

Case Report

Autologous Internal Limiting Membrane Transplants Successfully Close a Large Parafoveal Retinal Hole

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Parafoveal retinal holes (PRHs) are one of the complications that can occur after internal limiting membrane (ILM) peeling during macular surgery. Here we describe a patient in whom an exceptionally large PRH (1,069- μm dia.) was successfully closed by repeated autologous ILM transplantation.

Key words: autologous internal limiting membrane transplantation, parafoveal retinal hole, macular surgery

Parafoveal retinal holes (PRHs) are one of the complications that can occur after internal limiting membrane (ILM) peeling during macular surgery. Whether a PRH causes visual impairment depends on its distance from the fovea and its size. Although some patients with PRHs are asymptomatic and do not require any treatment [1], treatment is required when symptoms such as impaired vision, paracentral scotoma or metamorphopsia occur. However, there is no established treatment for PRHs.

We recently reported that autologous ILM transplantation could effectively close refractory macular holes, where the ILM had previously been peeled off [2]. Here we describe a patient in whom an exceptionally large PRH with a diameter of 1,069 μm was successfully closed by repeated autologous ILM transplantation.

Case Report

A 51-year-old Japanese woman was referred for treatment of a ruptured retinal arterial macroaneurysm in the right eye, which had caused both sub-foveal and

sub-ILM hemorrhages (Fig. 1A). The Snellen best-corrected visual acuity (BCVA) for this eye was 20/500. Initially we carried out a 25-gauge pars plana vitrectomy with cataract surgery, drained the sub-ILM hemorrhage, injected 0.1 ml of recombinant tissue plasminogen activator (4,000 IU/0.1 ml, GRTPA[®]; Mitsubishi Tanabe Pharma, Tokyo, Japan) subretinally [3, 4], and performed air tamponade. After surgery, a PRH formed superior to and temporal to the fovea (Fig. 1B). Therefore, 3 weeks later, we attempted to close the PRH by performing ILM peeling and a 20% SF₆ gas tamponade, but this was not effective (Fig. 1C, D).

The length of the major axis of the PRH, which was measured by the tool embedded in optical coherence tomography (OCT, DRI-OCT Atlantis, Topcon, Tokyo, Japan), was 1,069 μm . There were retinal cysts at the margin of the retinal hole, immediately adjacent to the fovea (Fig. 1D). The Snellen BCVA for the eye was 20/100, and the patient complained of paracentral scotoma.

Two weeks later, we carried out an autologous ILM transplant [2]. Sixteen days after that, the PRH had not closed, but was considerably smaller with a diameter of 280 μm (Fig. 1E, F). We therefore carried out a second

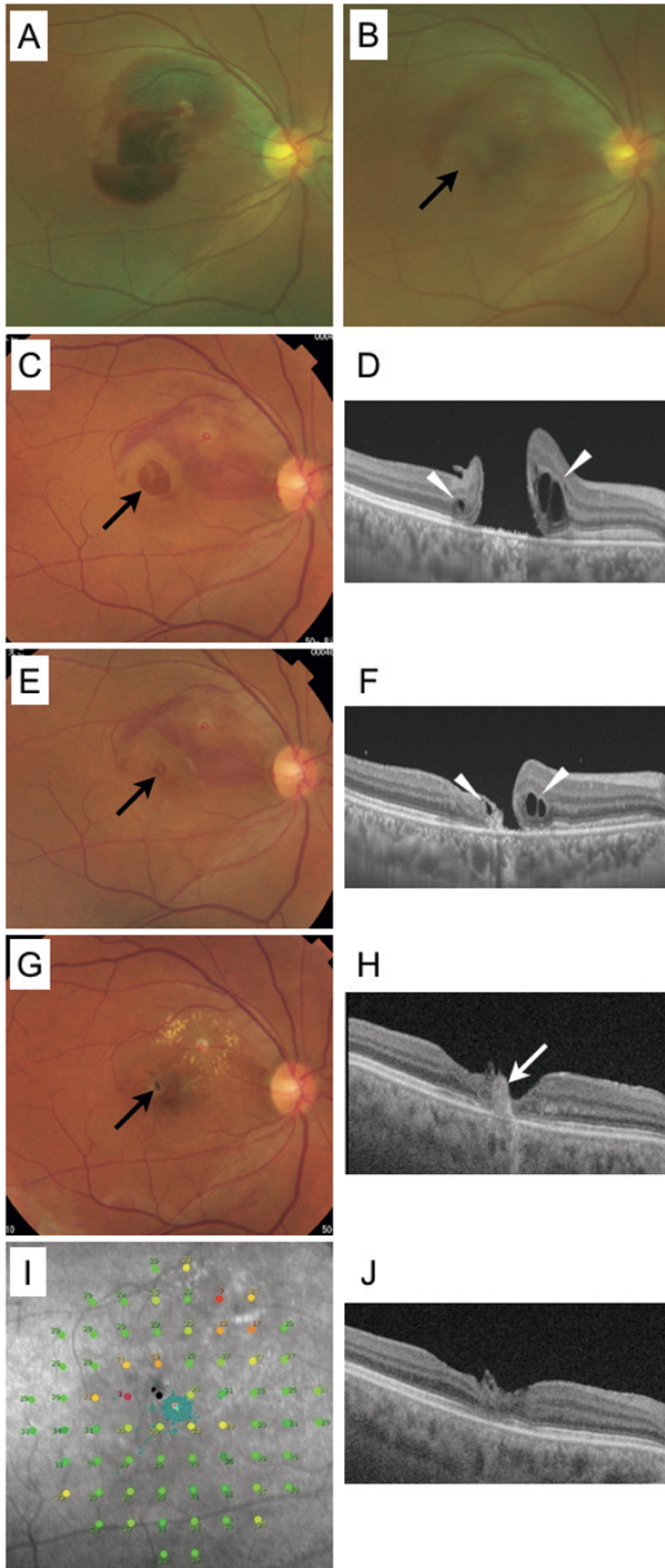


Fig. 1 Successful treatment of a parafoveal retinal hole (PRH) in the right eye of a 51-year-old woman. The PRH arose after treatment of a ruptured retinal arterial macroaneurysm. Fundus photographs at referral (**A**) and after the initial vitrectomy (**B**) showing the PRH (black arrow). A fundus photograph (**C**) and OCT scan (**D**) 3 weeks later, after the internal limiting membrane (ILM) peeling and 20% SF₆ gas tamponade were carried out, showing the PRH (black arrow) and retinal cysts (white arrowheads). Fundus photographs and OCT scans after the first autologous ILM transplant (**E, F**) and after the second autologous ILM transplant (**G, H**), showing the highly reflective area (white arrow). The black arrow in panel E indicates residual PRH. In panel G, the black arrow indicates the closed PRH. A microperimetry image (**I**) showing the paracentral scotoma (black dot). OCT scan (**J**) of the fovea at the 6-month follow-up.

ILM transplant and 2 days after that, the PRH had closed completely. Six months later, OCT confirmed that the PRH had closed, leaving a highly reflective area where it had been, and the OCT also showed that the marginal retinal cysts had disappeared (Fig. 1G,H). Although the patient was still aware of paracentral scotoma, which was detectable by microperimetry (Fig. 1I; MAIA; CenterVue, Padova, Italy), the outer retinal layers at the fovea were almost continuous (Fig. 1J) and the Snellen BCVA for the eye had improved to 20/16.

Conclusions

To the best of our knowledge, this is the first report of closure of a PRH hole by autologous ILM transplantation. Although asymptomatic cases of PRHs have been reported to require no treatment [1], in this patient we decided that treatment to close the PRH was needed for several reasons. First, the PRH was extremely large and so close to the fovea that it was causing paracentral scotoma. Second, there were accompanying cystoid changes immediately adjacent to the fovea, which had reduced the patient's visual acuity. Third, such large PRHs can cause retinal detachment.

The decision regarding the surgical procedure to use to close the retinal hole was based on our recent experience using autologous ILM transplantation to effectively close large macular holes in eyes that had previously undergone ILM peeling [2]. Although this patient required two ILM transplants, we finally succeeded in closing the PRH, and this improved both the cystoid changes in the eye and its visual acuity. This suggests that autologous ILM transplantation can be a useful therapeutic option for improving the anatomical and visual outcomes for patients with PRHs.

Although this case demonstrated that repeated transplantations of the ILM could effectively close a large PRH, the area of transplanted ILMs remained hyper-reflective and the laminar structure of the retina did not appear restored in OCT for at least 6 months after the surgery.

The process by which macular holes heal after ILM transplantation has been reported to involve glial cells proliferating and migrating along the implanted ILM, which acts as a scaffold for the glial cells and facilitates remodeling of the glial cells and transplanted ILM [2,5]. In this way, reintroducing the basement mem-

brane, in the form of the ILM transplant, enables the normal morphology of the macula to be restored. Indeed, in patients who underwent ILM transplantation for refractory macular holes, we have seen that the hyper-reflective areas seen in postoperative OCT gradually disappeared and the laminar structure of the macula was gradually restored [2]. These hyper-reflective areas seem to comprise a mixture of transplanted ILM and glial tissue [6,7]. Therefore our results suggest that only incomplete remodeling of these tissues occurred in this patient after PRH repair, possibly because there is a limit to the amount of glial tissue the retina can remodel.

In conclusion, autologous ILM transplantation may be a promising strategy for treating PRHs. However, this report describes only a single case with a relatively short follow-up period to date. Randomized controlled clinical studies of larger numbers of patients are needed to determine the impact of this surgical procedure on the management of PRH.

References

1. Sandali O, Sanharawi El M, Basli E, Lecuen N, Bonnel S, Borderie V, Laroche L and Monin C: Paracentral retinal holes occurring after macular surgery: incidence, clinical features, and evolution. *Graefes Arch Clin Exp Ophthalmol* (2012) 250: 1137–1142.
2. Morizane Y, Shiraga F, Kimura S, Hosokawa M, Shiode Y, Kawata T, Hosogi M, Shirakata Y and Okanouchi T: Autologous Transplantation of the Internal Limiting Membrane for Refractory Macular Holes. *Am J Ophthalmol* (2014) 157: 861–869.
3. Kimura S, Morizane Y, Hosokawa M, Shiode Y, Kawata T, Doi S, Matoba R, Hosogi M, Fujiwara A, Inoue Y and Shiraga F: Submacular Hemorrhage in Polypoidal Choroidal Vasculopathy Treated by Vitrectomy and Subretinal Tissue Plasminogen Activator. *Am J Ophthalmol* (2015) 159: 683–689.
4. Doi S, Kimura S, Morizane Y, Shiode Y, Hosokawa M, Hirano M, Hosogi M, Fujiwara A, Miyamoto K and Shiraga F: Successful displacement of a traumatic submacular hemorrhage in a 13-year-old boy treated by vitrectomy, subretinal injection of tissue plasminogen activator and intravitreal air tamponade: a case report. *BMC Ophthalmol* (2015) 15: 94.
5. Michalewska Z, Michalewski J, Adelman RA and Nawrocki J: Inverted Internal Limiting Membrane Flap Technique for Large Macular Holes. *Ophthalmology* (2010) 117: 2018–2025.
6. Ko TH, Witkin AJ, Fujimoto JG, Chan A, Rogers AH, Bauml CR, Shuman JS, Drexler W, Reichel E and Duker JS: Ultrahigh-resolution optical coherence tomography of surgically closed macular holes. *Arch Ophthalmol* (2006) 124: 827–836.
7. Oh J, Yang SM, Choi YM, Kim SW and Huh K: Glial proliferation after vitrectomy for a macular hole: a spectral domain optical coherence tomography study. *Graefes Arch Clin Exp Ophthalmol* (2013) 251: 477–484.