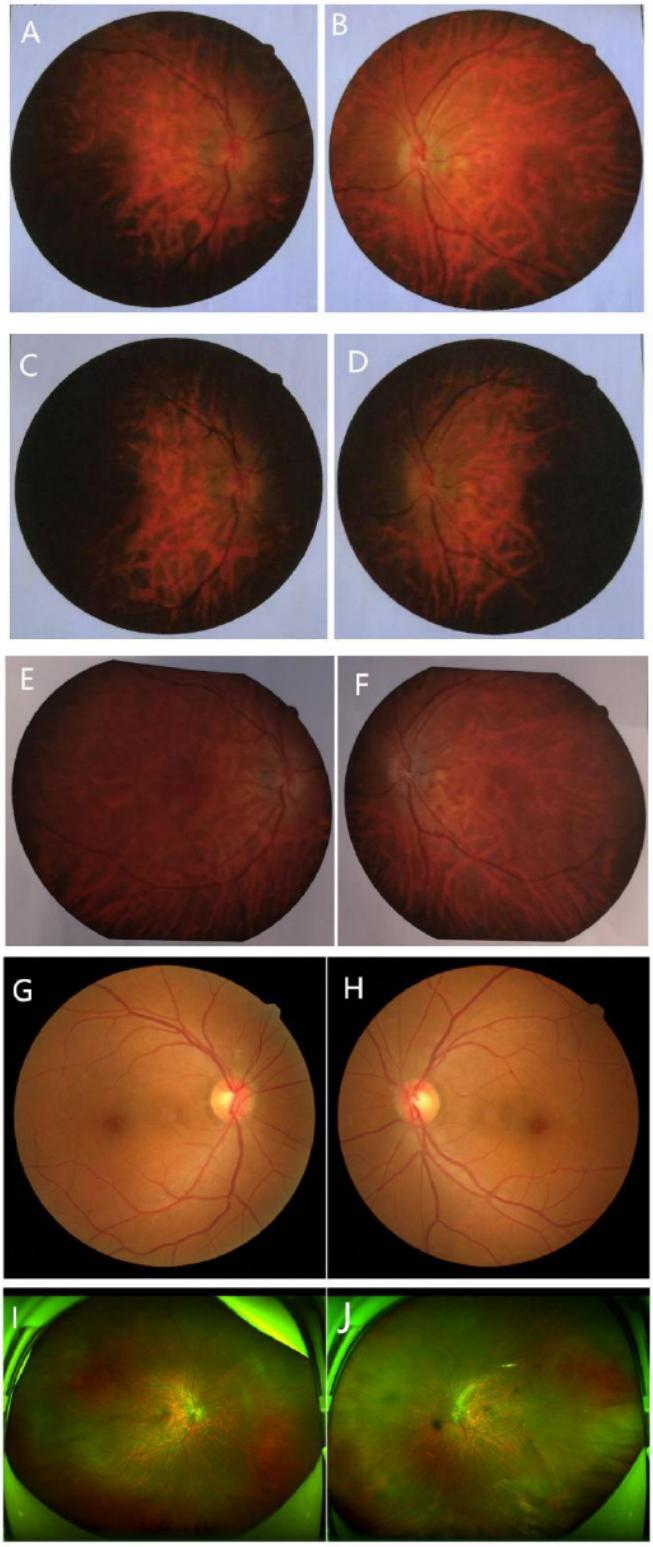

Figure 1: Fundus photos. **A**. Right eye at the first presentation in local hospital. **B**. Left eye at the first presentation in local hospital. **C**. Right eye at one week after injection. **D**. Left eye at one week after injection. E.Right eye at two weeks after injection. F. Left eye at two weeks after injection. **G**. Left eye before surgery. **H**. Right eye at the last visit (after surgical repair). **I**. Left eye at the last visit (after surgical repair). Macular hole were closed and the horse-shoe tear was surrounded by laser scar.

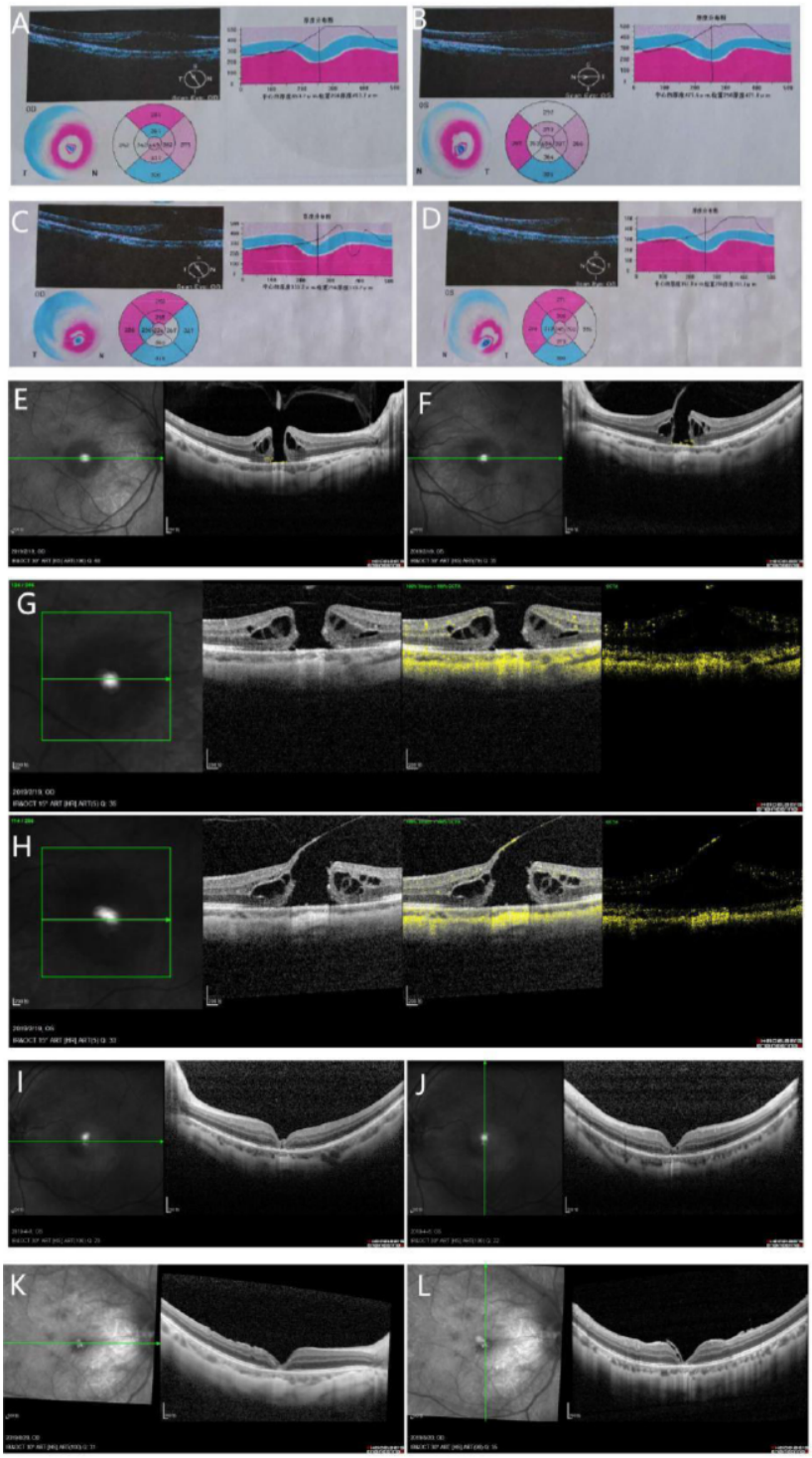

Figure 2: OCT scan. **A**. Right eye at the first presentation. **B**. Left eye at the first presentation. Dark space was shown in fovea with incomplete PVD in both eyes. **C**. Right eye at one week after injection. A full thickness macular hole was seen. **D**. Left eye at one week after injection. **E**. Right eye at two weeks after injection. A full thickness macular hole was seen. **F**. Left eye at two weeks after injection. A full thickness macular hole was seen. **G**. OCTA image of the right eye before surgery. **H**. OCTA image of the left eye before surgery. **I** and **J**. OCTA image of the left eye after surgery. The macular hole was closed in the left eye. **K** and **L**. OCTA image of the right eye after surgery. The macular hole was closed in the right eye.

DISCUSSION

Full-thickness macular hole formation is related to vitreo-macular traction although the exact pathogenesis is remain unclear. The macular hole formation associated with intravitreal Anti-VEGF injection has been reported as a rare situation. Moisseiev *et al.* [6] published a case of macular hole following intravitreal

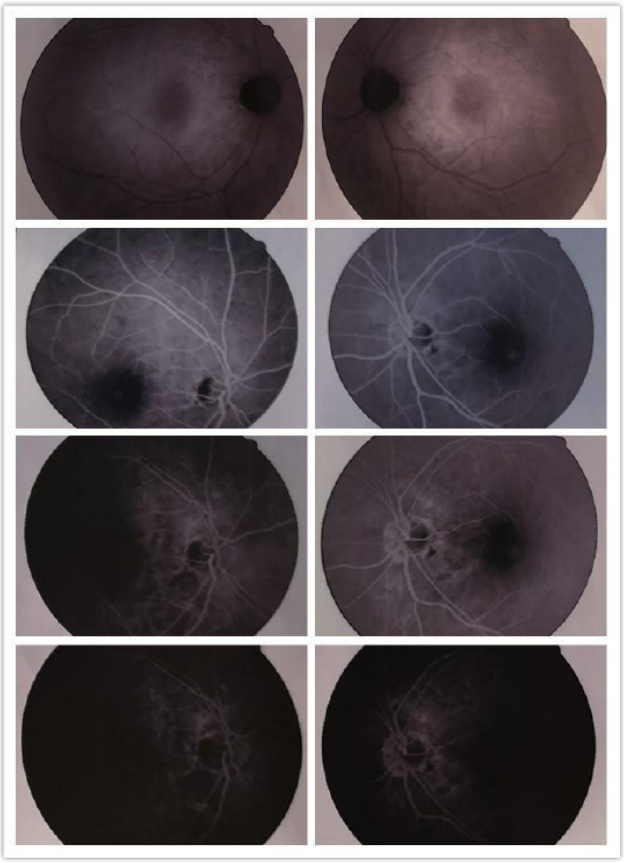

Figure 3: FFA images. From top to bottom, there were Auto fluorescence, early, middle and late phase of FFA. Window defect was found in fovea of both eyes. No exudation or pooling was seen in FFA.

Bevacizumab injection in neovascular AMD. The patient developed full-thickness macular hole in one eye after seven injections of Bevacizumab. The possible causes included the traction caused by Bevacizumab or the progression of retinal and RPE atrophy with AMD. Grigoropoulos *et al.* [7] and Raiji *et al.* [9] reported two cases of AMD-associated macular hole formation after ranibizumab injections. They considered the etiology as the tractional forces of vitreomacular adhesion and pushing or stretching forces of choroidal neovascular complex. Oshima *et al*. [9] reported a case of AMD-associated macular hole formation after three Aflibercept injections. The patient developed RPE tear after the first injection. They believed that the rolled RPE flap associated with traction of subretinal fibrosis caused the macular hole formation. Nawrocka *et al*. [10] reported a case of macular hole after ten months treatment of type 1 AMD was repaired successfully by surgery. Kayyaarasi *et al*. [11] reported 18 cases (19 eyes) developed macular hole after anti-VEGF injection. The average number of injections before the MH formation was four. MH developed after a mean follow-up of 5.1 months after the last injection. Most of the reported cases of macular hole formation after several anti-VEGF injection are AMD associated. The possible causes of macular hole formation were considered as increased fibrovascular scar tissue due to subretinal fluid resolution, neovascular membrane contraction, and the presence of PED, RPE tear, and ERM [6-10]. Lindeke-Myers A *et al*. [12] reported a case of PCV developed full thickness macular hole after intravitreal bevacizumab.

In this case, the high myopic patient received bilateral conbercept injection to treat “macular edema”. Although the quality of OCT image at baseline was very poor, we could find clue of myopic foveoschisis with incomplete PVD in both eyes, in stead of macular edema. FFA did not provide any evidence of anti-VEGF indication, neither macular edema nor myopic choroidal neovascularization. Thus, we have the reason to conclude that this case had myopic foveoschisis and was misdiagnosed as macular edema. The full-thickness macular hole formed in the right and left eye at 7 and 19 days after intravitreal conbercept injection, respectively. Through surgical repair, the macular holes in both eyes were closed. The possible explanations of full-thickness macular hole formation in this case could be: (1) The natural progression of myopic foveoschisis and PVD is coincident with the intravitreal injection of conbercept. (2) The tractional force from vitreomacular adhesion increased after intravitreal injection of conbercept. Anti-VEGF agent-Conbercept is a recombinant fusion protein developed and widely used in China in recent years. To the best of our knowledge, this is the first case report of full-thickness macular hole formation secondary to single dose of intravitreal conbercept injection; and the first case of bilateral full-thickness macular hole following intravitreal anti-VEGF injection. We should be aware that full-thickness macular hole formation could be a rare complication after anti-VEGF injection. To avoid unnecessary damage, the candidate for anti-VEGF injection should be selected appropriately.

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Conflict of Interests

Min Wu, none; Jie Min, none, Zhichao Sheng, none.

REFERENCE

[1] Shah CP, Hsu J, Garg SJ, Fischer DH, Kaiser R. Retinal pigment epithelial tear after intravitreal bevacizumab injection. Am J Ophthalmol. 2006; 142: 1070-2. https://doi.org/10.1016/j.ajo.2006.07.037

[2] Guber J, Praveen A, Saeed MU. Higher incidence of retinal pigment epithelium tears after ranibizumab in neovascular age-related macular degeneration with increasing pigment epithelium detachment height. Br J Ophthalmol. 2013; 97: 1486-7. https://doi.org/10.1136/bjophthalmol-2013-303978

[3] Chang LK, Flaxel CJ, Lauer AK, Sarraf D. RPE tears after pegaptanib treatment in age-related macular degeneration. Retina. 2007; 27: 857-63. https://doi.org/10.1097/IAE.0b013e3180342c42

[4] Doguizi S, Ozdek S. Pigment epithelial tears associated with Anti-Vegf therapy: incidence, long-term visual outcome, and relationship with pigment epithelial detachment in Age-related Macular Degeneration. Retina. 2014; 34: 1156-62. https://doi.org/10.1097/IAE.0000000000000056

[5] Duker J, Kaiser P, Binder S, Smet M, Gaudric A, Reichel E, *et al*. The International Vitreomacular Traction Study Group Classification of Vitreomacular Adhesion, Traction, and Macular hole. Ophthalmology, 2013; 120(12): 2611-2619. https://doi.org/10.1016/j.ophtha.2013.07.042

[6] Moisseiev E, Goldstein M, Loewenstein A, Moisseiev J. Macular Hole following Intravitreal Bevacizumab Injection in Choroidal Neovascularization Caused by Age-Related Macular Degeneration. Case Rep Ophthalmol. 2010; 1: 36-41. https://doi.org/10.1159/000319827

[7] Grigoropoulos V, Emfietzoglou J, Nikolaidis P, Theodossiadis G, Theodossiadis P. Full-thickness macular hole after intravitreal injection of ranibizumab in a patient with retinal pigment epithelium detachment and tear. Eur J Ophthalmol. 2010; 20: 469-72. https://doi.org/10.1177/112067211002000235

[8] Raiji VR, Eliott D, Sadda SR. Macular hole overlying pigment epithelial detachment after intravitreal injection with ranibizumab. Retin Cases Brief Rep. 2013; 7: 91-4. https://doi.org/10.1097/ICB.0b013e31826f090d

[9] Oshima Y, Apte R, Nakao S, Yoshida S, Ishibashi T. Full thickness macular hole case after intravitreal aflibercept treatment. BMC Ophthalmology, 2015; 15: 30. https://doi.org/10.1186/s12886-015-0021-3

[10] Nawrocka ZA, Nawrocka Z, Nawrocki J.Vitrectomy for full thickness macular hole developed during the course of anti-VEGF treatment of type 1 neovascular AMD.Eur J Ophthalmol, 2022 Sep; 32(5): NP5-NP8. https://doi.org/10.1177/11206721211002123

[11] Kayaarasi Ozturker Z, Akca Bayar S, Yaman Pinarci E, Kurt RA, Akkoyun I, Yilmaz G.Atypical macular hole formation after Anti-VEGF therapy for neovascular age-related macular degeneration: Coincidence or consequence? Arch Soc Esp Oftalmol (Engl Ed), 2021 Sep; 96(9): 455-461. https://doi.org/10.1016/j.oftale.2020.08.006

[12] Lindeke-Myers A, Kokame GT, Yeh S, Shantha J.Successful Treatment of Full-Thickness Macular Hole in Polypoidal Choroidal Vasculopathy with Anti-VEGF Therapy. J Vitreoretin Dis, 2020; 4(5): 433-436. https://doi.org/10.1177/2474126420909706

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