

Macular hole closure induced by intravitreal injection in diabetic macular edema

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Dear Editor,

Macular hole (MH) formation is uncommon in patients with diabetic macular edema (DME). Few cases of MH associated with DME treatment have been described, including a report of four out of eight eyes with MH and diabetic retinopathy (DR) having DME^[1]. However, no case of resolution of MH after DME treatment has been reported. We report three consecutive cases of MH closure achieved by intravitreal injection for DME treatment. This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital. The present study adhered to the tenets of the Declaration of Helsinki. Informed consent for using of medical record was obtained from each patients.

Case Presentation A 60-year-old woman who had visited our clinic for DME treatment complained of decreased vision in the right eye for one week. She had no significant medical or ocular surgical history other than a cataract surgery three years ago. She had been treated with panretinal photocoagulation for DR and intravitreal injection of bevacizumab, triamcinolone, and dexamethasone implant for DME for five years. The best-

corrected visual acuity (BCVA) of her right eye was 20/125. Fundus examination of the right eye revealed DME, an MH, and posterior vitreous detachment (PVD) identified as a Weiss ring. Optical coherence tomography (OCT; DRI OCT-1 Atlantis, Topcon, Tokyo, Japan) confirmed the presence of a stage 2 MH without vitreoretinal traction and showed thin epiretinal membrane (ERM) and perifoveal retinal edema (Figure 1A). MH was not observed in the OCT image of the visit one month ago. An intravitreal dexamethasone implant (Ozurdex[®], Allergan, Inc, Irvine, CA, USA) was injected on the same day to reduce the DME. After one week, OCT showed reduction of macular edema and closure of the MH. At three months, the BCVA was 20/63 and OCT showed recovery of the ellipsoid zone (EZ) and external limiting membrane (ELM; Figure 1B). A 60-year-old man with type 2 diabetes mellitus visited the clinic for DR screening. He had no complaints. He had no significant medical or ocular surgical history. The BCVA of his right eye was 20/40. Fundus examination of the right eye confirmed moderate non-proliferative DR, clinically-significant macular edema and PVD. There was perifoveal edema in the OCT image. Three days later, the patient visited the clinic for fluorescein angiography and a small MH was found that had not previously been presented. OCT scan was repeated and it revealed a stage 1 MH without vitreoretinal traction in addition to perifoveal edema (Figure 1C). Intravitreal bevacizumab (Avastin[®]; Genentech, Inc., South San Francisco, CA, USA) was immediately administered. After two weeks, OCT showed closure of the MH. Consecutive monthly bevacizumab injections were administered. At three months, the BCVA did not change, and recovery of the EZ and ELM was observed (Figure 1D). An MH was observed in a 74-year-old man at a routine follow-up for DR. He had no visual complaints or history of ocular treatment other than a panretinal photocoagulation performed five years ago. The BCVA of his right eye was 20/32. Weiss ring was seen at fundus examination. OCT showed stage 2 MH with diffuse macular edema without vitreoretinal traction and extrafoveal ERM (Figure 1E). There was no MH observed in the OCT image in the visit a month ago. Intravitreal bevacizumab was injected on the same day. After one month, his BCVA unchanged, but closure of the MH and reduced macular edema were observed (Figure 1F).

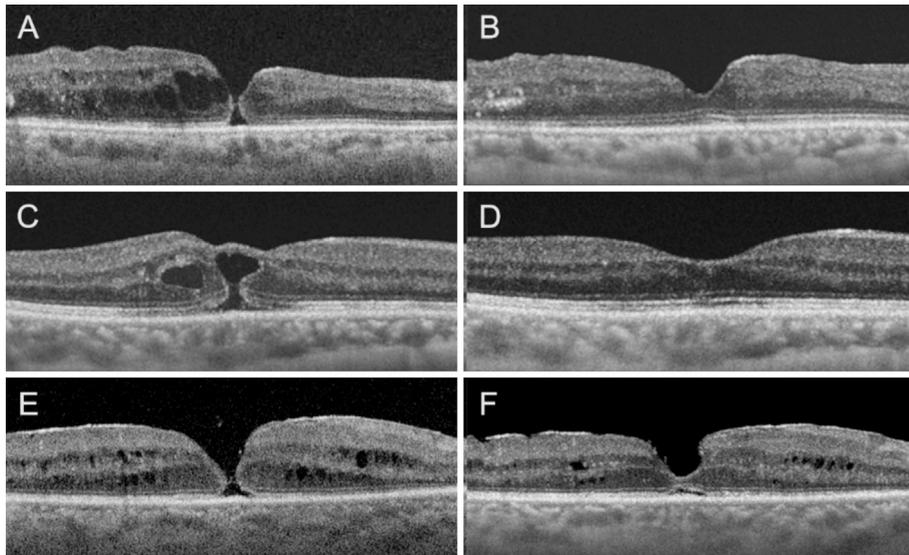


Figure 1 Cross-sectional optical coherence tomography images of the fovea of patients with a macular hole and diabetic macular edema A: OCT image of patient 1 demonstrating a stage 2 MH in the right eye, retinal edema and posterior vitreous detachment at the macular region are seen; B: Three months after intravitreal dexamethasone implant injection, macular edema has reduced and the MH is closed; C: OCT image of patient 2 demonstrating a stage 1 MH in the right eye, retinal edema and PVD at the macular region are seen; D: After three intravitreal bevacizumab injections that were administered monthly, reduced macular edema and closure of the MH are observed; E: OCT image of patient 3 showing a stage 2 MH and diffuse retinal edema in the right eye, PVD at the macular region is seen; F: After one month of intravitreal bevacizumab injections, macular edema has reduced and the MH has closed. MH: Macular hole; PVD: Posterior vitreous detachment.

DISCUSSION

MH is usually caused by vitreomacular traction or tangential traction of the vitreous cortex^[2]. However, Brazitikos and Stangos^[1] studied 8 eyes with DR which had developed MH and they found that 4 MHs were developed with DME. With this result, it is suggested that cystoid degeneration or vulnerable fluid accumulation in an atrophic retina may progress to MH in DME eyes. Kwon *et al*^[3] reported a case of MH closure induced by intravitreal triamcinolone injection in diabetic eye and insisted that macular edema treatment may lead to MH closure. In that case, however, unlike our case, there was a small subfoveal serous elevation before the vitrectomy for vitreous haemorrhage and DME was not observed at the time of MH. Although it is not the case of DME, a recent case showed the resolution of MH was induced by treatment of pseudophakic macular edema with oral acetazolamide, topical dexamethasone and ketorolac^[4]. In our cases, two patients with MH didn't have macular edema or MH at the last routine visit one month before MH development, and the other one patient with macular edema didn't show an MH on the first examination. Although injected drugs for reducing macular edema were different including bevacizumab and dexamethasone between patients, after intravitreal injection, it was confirmed that MHs were closed after 1wk to 1mo and well maintained for more than 3mo.

Since vitreomacular traction was not observed on OCT scan, PVD was shown in fundus photography and perifoveal or

parafoveal macular edema was exist in these cases, MHs can be caused by tangential traction rather than anteroposterior traction. As previously described, it is suggested that cystoid macular edema leads to a large cyst and the rupture of the inner wall result in MH in DR^[1]. In addition to the previous hypothesis, we suggest that macular edema forces the inner limiting membrane to be convex; due to its stiffness, the inner limiting membrane is not easily stretched, and this tension can be transmitted as tangential traction to the fovea^[5]. Due to this mechanism, the closure of MHs appears to be achieved after reduction of DME resulting in a decrease of tangential traction. In the present cases, the size of MHs were relatively small, below stage 2, and MHs occurred within 1mo before treatment. ERMs were observed in 2 cases and it could theoretically have an effect of the occurrence of MH, but the role of ERMs in these cases could be limited because MHs were closed only by the improvement of DME. The spontaneous closure rate of MH is less than 10%, and the closure rate of small MH ($\leq 250 \mu\text{m}$) is about 40%-60% in pharmacologic vitreolysis using ocriplasmin and is 29% in pneumatic vitreolysis. In small MH with DME like this case, it seems that DME treatment can be a treatment option^[2,6-7]. In conclusion, our findings indicate that in cases of DME with small MHs, treatment of macular edema can lead to MH closure.

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