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Spontaneous Lamellar Macular Holes Closure

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Key words: epiretinal proliferation (ERP), lamellar hole-associated epiretinal membrane (LHEP), lamellar macular hole (LMH), Müller glial cells, spectral-domain optical coherence tomography (SD-OCT).

Summary statement:

Lamellar macular hole is a macular lesion characterized by a partial thickness foveal defect and commonly associated with epiretinal proliferation. In this report we present two cases of spontaneous closure of lamellar macular holes by extension of epiretinal proliferation filling the retinal defect.

ABSTRACT:

Purpose: To report two cases of spontaneous closure of lamellar macular holes (LMH) with epiretinal proliferation (ERP).

Methods: Observational cases report.

Results: Two patients affected with LMH showed progressive and spontaneous closure of the hole associated with ERP development. At presentation, both patients presented with irregular foveal contour, and foveal cavitation with apparent loss of retinal tissue. In both cases, ERP, also called “lamellar hole-associated epiretinal proliferation” (LHEP), was present and increased in size over time. This proliferation progressively developed across the hole with apparent restoration of the foveal contour and preservation of visual acuity.

Conclusion: This report describes two cases of LMH in which ERP increased over time, resulting in LMH closure. Such observations may suggest a spontaneous healing process driven by glial cell proliferation.

45 INTRODUCTION

46 Lamellar macular hole (LMH) is characterized by an irregular foveal contour
47 with partial thickness retinal defect as seen on optical coherence tomography
48 (OCT).^(1,2) The pathophysiology of LMH remains poorly understood with suggestions
49 of an abnormal vitreoretinal interface and/or retinal degenerative processes playing
50 a role.^(3,4) The natural history of LMH includes the enlargement of the foveal
51 cavitation and progressive disruption of the ellipsoid zone resulting in visual acuity
52 loss.⁽⁴⁾ Pang et al. first noted that LMH is frequently associated with an epiretinal
53 proliferation (ERP), which they initially named “lamellar hole-associated epiretinal
54 proliferation” (LHEP).⁽⁵⁾ This dense material differs from conventional epiretinal
55 membrane by the absence of contractile activity and appears on spectral-domain
56 OCT (SD-OCT) as a thick, iso-reflective, epiretinal material.⁽⁶⁾ Although the
57 pathogenesis of ERP remains unclear, some authors hypothesized that it may be the
58 result of a healing process.⁽⁵⁾ Here we report two cases of LMH showing spontaneous
59 restoration of foveal contour with ERP increase over an extended follow-up period.

60

61 CASE REPORTS

62 Case 1

63 A 71-year-old gentleman was initially referred for a macula on
64 rhegmatogenous retinal detachment with multiple retinal tears in his pseudophakic
65 left eye. He underwent a combined pars-plana vitrectomy with scleral buckle. At
66 postoperative month one, the retina was attached and his vision was 20/20 Snellen
67 equivalent without macular abnormalities on fundus examination. Three years later,

the patient presented complaining of vision loss in his operated eye (20/30 Snellen equivalent). Examination of the posterior segment demonstrated an irregular foveal defect and a diagnosis of LMH was confirmed with SD-OCT (Figure 1A). The foveal contour appeared irregular with a partial thickness retinal defect and a disruption of both external limiting membrane (ELM) and ellipsoidal zone (EZ). An ERP was noted along the surface and the nasal internal edge of the lamellar hole (Figure 1A and 1B). Thirty-three months after the diagnosis of LMH, the proliferation had extended across the prior hole with restoration of the foveal contour (Figure 1C). The disruption of the ELM and EZ appeared to have improved over time. On clinical examination, his vision slightly improved to 20/25 Snellen equivalent.

Case 2

A 88-year-old gentleman was evaluated for a mild non-proliferative diabetic retinopathy. His visual acuity was 20/25 Snellen equivalent in his left eye. The patient was pseudophakic and the anterior segment examination was unremarkable. The posterior segment examination reported a blunted foveolar reflex in the left eye, and a LMH was diagnosed with SD-OCT examination (Figure 2A). Epiretinal proliferation was noted along the surface and at the edges of the LMH. Over time the proliferation progressively increased to completely filling the foveolar defect (Figure 2B and 2C). Thirty-three months after the initial diagnosis of LMH, the fovea had an apparent normal contour on SD-OCT (Figure 2D). His visual acuity remained stable over the follow-up period at 20/25, and both ELM and EZ appeared more regular compared to baseline examination.

DISCUSSION

92 We report two cases of LMH with an extended follow-up period, in which the
93 progression of ERP was associated with restoration of foveal anatomical contour and
94 preservation of visual acuity. Epiretinal proliferation is not an exclusive feature of
95 LMH as it has recently been associated with other retinal conditions such as full-
96 thickness macular hole, posterior uveitis, and epiretinal membranes.⁽⁷⁾ Therefore,
97 the term “epiretinal proliferation” (ERP) may be preferred instead of “lamellar hole
98 associated-epiretinal proliferation” or LHEP.⁽⁵⁾ This proliferation may originate from
99 inner retinal layers within the lamellar hole defect due to Müller cell proliferation.⁽⁵⁾
100 The exact pathogenesis of ERP is unknown but one theory is that the proliferation is
101 a reactive process to retinal injury.^(5,7)

102 Previous studies reported that visual acuity of LMH patients with ERP was
103 significantly worse than eyes without proliferation.^(6,8) However, in our cases, the
104 progressive increase in ERP did not impair visual acuity. In fact, the progression in
105 ERP correlated with restoration of foveal contour and ELM/EZ over time.
106 Remarkably, visual acuity remained stable over the follow-up period and even
107 slightly increased in the first case. This remodeling of foveal anatomy suggests a
108 spontaneous healing process such as the progressive growth of ERP over the foveal
109 surface.

110 Previous studies reported that the response of glial Müller cells to retinal injury
111 may be protective to retinal function with potential regeneration of all retinal cell
112 types including the photoreceptors.⁽⁹⁾ Hence, proliferation and migration of glial cells
113 present in the ERP may contribute to stabilization or regeneration of the retinal
114 layers including the photoreceptors. This could explain how the LMH patients in our
115 report showed preservation of visual acuity over their follow-up period.

Recommendations for surgical repair of LMH remains controversial.⁽¹⁰⁾ The two cases reported here may argue for observation given the possibility of spontaneous improvement. However, in cases where there is progressive decrease of vision with enlargement of the LMH and/or an increase of EZ disruption over time, surgical intervention might be considered. If a vitrectomy is performed, potential benefit of ERP noted in our cases support recent publications suggesting to use this proliferation to fill the hole at the end of the surgical procedure.⁽¹¹⁾

In 2012, using time-domain OCT, Theodossiadis et al. reported also two cases of spontaneous closure of what they named LMH.⁽¹²⁾ However, in this paper both patients showed a contractive ERM with no ERP. The authors attributed the favorable evolution to the spontaneous avulsion of the ERM with subsequent release of traction. In the present report, our both cases already had a posterior vitreous detachment and lacked a tractional ERM at baseline. The restoration of foveal profile involved the development of additional tissue, i.e epiretinal proliferation, thought to be a gliosis reaction in response to the loss of retinal tissue. A similar observation has recently been reported by Cutler and Singh, who also showed resolution of a LMH by extension of ERP.⁽¹³⁾ These different mechanisms highlight the distinctive pathogenesis between “tractional lamellar macular hole”, and “degenerative lamellar macular hole” which lacks tractional properties, as seen here in our two patients.⁽⁴⁾

In this report we describe two patients with LMH and progressive increase of ERP leading to spontaneous anatomical restoration of the foveal contour on SD-OCT, partial recovery of outer retinal layers, and preservation of the visual acuity.

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174 **FIGURES LEGENDS**

175 **Figure 1.** Case 1. Horizontal spectral-domain optical coherence tomography (SD-
176 OCT) scans over the follow-up period. At baseline SD-OCT imaging showed a
177 lamellar macular hole (LMH) (empty arrowheads) with epiretinal proliferation (ERP)
178 over the surface of the retina (arrows) (A). Large disruption of external limiting
179 membrane and ellipsoidal zone layers were noted above the retinal defect (B).
180 Thirty-three months later, the LMH was filled by the ERP which appears as an
181 isorefective tissue (arrows). The SD-OCT showed a regular foveal contour with
182 improvement of photoreceptors defect (C).

183

184 **Figure 2.** Case 2. Spectral-domain optical coherence tomography (SD-OCT) scans
185 showed initially a lamellar macular hole (LMH) visible as a partial thickness foveal
186 defect (arrowheads) with epiretinal proliferation (ERP) (arrows) (A). The area of
187 proliferation progressively increased over time (arrows) and filled the retinal defect
188 (arrowheads) (B and C). At the last examination the foveal contour appeared regular
189 with isorefective proliferation (arrows) overlying the previous foveal defect and
190 over the surface of the retina (D). Outer retinal layers were noted to be improved
191 from baseline to final examination (A and D).