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Case Report

Flap-Related Complications Following Temporal Inverted Internal Limiting Membrane Flap for Macular Hole Repair

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Abstract

Here we report three cases of flap-related complications following temporal inverted internal limiting membrane (ILM) flap technique for the repair of macular holes (MH). The first case showed a flap closure pattern in which the MH completely closed at 2 months spontaneously. The second case showed early anatomical and functional improvement provided by an immediate closure of the MH but developed flap contracture and nasally located epiretinal membrane (ERM) at postoperative 18 months. There was no functional deterioration, thus no further intervention was required. In the third case, early postoperative flap dislocation was observed and an additional surgery to reposition the flap was needed. The flap closure pattern observed with inverted ILM flap techniques may represent the ongoing healing process of large MHs and may be related to delayed spontaneous anatomical closure. ILM flap contracture and ERM formation may be a harmless long-term complication. Dislocation of the ILM flap is an unexpected early postoperative complication that may necessitate a second surgery for flap repositioning.

Keywords: Macular hole, vitrectomy, inverted internal limiting membrane flap, flap contracture, flap dislocation, flap closure

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Introduction

Macular hole (MH) is a full-thickness break in the foveal retina. The closure rate of MHs has greatly improved since the introduction of internal limiting membrane (ILM) peeling, which became important in MH surgery. However, failure rates remained high for large MHs. The inverted ILM flap technique, described by Michalewska et al.,[1] has shown superiority to the traditional ILM peeling technique for the surgical treatment of large MHs, with higher closure rates. The closure rate of large MHs with the inverted ILM flap was reported as 98%, compared with the 88% closure rate attained with conventional vitrectomy and ILM peeling. The temporal inverted flap technique, a modified form in which ILM peeling was limited to the temporal fovea, was later introduced by the same group in 2015 and found to be as effective as the original technique with less surgical trauma.[2]

As the popularity of inverted flap techniques increase, structural macular changes and complications associated with the technique have started to emerge. Besides the most common closure patterns described in the literature (U-shaped closure, V-shaped closure, and W-shaped closure),[2,3] a distinct "flap closure" pattern was noted in approximately 15% of cases.[2,3,4,5] In these cases, the MH was covered by a thin layer of inverted ILM that acted as a bridge between the edges, and anatomical closure was eventually achieved. It is believed that the ILM flap induces migration and proliferation of glial cells in the retinal layers. While this brings about closure of the defect, it may also result in long-term adverse morphologic changes in the retina. However, to our knowledge, there are only a few reports on postoperative structural changes that may lead to complications associated with inverted ILM flaps.[6,7,8,9,10]

Herein, we report three cases of inverted ILM flap-related complications: the first is late MH closure with flap closure pattern, the second is late flap contracture, and the third is early postoperative flap dislocation.

Case Reports

Case 1

A 61-year-old woman presented with blurry and distorted vision in her left eye. She noticed this by chance one month earlier after covering the fellow eye. Best corrected visual acuity (BCVA, decimal) was 0.15 and fundus examination revealed a MH in the left eye.

Spectral domain optical coherence tomography (SD-OCT; SPECTRALIS, Heidelberg, Germany) demonstrated a large MH, the diameter of which was 459 µm at its narrowest point and 943 µm at its base, with cystoid spaces at the edges (**Figure 1A**). Ocular examination of the right eye was normal. Pars plana vitrectomy (PPV) was performed in left eye with 360-degree ILM peeling around the macula and temporal ILM flap isolation and inversion over the hole. ILM forceps were used to peel the ILM off at the nasal side of the MH, which was removed completely. Then, the temporal ILM was peeled in an area of two disc diameters. During this peeling, the ILM was not removed completely from the retina and was left attached to the temporal edge of the MH, then inverted and placed over the MH. Fluid-air exchange was performed, which ensured the flap lay flat over the hole. Then air-gas exchange was performed with 20% sulfur hexafluoride (GOT Multi SF6;Alchimia, Beijing) gas. The patient was instructed to stay in face-down position for the next 3 days. She was prescribed dexamethasone and moxifloxacin drops for 2 weeks and then tapered within a month. Postoperative progress was monitored with serial visual acuity measurements and OCT images.

The patient was seen at postoperative 10 days, following partial resorption of the gas. OCT revealed a flap closure pattern, marked by persistence of the full-thickness MH with the ILM flap bridging the edges (**Figure 1B**). This pattern remained almost the same at the 1-month visit except for slight thickening of the flap (**Figure 1C**). Full closure with a regular foveal contour was observed 2 months after surgery (**Figure 1D**). Her vision improved to 0.6 with a small ellipsoid zone defect in the fovea. One year later, the patient returned with decreased vision due to nuclear sclerosis and underwent cataract surgery. Thereafter, her BCVA reached 1.0 and was maintained during 16-month follow-up. The outer retinal defect became smaller on OCT within this period (**Figure 1E**).

Case 2

A 63-year-old woman presented with floaters in the right eye. BCVA was 0.4 in the right eye and 1.0 in the left eye. Fundus examination and SD-OCT revealed a small MH with cystoid edges in the right eye and focal vitreomacular traction (VMT) in the left eye. The diameters of the MH were 213 µm at its narrowest point and 843 µm at the base (**Figure 2A**). While the patient was scheduled for surgery on the right eye, she returned a month later with photopsia and blurry and distorted vision in the left eye. BCVA had decreased to 0.5 and a small MH with a minimum diameter of 100 µm and a base diameter of 200 µm was detected in the left eye (**Figure 3A**). PPV combined with phacoemulsification and intraocular lens implantation was performed in the right and left eyes, respectively, 2 weeks apart. In both eyes, surgery included a large temporal inverted ILM flap while the nasal ILM was preserved. Fluid-air exchange followed by air-gas (20% SF6) exchange was performed as described in the first case.

At the postoperative 10-day visit, BCVA was 0.6 in the right eye, and SD-OCT showed closure of the inner layers of the MH with a gap in the outer layers (**Figure 2B**). The outer layer defect was healed and BCVA improved to 1.0 at the 2-month visit (**Figure 2C**), after which the findings remained stable over 2-year follow-up.

The left eye showed excellent closure of the MH with almost normal foveal contour and BCVA improvement to 1.0 at 10 days postoperatively. However, an ILM flap traversing the foveal contour, presumably bridging the edges of the previous MH, was noted on SD-OCT (**Figure 3B**). Vision and OCT findings remained stable within the first 6 months postoperatively.

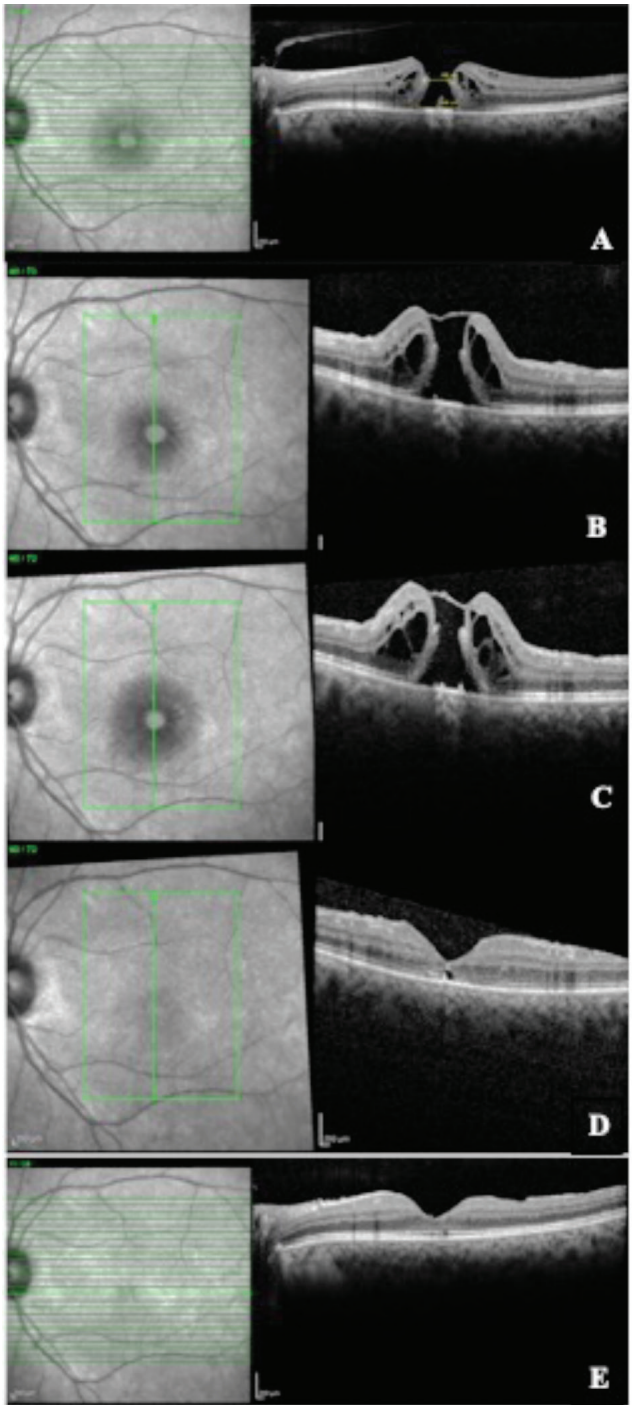

Figure 1. Case 1: A) Spectral domain optical coherence tomography (SD-OCT) shows a large full-thickness macular hole (MH) at baseline. B) SD-OCT showing the "flap closure" pattern with persistence of the MH with internal limiting membrane flap at the top bridging the cystic edges of the hole at postoperative 10 days. C) Persistent "flap closure" appearance with slightly thickened flap and outer retina at 1 month. D) Complete closure of the MH with a small defect in the ellipsoid zone at 2 months. Visual acuity improved to 0.6. E) SD-OCT at the 16-month follow-up demonstrating a smooth foveal contour and restoration of the outer retinal layers

At postoperative 18 months, SD-OCT revealed ILM flap contracture accompanied by a nasal epiretinal membrane (ERM) causing irregularity of the inner retinal layers (**Figure 3C**). However, BCVA remained 1.0 with mild metamorphopsia. The patient was observed without intervention, and her symptoms and OCT findings remained stable during the 2-year follow-up.

Case 3

A 76-year-old woman presented with a sudden loss of vision in the right eye. She stated that her vision had already been subnormal in both eyes for a long time. Her BCVA was 0.04 in the right eye and 0.2 in the left eye. Slit-lamp examination showed bilateral corticonuclear cataract. Fundus examination revealed yellowish flecks at the level of retinal pigment epithelium in both eyes and a MH in the right eye. The left eye had a focal VMT and subfoveal vitelliform material on SD-OCT, which showed corresponding hyperreflectance and hyperautofluorescence on the infrared and fundus autofluorescence imaging consistent with adult-onset foveomacular dystrophy (**Figure 4A,B**). SD-OCT of the right eye showed a large full-thickness MH with a minimum diameter of 800 µm, accompanied by VMT, cysts at the edges, and RPE atrophy leading to prominent choroidal hyper-transmission (**Figure 4C**). Fluorescein angiography showed no sign of neovascularization. PPV combined with phacoemulsification and intraocular lens implantation was performed in the right eye. PPV included a temporal inverted ILM flap over the MH while the nasal ILM was preserved. Fluid-air exchange followed by air-gas (20% SF6) exchange was performed. At the 10 days postoperatively, following partial resorption of the gas, SD-OCT revealed

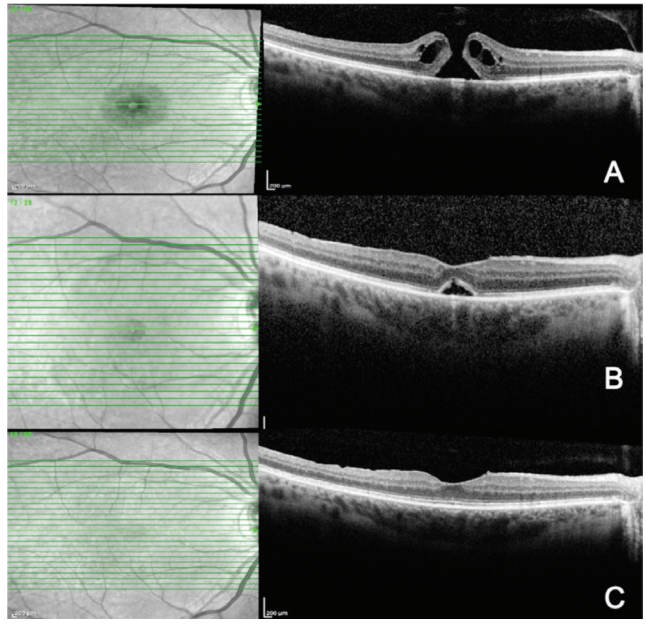

Figure 2. Case 2, right eye: A) Spectral domain optical coherence tomography (SD-OCT) shows a small full-thickness macular hole (MH) at baseline. B) SD-OCT on postoperative day 10 shows closure of the inner layers of the MH, with a large gap in the outer layers. C) MH was totally closed at postoperative 2 months and remained stable throughout 2-year follow-up

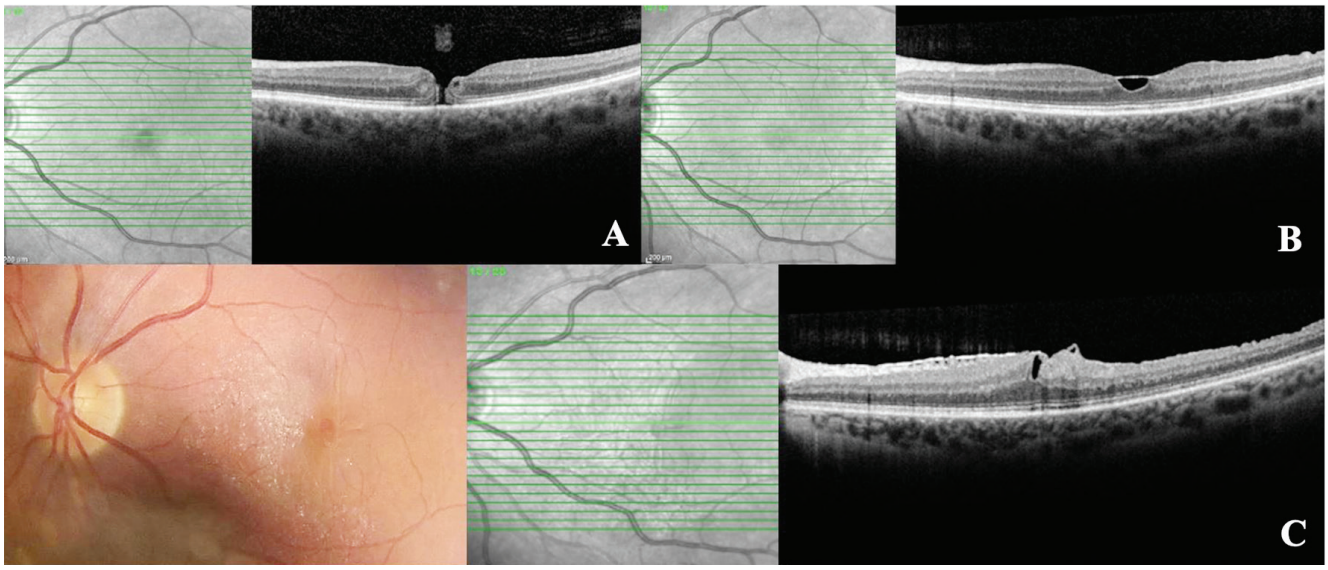

Figure 3. Case 2, left eye: A) Spectral domain optical coherence tomography (SD-OCT) shows a small full-thickness macular hole (MH) at baseline. B) SD-OCT on postoperative day 10 shows the internal limiting membrane flap bridging the edges of the closed MH. This appearance remained stable in the following 6 months. C) Color fundus image and the corresponding OCT at postoperative 18 months revealed contracture of the flap which caused inner layer irregularities and was accompanied by an epiretinal membrane on the nasal side

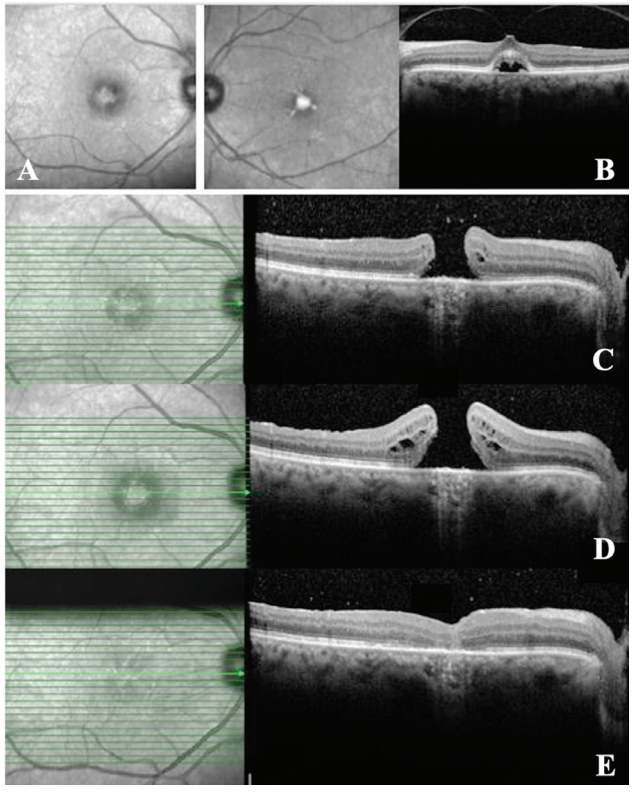

Figure 4. Case 3: A,B) Infrared retinal images and spectral domain optical coherence tomography (SD-OCT) of the left eye suggesting pattern dystrophy as a background pathology in this patient. C) In the right eye, SD-OCT shows a large full-thickness macular hole (MH) with a minimum diameter of 800 µm at baseline. D) The MH remained open at the postoperative 1 month. The underlying cause of persistence of the MH was the detached internal limiting membrane flap. E) MH closure was observed 2 weeks after repositioning surgery, and was stable throughout 18-month follow-up

persistence of the MH, which was confirmed to be still open at the postoperative 1-month (**Figure 4D**). Reoperation was performed at postoperative 3 months. During surgery, the ILM flap was found to have returned to its original temporal position. The nasal ILM was peeled, the previous temporal ILM flap was remobilized to form a temporal flap and repositioned over the MH, and 12% perfluoropropane (C3F8) gas tamponade was given. The patient was instructed to stay in face-down position for a week. At postoperative 2 weeks, OCT demonstrated closure of the MH, accompanied by ellipsoid zone atrophy (**Figure 4E**). The BCVA improved to 0.4 and was maintained during 18 months follow-up period. The MH remained closed and the outer layer defect has been stable within the follow-up period.

Discussion

In this report, we examined three MH patients who were treated with temporal inverted ILM flap technique and developed unexpected flap-related morphological changes and complications in the postoperative period.

The first case demonstrated late MH closure associated with the flap closure pattern, a newly described pattern after the emergence of inverted flap techniques.[2] This pattern, as occurred in case 1, was recognized as a thin hyperreflective band of ILM extending across the inner retina surface on both sides of the previous MH following surgery with inverted flap technique.[1,2] Reported rates of flap closure pattern range between 14% and 27% in the early postoperative period and decreases over time.[1,5,8,11] Boniṅska et al.[5] showed that flap closure persisted in only one-third of the eyes at the end of 1 month, and completely disappeared and turned into other closure patterns at the end of the 3 months. Tsui and Yang[12] reported the mean time to disappearance of the flap closure as 2 months, which was similar

to case 1 in this report. However, in some eyes, the ILM flap may persist much longer while MH closure takes place. Michalewska et al.[2] reported that flap closure remained at postoperative 6 months in 11% of the original inverted ILM flap group and 3% of the temporal inverted ILM flap group. By postoperative 12 months, 3% of original inverted ILM group still showed the flap closure pattern, but MH closure was eventually achieved in all cases.

The proposed mechanism of MH closure with the inverted ILM flap technique is that the ILM flap acts as a scaffold for glial cells to proliferate, as well as provides a barrier to the entrance of fluid from the vitreous cavity to the MH.[5] In this regard, the flap closure pattern represents an ongoing physiological healing process of large MHs that may remain open if standard ILM peeling were used. Closure of large MHs with postoperative flap closure pattern is very likely. However, full closure may take a longer time, and the decision to perform revision surgery should not be made hastily.

Our second patient also demonstrated bridging by the ILM flap, but this time over the closed MH. Following a long and stable persistence, the flap tissue showed contraction 18 months postoperatively. This was accompanied by a newly ERM in the nasal quadrant, where the ILM had been previously preserved. Contracture and thickening of the ILM flap is defined as the first step of the regeneration process, followed by formation of gliosis on the retinal side of the flap, which eventually fills the cavity and results in anatomical closure of the MH within 1-4 months postoperatively.[12] While the ILM flap forms a bridge and improves the integrity of the foveal structure, it may also persist as an additional tissue after hole closure. Previously, Boniṅska et al.[5] reported hyperreflective ILM remnants on the retinal surface in 44% of eyes with an inverted ILM flap. Later, Tsui and Yang[12] pointed out a higher incidence of persistent ILM tissue, showing a rate of 66% in their series. Both studies suggested that these remnants remained stable over time and had no influence on the vision. However, recently Hirata et al.[8] quantitatively demonstrated contracture of ILM flaps in 23% of eyes that underwent MH surgery with temporal inverted ILM flap. Of these, one required ILM peeling 12 months after the initial surgery due to severe flap contraction causing decreased vision and metamorphopsia. This case also had an ILM flap overlying a closed MH in the early postoperative period. At postoperative 6 months, the ILM flap integrated into the retinal layers and transformed into an epiretinal membrane.[9,10] Several other reports also showed ERM formation following inverted ILM techniques. In a case report by Kanda et al.,[9] histopathological examination of the surgically removed ERM showed cellular proliferation between overlapping ILMs. Authors proposed that cells and collagen remaining on the vitreous side of the ILM may have served as a scaffold for cell proliferation. In these reports, ERMs occurred 3-6 months postoperatively and coincided with the position of the ILM flaps. In contrast, the ERM in our patient originated from the nasal macula and formed later. This may indicate that a nasal ERM may be a long-term consequence of gliotic proliferation of the nasal retina where the ILM is left in place. Late contracture of the flap could be attributed to the tangential force applied by the nasal ERM and/or "reverse" gliosis developing on the vitreous side of the flap. Although vision was not affected except for mild metamorphopsia in our case, removal of the nasal ILM may be safer, especially if there is a suspicion of residual epiretinal membrane. Moreover, conventional ILM peeling would have been preferable for primary treatment in this particular case because the MH was small. Although our clinical experience suggests that the inverted flap technique provides a much smoother and better foveal contour, it may have some disadvantages in small MHs in the long term, as demonstrated in this case. Apart from removing the nasal ILM, the conventional technique would also eliminate the potential of any ILM flap tissue contributing to the formation of ERM in such small holes.

Our third case showed early postoperative dislocation of the ILM flap. This is a rather unexpected complication, because the temporal inverted flap technique provides a wider connection to retina, thereby decreasing the likelihood of spontaneous detachment or flipping of the flap during fluid-air exchange compared to the original inverted ILM flap technique. Previously, Kawamata et al.[7] described a case of partial flap detachment following a superior inverted flap technique, which recovered spontaneously within 3 months without any further intervention. Total dislocation in our case would have made the spontaneous recovery unlikely, if not impossible. Therefore, after discussing the options with the patient, we decided on a repeat surgery at 3 months. Dislocation of the flap could be attributed to inadequate postoperative head positioning of the patient, resulting in an insufficient tamponade effect. Although preservation of the nasal ILM provides a more stable flap and decreases the risk of flap loss and free flap formation, it might also contribute to persistence of the MH and the need for repeat surgery once a dislocation occurred. Some precautions may be taken to prevent early postoperative flap dislocation, such as efficient drying of the fluid in the posterior pole during fluid-air exchange, or using perfluorodecalin to stabilize and secure the flap tissue in place. Positioning of the head slightly nasally and waiting for some time may allow accumulation of residual fluid on the optic nerve. Also, local anesthesia may be preferred to general anesthesia to ensure appropriate head positioning immediately after surgery.

In conclusion, we addressed three different complication scenarios following use of temporal inverted ILM flaps and their related mechanisms. Flap closure pattern may be inherently associated with delayed closure of MHs. MH dimensions may have some effect on flap closure pattern, which needs to be further investigated. ILM flaps may show contraction in the long-term in association with secondary ERM formation, which may be prevented by peeling off the nasal ILM during temporal inverted flap surgery and creating a smaller overlapping area of ILM tissue. Finally, flap dislocation should be considered in MH

cases that fail to close following inverted ILM flap surgery, and may require reoperation for flap repositioning.

Ethics

Informed Consent: This case report was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information was performed in a Health Insurance Portability & Accountability Act (HIPAA)-compliant manner.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.Ö., Concept: G.D.G.İ., E.Ö.Z., Ş.Ö., Design: G.D.G.İ., E.Ö.Z., Ş.Ö., Data Collection or Processing: G.D.G.İ., E.Ö.Z., Analysis or Interpretation: G.D.G.İ., E.Ö.Z., Ş.Ö., Literature Search: G.D.G.İ., Writing: G.D.G.K.

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