Inverted ILM flap technique in Optic Disc Pit Maculopathy: An Iranian experience with review of the literature

Ali Tavallali
Tavallali Eye Infirmary, Shiraz, Iran
Yasaman Sadeghi
Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA
Seyed-Hossein Abtahi (Shf.abtahi@yahoo.com)
Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran https://orcid.org/0000-0002-1459-6752
Hosein Nouri
Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran https://orcid.org/0000-0003-1808-0443
Mitra Rezaei
Virology Research Center, National Research Institute of Tuberculosis and Lung diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran
Mehdi Mazloumi
Eye Research Center, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

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Research Article

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Abstract

Purpose

To present the outcome of optic disc pit maculopathy (ODPM) managed successfully with inverted internal limiting membrane (ILM) flap over the optic disc.

Methods

This prospective case series included three patients with ODPM who underwent pars plana vitrectomy with posterior vitreous detachment induction, followed by inverted ILM flap over the optic disc and gas tamponade. Patients were followed for 7-16 weeks as regards their functional and anatomical findings. A narrative review is also provided about Pathology, Pathogenesis, and surgical techniques in the treatment of ODPM

Results

Three adult patients (25–39 years old) were evaluated, with a mean duration of decreased visual acuity of 7.33 ± 2.40 months (4-12 months). Postoperatively, BCVA improved dramatically in one patient from 2/200 to 20/25. BCVA in the other two improved two and three lines, to 20/50 and 20/30, respectively. Significant anatomic improvement was achieved in all patients.

Conclusion

Vitrectomy with inverted ILM flap insertion over the optic disc can yield favorable anatomical improvement in patients with ODPM.

Precis

Optic disc pit maculopathy (ODPM) develops in 25%-75% of congenital optic disc pit cases. We reported three ODPM patients treated with vitrectomy, inverted internal limiting membrane flap insertion over the optic disc, and gas tamponade, which achieved near-complete macular anatomy restoration and two or more lines of improvement in visual acuity.

Introduction

Optic disc pit (ODP) is a rare excavated anomaly of the optic nerve head (ONH), with an estimated prevalence of about 2/10,000 and no gender or racial predilection (1). ODP is most frequently found at the temporal or inferotemporal sections of the ONH and is assumed as an atypical coloboma of the ONH with dysplastic primitive retinal tissue herniating posteriorly into the subarachnoid space through a defective lamina cribrosa (2). Non-complicated ODP is mostly asymptomatic; however, 25%-75% of cases may develop ODP maculopathy (ODPM), characterized by cystoid macular changes and/or serous macular detachment (3). ODPM occurs unpredictably and typically in early adulthood, leading to severe visual deterioration, especially in long-standing cases due to the lamellar/full-thickness macular hole development, retinal pigment epithelium (RPE) atrophy, and cystic macular degeneration (4). Therefore, timely diagnosis and appropriate management of ODPM is warranted; however, given its rarity and controversial pathophysiological aspects, no single treatment modality is widely accepted and agreed upon yet (3). Management strategies mainly include pars plana vitrectomy (PPV) and posterior vitreous detachment (PVD) induction, with or without peripapillary barrier laser photocoagulation, gas tamponade, and internal limiting membrane (ILM) peeling (4).

Here, we describe three cases of ODPM successfully managed with PPV, PVD induction, transplantation of inverted autologous ILM onto the ONH (reverse ILM-flap technique), and gas tamponade with non-expansile concentration (16%) of C3F8 by a single surgeon (AT). Further, we discuss the current understanding of ODPM pathophysiology and review different treatment strategies described in the literature.

Methods

This prospective interventional case series was implemented from January 2018 to November 2019. Consecutive cases with ODPM were included. All of the surgeries were performed by a single surgeon (A. T.).

Outcome measures included central macular thickness (CMT) and retinal morphology; and the Snellen visual acuity. Preoperative and postoperative examinations included best-corrected visual acuity (BCVA), slit-lamp and funduscopic examinations, complications, and structural optical coherence tomography (Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany). The study adhered to the principles of the Helsinki declaration. Informed consent was obtained from all participants.

Operative Technique

Under general anesthesia, a three-port, 23 gauge transconjunctival PPV was performed, followed by induction of PVD. ILM was visualized by Membrane-Blue-Dual dye staining (DORC International, EEC). Using a 25Ga+ ILM forceps (Grieshaber advanced DSP tip ILM forceps, Alcon Grieshaber AG, Switzerland), a large ILM flap was peeled from 1mm temporal to the fovea up to its pedicle at 0.2mm temporal edge of the ONH. The peeled ILM was then inverted and flattened on the optic disc, covering the pit. Finally, fluid-air exchange was performed, and C3F8 (16%) was injected to stabilize the ILM flap over the ODP, and the patient was instructed to remain in a prone position postoperatively.

Case Presentation

Case 1

A 39-year-old white woman presented with complaint of progressive decrease of vision in her left eye, evolving for the last six months. Best-corrected visual acuity (BCVA) was 20/20 and 2/200 in her right and left eye, respectively. Fundoscopy of the right eye was unremarkable, whereas an ODP at the inferotemporal aspect of the optic disc and cystoid macular edema were revealed in the left eye. OCT of the left eye showed large, schisis-like cystoid spaces in inner and outer retinal layers, with a large intraretinal cyst underneath a very thin overlying fovea. CMT was 685 μm (Fig. 1A).

At one-month post-operation follow-up, the BCVA of her left eye was 20/40. OCT scan revealed an ODP with a large gap in lamina cribrosa connected with perineural space covered with wrinkled ILM (Fig. 1B). Two months after the surgery, BCVA improved to 20/25. Remnants of ILM were observed at the disc margin and significant remodeling in the ODP cavity, closing the gap to a large extent (Fig. 1C). Intraretinal fluid (IRF) was resolved with only a small amount of residual subfoveal fluid. The mean CMT was reduced to 247 μm (Fig. 1D).

Case 2

A 27-year-old white man presented with a one-year history of decreased vision in his right eye; his medical history was otherwise unremarkable. Upon examination, his BCVA was 20/100 in the left eye and 20/20 in the right eye. Fundoscopic examination of the right eye was normal; a laterally-located ODP and macular detachment were noted on the left eye fundoscopy. OCT scans of the left eye showed a very high mean CMT of 912 μm, multilayer inner retinal schisis nasal to the fovea, marked intraretinal fluid in the Henle's layer, and serous neurosensory detachment of the fovea (Fig. 2A). The patient underwent the same procedure as the first case. At the 7th week follow-up, the macular detachment had collapsed, the mean CMT reduced to 367 μm, and significant anatomic restoration was achieved (Fig. 2B); BCVA improved to 20/50.

Case 3

A healthy, white, 25-year-old-woman presented with a history of painless, progressive reduction of central vision in her right eye for four months. The BCVA was 20/70 in the right and 20/20 in the left eye. Fundoscopy of the right eye revealed a large inferotemporal ODP and macular edema. In the OCT scan of the right eye, large intraretinal fluid in the Henle's layer was observed similar to the aforementioned case; mean CMT was 957 μm. (Fig. 3A). The same procedure as described was undertaken. Sixteen weeks postoperatively, her right eye BCVA was 20/30, and retinal edema had significantly resolved. The mean CMT was reduced to 330μm (Fig. 3B).

Discussion

Over time, BCVA of eyes with ODPM can deteriorate to 20/200 or worse in many cases; Of course, spontaneous remission has notably been reported in about 25% of cases (5, 6). With spontaneous remission, however, cystic changes of RPE and neurosensory retina and lamellar or full-thickness macular hole are likely to develop, with risk of permanent visual loss (5); serous macular detachment may also recur (7). Even in pediatric cases, whose chances for spontaneous resolution are higher (8), postponing the surgical interventions to monitor the natural course of maculopathy carries the risk of amblyopia development – resulting from visual impairment and changes in visual centers innervated by the affected ganglion cells (9). Hence, primary surgical management of ODPM is recommended, especially in cases with subretinal fluid (SRF) accumulation (1).

Pathology and pathogenesis in the literature

Historically, vitreous has been suggested as the primary source of fluid leakage into the retina through a thin porous membrane, constituted of dysplastic retinal tissue covering the ODP (10). Through serial histopathology sections of electron microscopy, Christoforidis et al. could visualize holes in the diaphanous membrane overlying the ODP bridging with a schisis-like cavity in the retina (11). SRF drainage through pores in the ODP roof was successfully performed by Johnson and Johnson (12) and Postel et al. (13). One hypothesis is that a negative pressure created by posterior hyaloid traction over the porous ODP-covering membrane generates an inward gradient of liquified vitreous into the retina (11, 14).

Although inconsistently, vitreous strands over the ONH and peripapillary retina have been detected on OCT scans and electron photomicrographs of patients with ODPM (2, 14). The role of vitreous traction in ODPM pathogenesis is amply supported by encouraging remission of maculopathy following vitrectomy (15) or spontaneous PVD (16). Strong vitreoretinal attachment at the disk margin has been reported during surgically-induced vitreous detachment (7). In addition to the role of posterior hyaloid traction, the tangential traction on the retina caused by ILM is also proposed to exert elevational traction on the retina, maintaining the inward fluid gradient into the retina (via ODP) (17). Post-vitrectomy subretinal migration of gas and silicone oil further supports the existence of communication between vitreous cavity and subretinal space through ODP; curiously, it happens when no vitreoretinal traction exists, indicating the involvement of other pathogenic mechanisms (12).

Cerebrospinal fluid (CSF) oozing from the adjacent subarachnoid space is the second plausible fluid source; it was first proposed in 1964 (18) after Regenbogen and colleagues noticed a pulsating transparent membrane over the ODP during surgery, which they attributed to CSF pressure fluctuations. Akiba et al. had a similar observation, which they ascribed to intravitreal traction caused by anomalous Cloquet's canal (19). Friberg and colleagues reported free pulsation of glial and vitreous remnant overlying ONH into and out of ODP in an eye with visible PVD (20). They also recognized a retrobulbar cyst communicating with the vitreous cavity through B-scan ultrasonography and documented a constant relative hypotony in the affected eye, presumably due to intraocular fluid drainage into the cyst and ultimately the subarachnoid space (20). In 2006, intracranial migration of silicone oil was noted on brain magnetic resonance imaging scans of a patient with ODPM presenting with a headache after vitrectomy and silicone oil injection (21). The direct communication of intraretinal cystoid spaces and the lamina cribrosa gap in the ODP (22) and their connectivity with the vitreous cavity were later visualized using high resolution, enhanced depth imaging (EDI) and swept-source (SS) OCT scans (23–25). As theorized by Johnson and Johnson (12), anomalous inter-connection and fluctuation of pressure gradient between intra- and extraocular spaces enable CSF and vitreous aqua to move through the ODP. When intracranial pressure (ICP) decreases, syneretic vitreous is sucked toward the communicating perineural space, and then with a rise in pressure, trapped vitreous and/or CSF is ejected into/under the adjacent retina and posterior vitreous cavity. The same mechanism could explain subretinal migration of gas and oil, post-vitrectomy, and occurrence of maculopathy in pediatric ages when liquified vitreous is uncommon (12).

As to the morphology and progression of ODPM, Lincoff et al. (26) first introduced the so-called bilaminar retinoschisis concept, in which liquid accumulation emanates from the inner neurosensory retina, extending outwards through outer layer lamellar holes. They proposed that true serous macular detachment occurs merely as a complication of longstanding intraretinal edema. Although this view has been widely accepted (23), it has been challenged by occasional observations of an outer layer hole in OCT scans (27, 28) and cases of ODPM with macular detachment, where no inner retinal schisis-like cavity was found (29). Todorich et al. reported a case of ODPM with direct connection of SRF to ODP, as detected on spectral-domain (SD)-OCT scans (30). Using high-resolution OCT, Imamura et al. showed that fluid could move straightly from ODP to multiple retinal layers, including the sub-ILM space, ganglion cell layer, inner and outer nuclear layers, and subretinal space (28). The outer nuclear layer is usually affected – as seen in our cases; one interpretation could be that in the majority of cases, the inner retina and/or subretinal space are involved secondarily to an initial passage of fluid through the outer retina (31). Intriguingly, Skaat et al. described two distinct OCT patterns in their cases: i) a predominant serous detachment pattern, with no to minimal schisis-changes of the photoreceptor layer in pediatric patients (mean age: 9 years old), versus ii) a multilayer schisis pattern in older adults (mean age: 31.7 years old) (32). The former pattern in younger patients has been reported by others as well, but it was not confined to the pediatric population (33). Although direct SRF conduit from ODP is rare (1), perhaps when present, it allows fluid passing beneath the retina much sooner than expected for conversion of asymptomatic ODP to ODPM in early adulthood. ODPM does occur unpredictably; however, blunt ocular and head trauma has been suggested as a potential trigger, especially in pediatric-onset cases; Rii et al. have attributed this to the severe hyaloid face adhesion in pediatric patients exerting an anteroposterior tractional pull on the macula following trauma (34). Another explanation could be the sudden rise in ICP after the trauma, forcing the CSF into/under the retina (3).

In summary, it could be reasonably inferred that both vitreous and CSF could serve as the pathogenic source of the accumulated fluid, passing into the retina through multiple layers, most commonly the outer nuclear layer (11). Moreover, both vitreoretinal traction and ICP pressure fluctuation play a role in the pathogenesis of the disease, either being prominent at certain ages and/or under different circumstances. We also suggest that a direct subretinal connection with the ODP cavity together with a traumatic experience may act as risk factors for accelerated progression toward ODPM in cases with asymptomatic ODP.

Surgical techniques in the literature

As previously mentioned, tractional forces over the ONH allow for the fluid entrance through the ODP, and the traction exerted upon the peripapillary and macular area could promote schisis separation of retinal layers, facilitating the fluid migration into the retina. Therefore, complete vitrectomy with PVD induction is the mainstay of ODPM treatment (3, 27). Hirakata et al. showed that complete retinal attachment in 7 of 8 eyes was achieved with isolated PPV and PVD induction, although it took up to a year (35). An alternative surgical approach is placing scleral buckles between the optic disc and macula, with a similar success rate of 85% as PPV and PVD induction. Besides alleviating vitreoretinal traction, scleral buckling is suggested to obstruct the fluid passage from ODP (36). However, this tricky technique is rarely applied in the management of ODPM (4).

ILM peeling, gas tamponade, and juxtapapillary endolaser photocoagulation are commonly utilized adjunctive procedures alongside PPV. The rationale behind these procedures and their additional benefit to vitrectomy is still controversial. Pneumatic retinopexy alleviates vitreomacular traction by inducing PVD and displacing accumulated fluid (37), but when applied without PPV, it has a temporary effect (38) and retinal reattachment rate of 50% with a mean number of 1.8 injections (39). Laser application is tentatively proposed to seal the route of the ODP to the fovea, but it has a very low success rate (40), probably because choroid and deep retinal layers absorb much of the laser energy. It also bears the risk of causing significant visual field defects (41). Combined gas tamponade and laser application had 75% success rate, but re-intervention was needed in 40% of the cases (42). After unsuccessful photocoagulation or pneumatic retinopexy, PPV and fluid air exchange, with or without laser treatment, have yielded an 88% reattachment rate (6). More recently, ILM peeling has been suggested to ensure the removal of all anteroposterior and surface-parallel tractional forces from the retina (43). Three multicenter studies evaluated the surgical success rates gained with PPV and PVD induction +/- ILM peeling, gas tamponade, and juxtapapillary endolaser and evaluated the extra therapeutic gain associated with each of these adjunctive treatments (1, 15, 44). They showed an overall 75–86% retinal attachment success rate, but none found a significant improvement gained with ILM peeling or temporal laser application; only gas tamponade showed additional efficiency in the study by Avci et al. (44); however, all these studies suffer from small sample sizes and heterogeneities in surgical procedures employed (1).

Marticorena et al. reported a case successfully treated with peeling of ILM after an initial failure of PVD and laser application (45). PVD induction, gas tamponade, and ILM peeling resulted in favorable outcomes in three ODPM cases within a few months, as described by Georgalas et al. (46). In a retrospective analysis of five patients who underwent PPV plus gas injection with or without ILM peeling, Skaat et al. reported complete SRF resolution in the former group whereas macular detachment persisted in patients for whom ILM peeling was not performed (32). Even considering the different clinical and morphological characteristics of the two groups, it could still be inferred that ILM peeling is a critical surgical maneuver for alleviation of maculopathy. Despite the formation of macular holes in 57% of the eyes operated, Shukla et al. achieved excellent results with vitrectomy, ILM peeling, and tamponing in 7 cases. 3 out of 4 holes were closed spontaneously, and the final visual outcome was unaffected by macular hole development during the recovery course (43). Fovea-sparing ILM peeling has been suggested to minimize the risk of macular hole formation (47); however, leaving a central island of ILM on the macula showed no protection against macular hole formation in one out of two eyes undergone the procedure (43). Moreover, full-thickness macular hole formation has been reported following PVD, gas tamponade, and laser photocoagulation without ILM peeling (48); as Shukla et al. proposed, most of the risk could be attributed to removing the strongly adherent posterior hyaloid face (43).

Spaide et al. introduced another adjunctive maneuver beside PPV, i.e., partial-thickness fenestration of the retina, radial to ONH. It is proposed to allow fluid redirection toward the vitreous cavity instead of the intra-/sub-retinal layers (49). They later achieved 94% foveal fluid resolution with this technique (50). However, a previous attempt to create a fenestration connected to schisis cavities by Slocumb and Johnson resulted in persistent macular detachment due to premature closure of the fenestration soon after surgery (51). Moreover, this technique will not be effective in the presence of a direct conduit beneath the retina.

Sealing the congenital pit with platelet-rich plasma (PRP) or fibrin glue has shown promising results and seems to shorten the long duration of restoration following surgery (30, 52). However, the plugs are temporary and cannot be regarded as a permeant solution. Long-term safety of

PRP is unknown as it can theoretically trigger proliferative vitreoretinopathy (30). The use of fibrin glue bears the risk of allergic reactions and microbial transmission (53).

Insertion of inverted ILM flap over the ODP has recently been suggested; the flap could act as a physiologic physical barrier against vitreous and oil migration and induce gliosis and cell proliferation within the ODP cavity (54). We observed pit remodeling and partial closure as soon as two months after complete PVD induction, ILM peeling, reverse ILM flap insertion, and gas tamponing. Moreover, we did not observe any macular hole formation in the three eyes operated, consistent with previous case reports using this technique (55, 56). Following a similar rationale, scleral autograft has also been proposed (57) but has an inherent risk of optic nerve damage (58).

Conclusion

Aside from removing traction over the ODP, PVD and ILM peeling are necessary to release the elevating stress from the retina per se. Removing all the tractional forces that promote schisis separation allows retinal layers to reattach over time. However, in the presence of communicating fluid sources, the restoration process is generally slow because intermittent pressure gradient caused by fluctuations in CSF pressure could still push fluid into the retina.

In our experience, the inverted ILM flap procedure is efficacious and safe in the management of ODPM. This emerging surgical technique invokes cellular proliferation and tissue construction inside the ODP and closes the communicating cavity, substantially facilitating the remission. Gas tamponade further facilitates egressing fluid and keeps ILM over the ODP long enough to induce and maintain cellular growth and tissue remodeling inside the pit.

Declarations

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Consent for publication: After briefing participants on the content prepared for publication, signed informed consent letters were obtained.

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Figures

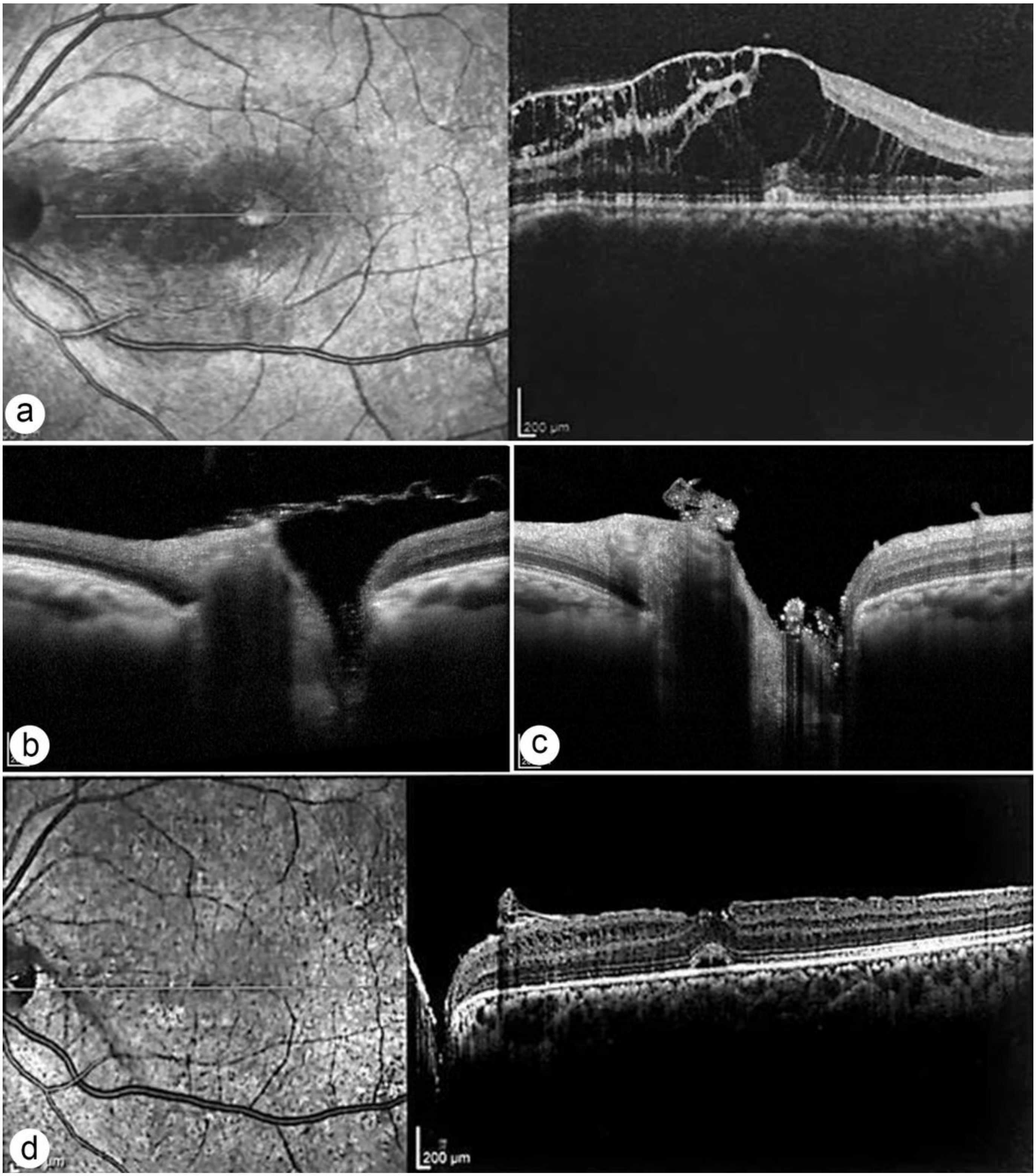

Figure 1

OCT findings in case no. 1. (a) Before surgery; schisis-like cystoid spaces in the inner and outer retinal layers and an ample cystoid space in the inner fovea. (b) One month post-surgery; optic disc pit (ODP) is covered with an ILM flap; a large gap in lamina cribrosa in connection with perineural space is visible. (c) Two months post-surgery; ILM remnants appear at the disc margin; ODP cavity remodeling has nearly closed the gap in lamina cribrosa. (d) Minimal Schises in the inner nuclear layer are noted, and the macula is reattached with small residual sub-foveal fluid.

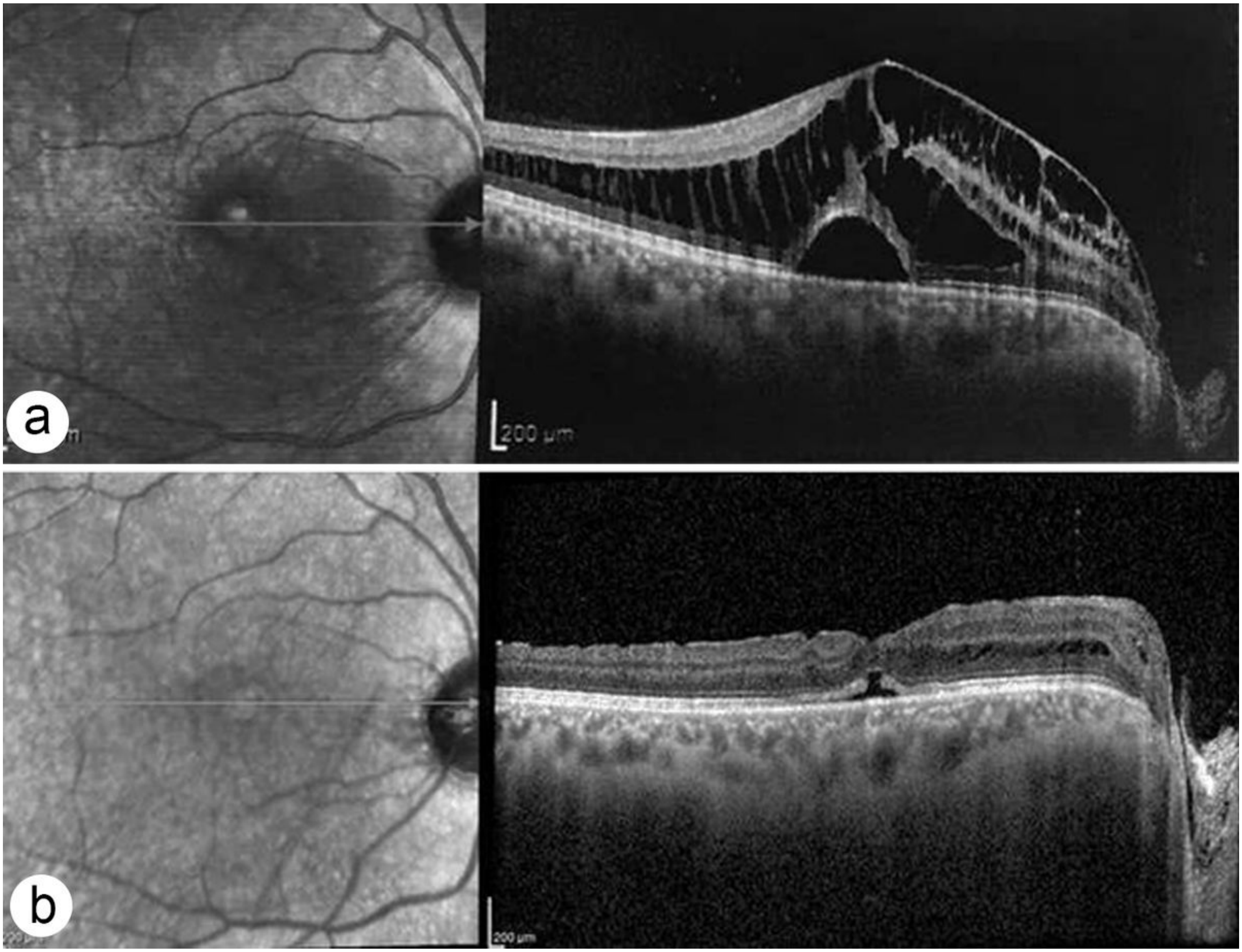

Figure 2

OCT findings in case no. 2. (a) Before surgery; note the multilayer inner retinal schisis nasal to the fovea, considerable edema of the Henle's layer, and serous detachment of the macula. (b) Seven weeks post-surgery: minimal residual fluid beneath the fovea and in the Henle's layer.

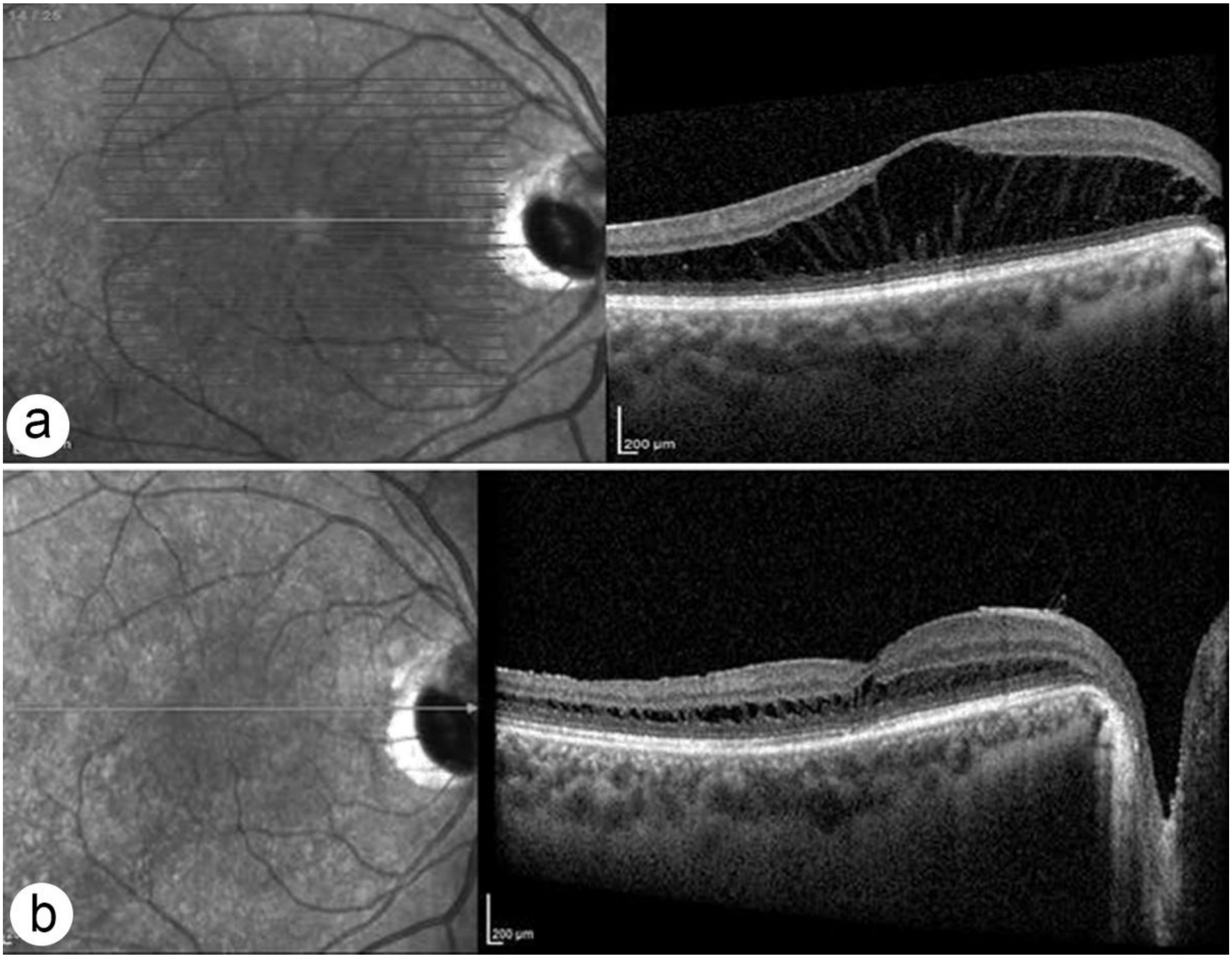

Figure 3

OCT findings in case no. 3. (a) Before surgery; huge schisis cavities are visible in the Henle's layer. (b) Sixteen weeks post-surgery: small residual schisis cavities are left.