



Brief communication

Development of macular holes in diabetic retinopathy with fibrovascular proliferation: Report of four cases



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ABSTRACT

There are yet no reports in the literature describing the mechanism of macular hole (MH) formation associated with fibrovascular proliferation in proliferative diabetic retinopathy. We report four cases of MHs in diabetic retinopathy with fibrovascular proliferation; formation of MHs were studied using sequential pre-MH optical coherence tomography (OCT). In Case 1, initial OCT revealed tractional schisis and cysts with fovea detachment. An MH with bowl-shaped detachment was noted within 6 weeks. In Case 2, initial OCT revealed thickened posterior hyaloid membrane with vitreomacular traction. Five and a half years later, OCT showed MH formation with possible vitreomacular separation. Some epiretinal membrane was also noted in the macula area. In Case 3, initial OCT revealed tractional retinal elevation from the superonasal area to the fovea with macular thinning. An MH with detachment developed 7 weeks later. In Case 4, initial OCT revealed macula-involved retinal detachment with traction. An MH was noted 4 weeks later. The analysis of sequential OCT findings in these four cases suggests that strong vitreoretinal adhesion and traction of fibrovascular proliferation may induce an MH without going through the same evolutionary phases as those characteristic of idiopathic MHs.

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1. Introduction

Full-thickness macular holes (FTMHs) most commonly occur in senile patients without an apparent underlying cause. It may also develop after ocular trauma or in association with high myopia, rhegmatogenous retinal detachment, or diabetic retinopathy (DR).^{1–3} In proliferative diabetic retinopathy (PDR), macular holes (MHs) may develop in eyes with or without fibrovascular proliferation (FVP). Some studies have demonstrated that the structural changes, treatment, and outcomes of MHs in DR without FVP are similar to those in idiopathic conditions.⁴ By contrast, an MH in DR with FVP has characteristics that are distinct from those of idiopathic MHs.⁵ Our previous study reported the clinical characteristics and treatment results of MHs associated with FVP.⁵ However, whether the development of an MH in DR with FVP follows a similar process to that occurring in the case of idiopathic holes

remains unclear. In this study, we report four cases of diabetic MHs in DR associated with FVP that had undergone optical coherence tomography (OCT) before MH formation. By studying the pre-MH changes from clinical examinations and OCT, we hope to increase our understanding of the mechanism of MH formation in this unique clinical condition.

2. Methods

We reviewed sequential OCT images from FTMHs in DR patients with visible FVP prior to and after FTMH formation from July 2007 to January 2013. Fundus photography and standard 6 mm or 9 mm OCT (Stratus OCT; Carl Zeiss Meditec, Inc., Dublin, CA, USA), or spectral domain OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Inc.) of the macula were carried out in all participants. Features of the macular structural changes as well as the vitreoretinal relationship, including premacular tissue presence and posterior hyaloid status, were recorded. The morphological definition of MH was a full-thickness retinal defect in the macular area with or without surrounding subretinal fluid cuff. Retinal detachment was defined as retinal elevation, with the subretinal fluid being more extensive than the surrounding cuff adjacent to the hole.

Conflicts of interest: The authors have no financial interest in any materials or equipment used in the study. All authors declare no conflicts of interest.

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3. Case reports and results

3.1. Case 1

The first case was a 54-year-old woman having DR who presented with blurred vision in the left eye. The best-corrected visual acuity (BCVA) was 20/25 in the right eye and 20/63 in the left eye. Anterior segment examination results, pupils, and intraocular pressure were normal. Fundus examination of the left eye showed PDR with FVP tissue on the temporal lower and superonasal areas of the macula associated with an elevation of the paramacular tissue (Fig. 1A). OCT revealed tractional schisis and a cyst with fovea detachment (Fig. 1B and C). A follow-up examination 6 weeks later revealed an FTMH with a subfoveal fluid pocket and outer retinal tissue dehiscence. The edge of the hole was flat without cystic change (Fig. 1D–F).

3.2. Case 2

The second case was a 60-year-old man who presented with blurred vision in both eyes. He had diabetes mellitus for many years. BCVA was 20/200 in the right eye and 20/32 in the left eye.

Anterior segment examination in both eyes was unremarkable and intraocular pressure was normal. Fundus examination showed PDR in both eyes, with tractional retinal detachment in the right eye and FVP mainly situated at the midperipheral temporal retina in the left eye (Fig. 2A). The right eye was operated on, and a follow-up examination of the left eye 1 year later showed no increased FVP. However, OCT showed a thickened posterior hyaloid, specifically vitreomacular separation with vitreofoveal adhesion, which caused foveal tenting with cyst formation, although the outer retinal and photoreceptor layers were undisturbed (Fig. 2B). Three years later, OCT showed inner cyst disruption. The thickened posterior hyaloid seemed distanced from the retina, but the macular configuration suggested persistent vitreofoveal traction (Fig. 2C). A subsequent follow-up study performed 5 years after the first visit showed disruption of the outer lamina and formation of an MH (Fig. 2D and E).

3.3. Case 3

Case 3 was a 54-year-old woman having DR who presented with blurred vision in both eyes. BCVA was 20/125 in the right eye and 20/200 in the left eye. The anterior segment was

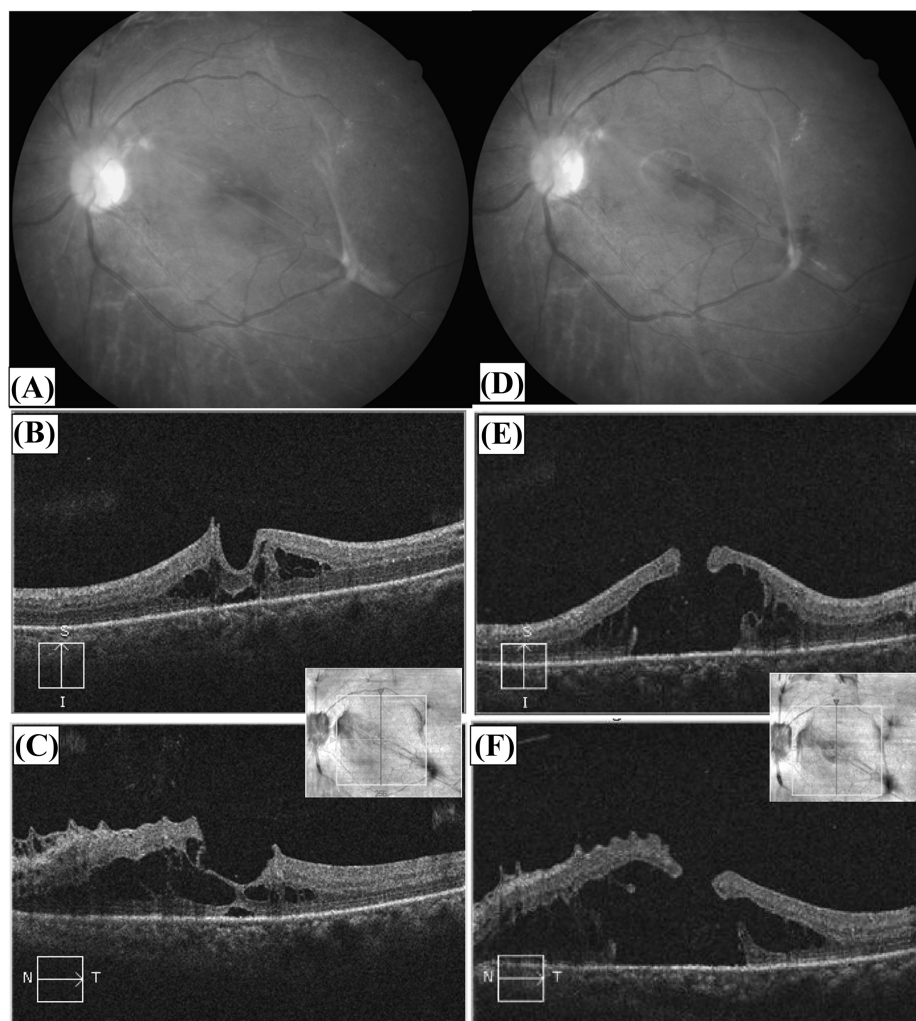


Fig. 1. Case 1. (A) Fundus photography shows the FVP tissue on the temporal lower and superonasal areas of the macula associated with elevation of the paramacular tissue. (B and C) OCT reveals foveal detachment with localized traction schisis. (D) An MH is noted 6 weeks later. (E and F) OCT shows an FTMH with a subfoveal fluid pocket and outer retina tissue dehiscence. The hole margin is flat without cystic change. FTMH = full-thickness macular hole; FVP = fibrovascular proliferation; MH = macular hole; OCT = optical coherence tomography.

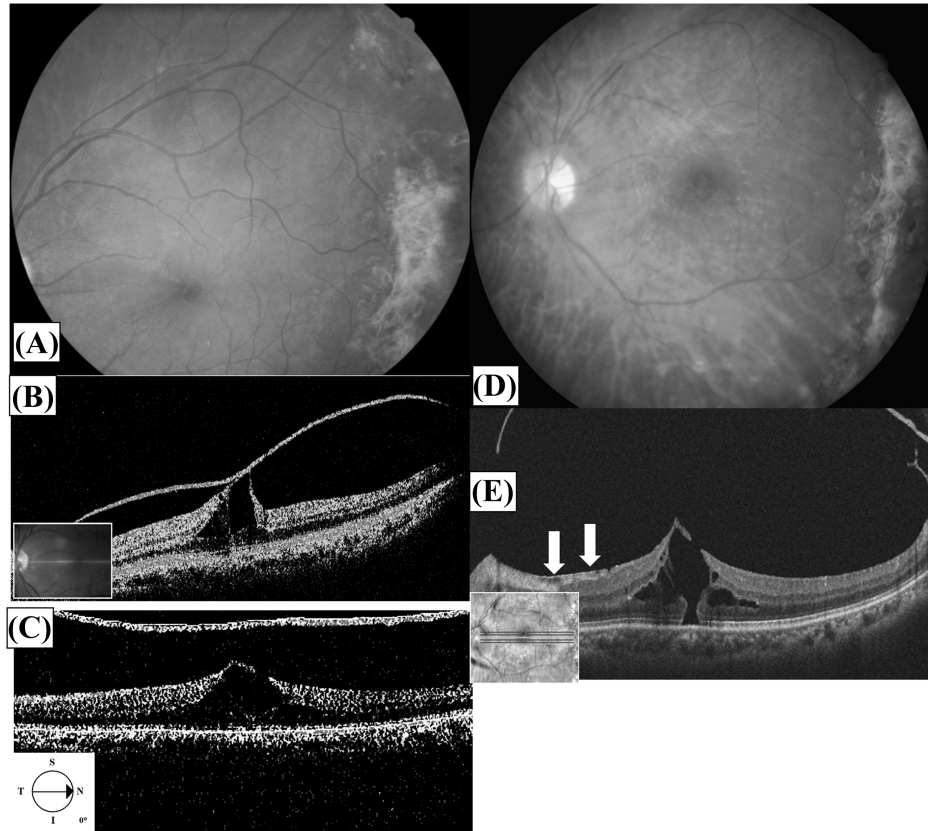


Fig. 2. Case 2. (A) Fundus photography shows that the FVP is situated mainly at the midperipheral temporal retina. (B) OCT 1 year later shows thickened posterior hyaloid and vitreomacular separation with vitreofoveal adhesion. Foveal tenting with cyst formation is also noted. (C) Three years later, disruption of the inner cyst is noted. The thickened posterior hyaloid seems to be away from the retina, but the macular configuration suggests persistent vitreofoveal traction. (D and E) One and a half years later, disruption of the outer lamina with MH formation is noted. ERM (arrow) is revealed from the nasal to the macula area. ERM = epiretinal membrane; FVP = fibrovascular proliferation; OCT = optical coherence tomography.

unremarkable. Fundus examination showed PDR with FVP in both eyes. OCT of the right eye revealed the presence of FVP tissue that exerted traction on the macular area from the nasal side, causing elevation and cystic change of the nasal macula, as well as thinning of the fovea (Fig. 3A). The FVP extended from the temporal and upper juxtapapillary areas to the upper arcade, and to the superonasal area at one end and the superotemporal midperiphery at the other end (Fig. 3B). A follow-up examination 2 months later revealed an FTMH and localized detachment in the right eye. No foveal detachment or inner retinal cyst formation was detected (Fig. 3C).

3.4. Case 4

The fourth case was a 30-year-old woman who presented with blurred vision in both eyes. She had diabetes mellitus for many years. BCVA was 20/32 in the right eye and 20/100 in the left eye. The anterior segment was unremarkable. Fundus examination showed PDR and FVP in both eyes with tractional retinal detachment of the left eye. FVP in the right eye was located mainly on the upper retina (Fig. 4A), and OCT revealed condensed hyaloid and vitreofoveal adhesion associated with tractional macular detachment (Fig. 4B). A follow-up examination 1 month later revealed an FTMH in the right eye (Fig. 4C and D).

Case 3 had been lost to follow-up without surgery. The remaining three cases required surgical intervention. Hole closure after operation was achieved in two cases (Cases 1 and 2), and in one (Case 4) a small gap remained 2 years after surgery.

4. Discussion

In our previous study, we found several distinctive morphological characteristics of MHs associated with FVP, including the typical flat hole margin with minimal cystic change, a larger detachment area around the hole as opposed to the simple cuff found in the idiopathic hole, and a thickened premacular membrane.⁵ Although these changes suggest different mechanisms of MH formation between DR with FVP and idiopathic cases, the literature had previously not investigated the prehole condition of the macula and the pathways leading to MHs. In this brief report, we found diverse mechanisms that might result in MHs in DR with FVP.

It is now widely accepted that the early event leading to an idiopathic MH is the persistent adherence of the cortical vitreous to the fovea with adjacent vitreoretinal separation. The resultant traction on the fovea causes foveal detachment or an intraretinal space termed a pseudocyst. Further traction leads to dehiscence of the foveal tissue, resulting in FTMH formation.^{6–9} After complete posterior vitreous detachment, epiretinal membrane exerting tangential traction on the fovea can be another cause of FTMH formation.^{10,11}

In our study, however, an analysis of the OCT findings of MHs in PDR associated with FVP showed different formation steps from those of idiopathic MHs.

In the first case, the FVP tissue caused an elevation of the paramacular tissue and exerted tangential traction on the macula. The macula first developed foveal detachment with localized tractional

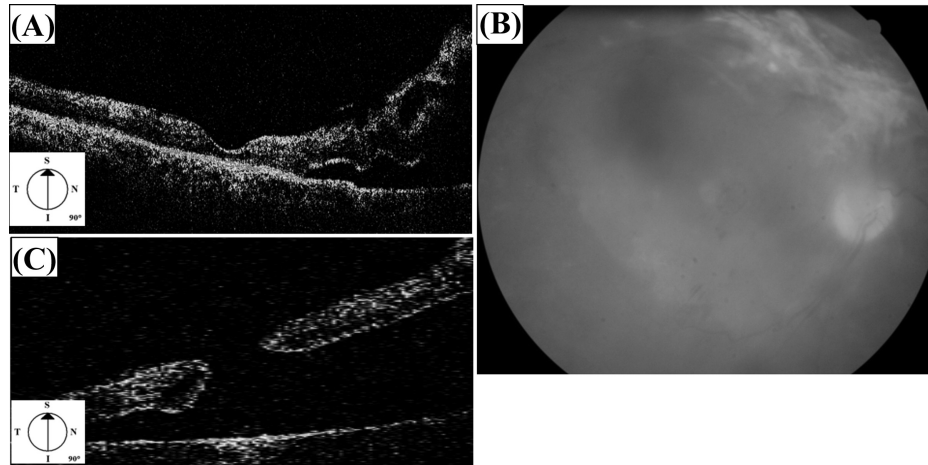


Fig. 3. Case 3. (A) OCT shows that the FVP tissue exerted traction on the macular area from the nasal side, causing elevation and cystic change of the nasal macula, as well as thinning of the fovea. (B) Fundus photography 2 months later shows that the FVP tissue extends from the temporal and upper juxtapapillary area to the upper arcade and to the upper nasal area. (C) OCT shows an MH and localized detachment. FVP = fibrovascular proliferation; MH = macular hole; OCT = optical coherence tomography.

schisis, different from the usual prehole condition of inner foveal cyst in the idiopathic condition. Structural changes rapidly went through outer lamina disruption, inner wall dehiscence, and schisis lining tissue breakdown to form a cavity with an elevated opening without cystic changes at the margin of the MH. This unique configuration was a result of the progressive and persistent traction on both the inner and the outer macula, which caused significant tissue dehiscence. The flat margin of the MH indicates that cystoid macular edema did not play a major role in the formation of the FTMH in this case.

In the second case, the FVP was mainly situated at the mid-peripheral temporal retina. The thickened posterior hyaloid developed vitreomacular separation with vitreofoveal adhesion

similar to the prehole condition in idiopathic cases. However, the vitreomacular traction was usually released after disruption of the inner cyst in idiopathic cases.^{12,13} However, in our case, the traction persisted even after foveal inner lining disruption and a possible separation of the thickened posterior vitreous membrane from the macular area, and resulted in the formation of FTMH 1½ years later. Color photography and OCT suggested epiretinal membrane formation in the macular area. We postulated that the presence of the epiretinal membrane might have sent traction from FVP to the foveal area and have an important contribution to the development of the MH.

In the third case, OCT showed that the FVP tissue exerted traction on the macular area from the nasal side, causing elevation and

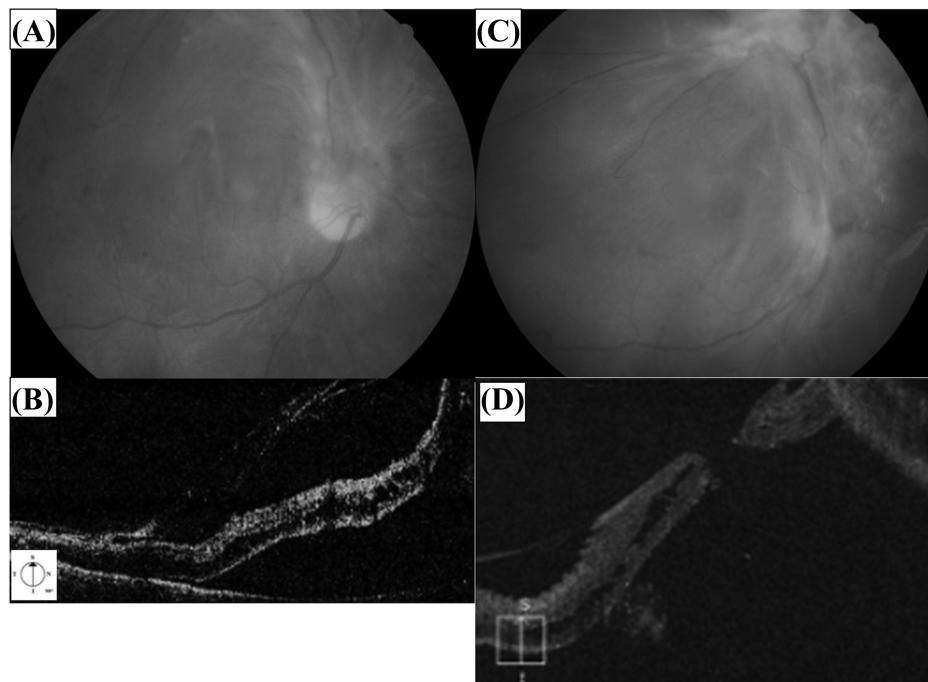


Fig. 4. Case 4. (A) Fundus photography shows that the FVP is located mainly on the upper retina. (B) OCT reveals that the FVP exerts oblique macular traction through condensed hyaloid and vitreofoveal adhesion, causing tractional macular detachment. (C and D) Fundus photography and OCT shows an MH and RD 4 weeks after the RD was detected. FVP = fibrovascular proliferation; MH = macular hole; OCT = optical coherence tomography; RD = retinal detachment.

cystic change of the nasal macula, as well as thinning of the fovea. An FTMH developed within just 2 months. The serial images and the time sequence suggest that the FTMH was formed without going through the stages of foveal changes typical of an idiopathic MH. There was tractional retinal elevation in the superonasal area with macular thinning before MH formation, suggesting that the MH was induced by the tangential force of FVP. Again, the margin of the hole was flat, indicating that the tangential traction, and not the cystoid macular edema, was the main contributor to the FTMH formation.

In the fourth case, the tractional macular detachment was associated with oblique macular traction from the condensed hyaloid and the FVP. Instead of tension release after the development of macular detachment, the nondetached vitreous hyaloid along with FVP tissue maintained tangential traction on the macula, causing disruption of the fovea and formation of the MH. Development of the FTMH in this case emphasized the continuous traction after macular elevation.

In conclusion, our case report reveals that varied pathways of FTMH formation exist in DR cases with FVP, and all these pathways were different from those in idiopathic conditions. We noted that in a case with traction schisis (Case 1) or macular thinning (Case 3), the tangential traction force induced by FVP might be severe enough to induce FTMH formation within a short period of time without slowly progressing from foveal cysts or foveal detachment. Alternatively, the fovea may be subject to an anterior–posterior traction force, in addition to tangential and oblique tractions by the adherent fibrovascular tissue. This complex and strong traction could possibly induce foveal tears from the attached retina (Case 2) or after macular detachment (Case 4).

Further analysis with larger case numbers is necessary to elucidate the diverse mechanisms of FTMHs in PDR with FVP.

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