ORIGINAL ARTICLE

REPORT ON AMNIOTIC MEMBRANE FOR SURGERY OF PERSISTENT MACULAR HOLE

Lipková B.[1], Rosocha J.[2], Maurská A.[1]

[1]Ophthalmology Department, Faculty Hospital Žilina, Slovakia
[2]Associated Tissue Establishment of the L.Pasteur University Hospital and Medical School of the P. J. Šafárik University in Košice, Slovakia

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MUDr. Blandína Lipková, Ph.D.
Očné oddelenie, Fakultná Nemocnica s Poliklinikou Žilina
V. Spanyola 43
012 07 Žilina
E-mail:
blandina.lipkova@gmail.com

SUMMARY

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Purpose: To evaluate the results of 3 cases with persistent macular holes (MH) treated by 23-gauge vitrectomy, extension of internal limiting membrane peeling, a human amniotic membrane (hAM) plug insertion into the subretinal space through MH and expanding gas endotamponade.

Material and methodology: The diagnosis of persistent MH in three patients was unilaterally confirmed using SD-OCT. In the first patient, a primary MH was present. In the second patient, a secondary MH occurred after cystoid macular edema because of central retinal vein occlusion. The third patient suffered with sustained atrophy of the retinal pigment epithelium (RPE) in the foveola several years before the development of MH. All patients were females. The first two patients underwent reoperation four months after the primary surgery; the third patient underwent two previous pars plana vitrectomies (PPVs), the last one 11 years ago. Firstly, a revision of the periphery and removal the vitreous remnants were performed; the ILM peeling zone was extended. The plug from the dehydrated hAM was prepared. Subsequently, the hAM plug was inserted via MH subretinally. Standard cryopexy behind the sclerotomies, fluid-for-air exchange, and vitreous cavity tamponade with expansile gas were performed.

Results: Two patients achieved MH closure; in the third patient, surgery significantly reduced cystoid edema of the MH edges and the MH diameter, but the MH remained open. All patients experienced a mild improvement in visual acuity and loss of disturbing visual phenomena.

Conclusion: We have confirmed that hAM plug insertion is feasible for persistent MH, even of large sizes. It is essential to orient the basal membrane of the plug towards the neurosensory part of the retina and the chorionic side to the RPE due to growth factors, but also for the concavity of the plug towards the RPE. It is possible that the use of tamponade with perfluoropropane (C3F8) is preferable to tamponade with sulfur hexafluoride (SF6). The time of reoperation approximately 3–4 months after the first failed vitrectomy can be considered optimal.

Keywords: macular hole, human amniotic membrane, plug from human amniotic membrane, pars plana vitrectomy, expansile gas

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INTRODUCTION

The macular hole (MH) belongs to the pathology of the vitreoretinal interface, which arises in the fovea by disrupting the layers of the retina, from the internal limiting membrane (ILM) to the retinal pigment epithelium (RPE). The Classification of Vitreomacular Adhesion, Traction, and Macular Hole compiled by The International Vitreomacular Traction Study Group is currently used. [1]

A primary MH is caused by the traction of the vitreous; a secondary is the direct result of pathology other than vitreomacular traction (VMT). Full-thickness MH is subclassified according to the size of the hole on the OCT examination and according to the presence or absence of VMT. In current literature, the term "idiopathic" is no longer used, since the cause of the formation of the macular hole is the traction of the vitreous [2]. The prevalence of the primary macular hole in the population varies from 0.2 to 3.3 per 1 000 inhabitants. It occurs between the 6th and 7th decade of life, more often in women. A main breakthrough in the treatment of MH came in 1991, when Kelly and Wendel first described the positive effect of pars plana vitrectomy (PPV), with the removal of posterior cortical vitreous (PCV) for the closure of MH. The success rate was 58 % [3]. Since then, various procedures and postoperative strategies have been used to improve anatomical and functional outcomes. In 2010, Michalewska et al. described an innovative inverted ILM flap technique. It was a recommended and effective surgical procedure in primary and myopic macular holes, with a success rate of up to 98 % [4].

The current commonly used surgical method for the treatment of MH – pars plana vitrectomy with peeling of the internal limiting membrane (ILM) and with the intravitreal application of expansion gas – leads to improvement of central visual acuity, as well as to the adjustment of changes in the Watzke Allen test and the disappearance of central scotoma [5].

The ILM flap is believed to serve as a construction for the proliferation of glial cells, allowing Müller cells and photoreceptors to take an anatomical position similar to healthy foveola [6].

Persistent MHs are considered as those that remain open even after surgery, and recurrent MHs are those that reopen after their initial closure. This may be due to persistent epiretinal traction, insufficient gas tamponade, non-compliance of the patient concerning face-down positioning, or unknown causes [7].

Reoperation involves 3 groups of methods. In the first group, the tissue causing tangential traction in the macula, which prevented the edges of the hole from approaching, is removed by extending the ILM peeling which should be at least 1.5–2 papillary diameters (PD) from the fovea radially in 360 degrees between arcades. However, it is most effective to supplement peeling up to the temporal arcades [8,9].

Some authors have managed to release traction by cutting the edges of the macular hole, but they warn that this procedure may cause irreversible destruction of the inner layer of photoreceptors [10].

The second group of reoperations includes relaxing maneuvers, such as ILM abrasion using a Flex handle or diamond sweeper, where centripetal movements on the surface of the retina disrupt the tissue that becomes loose and the edges of the MH more easily fit closely to each other [11].

In recent years, transplantation or plug has been used in the treatment of a persistent macular hole. The plugs represent the third group of MH reoperations. As a plug for the closing of MH, we can use various anatomical alternatives, such as platelet-rich plasma which contains growth factors and other molecules involved in tissue regeneration [12]. Another possible alternative is the transplantation of a flap from the anterior or posterior lens capsule [13]. With a higher operational risk, it is possible to use the free flap of the neuroretina, either so that the photoreceptors of the flap point towards the retinal pigment epithelium, or so that the photoreceptors point towards the residual photoreceptors in the hole area [14].

The technique of treating a macular hole with a laser is also mentioned in the older literature. Laser spots were applied to the pigment epithelium in the MH bottom until it faded. It is supposed that cell proliferation occurred and allowed the closure of MH by the contraction of its edges. The success rate of this method was 33 % [15].

In the Ophthalmology Department of Faculty Hospital Žilina, in three cases of persisting macular holes, we performed a technique using a plug from the human amniotic membrane (hAM plug), designed by Rizzo and the collective in 2019 [16].

MATERIAL AND METHODOLOGY

The diagnosis of persistent macular hole (MH) was unilaterally confirmed in three patients by optical coherence tomography (SD-OCT). In the first patient, it was a primary macular hole (Figure 1A, 2A); in the second patient, it was a secondary hole after cystoid macular edema, because of the central retinal vein occlusion (Figure 3A, 4A), and in the third patient (Figure 5A, 6A), RPE atrophy in the central area was described even before the development of the macular hole. The MH diameter was in the range of 306–810 μm and the base diameter was 1295–1910 μm. Two patients underwent previous unsuccessful surgery 3–4 months before reoperation; the third patient underwent two previous vitrectomies, the last one 11 years ago. We always first performed the revision of peripheral vitreous with its residual removal at the beginning of the surgery. After staining with blue dye (a mixture of trypan and brilliant blue), we extended the ILM peeling zone. Consequently, we prepared the plug from the dehydrated human amniotic membrane. We used vitreoretinal microsurgical scissors under the control of an operating microscope to prepare the plug. Determination of the plug size was done according to the diameter of the MH base. The dehydrated amniotic membrane is supplied to us by the Associated Tissue Establishment of the L. Pasteur University Hospital and Medical School of the P. J. Šafárik in Košice. We inserted the prepared plug, using the vitreoretinal microforceps into the vitreous cavity through a 23-gauge trocar, unlike all available authors, without removing the valve. It is ideal to place the amnion right on the MH area. With consecutive maneuvers, we placed the plug via MH into the subfoveal area. In the case of the first operation, we did not pay attention to the orientation of the hAM plug. In the other two cases, we inserted the plug with the basal membrane upwards and the chorionic side towards the RPE. We performed standard cryopexy behind the sclerotomies, fluid-air-exchange, and the application of expansion gas C_3F_8 or SF_6 in discrete expansion concentration into the vitreous cavity. In all patients, sclerotomies were secured with a suture. The expansile gas tamponade presented 90–100 % of the vitreous cavity volume, so we instructed patients to lie in a face-down position only while sleeping and to avoid the position of lying on the back. In the first patient, a peripheral retinal tear was detected after gas resorption, which did not cause any complications thanks to sufficient laser coagulation treatment.

RESULTS

The monitored preoperative and postoperative parameters are provided in Tables 1 and 2. The closure of the macular hole after reoperation – vitrectomy with ILM peeling extension, hAM plug insertion subretinally and expansion gas application – was observed in two patients (Figures 1B, 2B, 3B, 4B). In the third case of MH (Figure 5B, 6B), the diameter of the macular hole decreased and the cystoid edema of its edges was significantly reduced, but MH remained open. Our patients experienced only a slight improvement in visual acuity, but above all, they lost disturbing visual phenomena in the center of the visual field. We have confirmed that the insertion of the hAM plug into the subretinal space is fully indicated for eyes with a persistent macular hole, despite its large size that has not closed after previous pars plana vitrectomy with ILM peeling. In the first patient, we detected a retinal tear on the periphery at No. 2, which we treated with a laser barrage. It did not cause any further complications. In the patient whose MH remained open after reoperation, the interval from the previous operation was considerable – 11 years. We used an expansion gas with faster resorption (SF6 instead of C3F8) within her reoperation, unlike in the two other patients.

DISCUSSION

We performed a relatively new surgical technique, introduced by Rizzo et al. in 2019. The dehydrated human amniotic membrane can easily be obtained from the Associated Tissue Establishment of the L. Pasteur University Hospital and Medical School of the P.J. Šafárik University in Košice. Dehydrated hAM is easy to handle. Procedures with transplants from other material – from the lens capsule and neuroretina – require a longer surgery time, show a higher risk of complications, and do not provide the potential for neurosensory retina regeneration by growth factors [17,18].

When using hAM, two possible MH closure mechanisms are foreseen. This may be due to the regenerative effect of the hAM plug on the neurosensory retina, with a progressive shift of the edges over the membrane. The second option of the macular hole closing principle, after insertion of the hAM plug under the neurosensory layer of the retina, is the movement of the MH edges together, simply by amniotic membrane wrinkling [18,19].

The question is the orientation of the plug which needs to be oriented towards the RPE. It is important that the plug is directed by the chorionic side towards the retinal pigment epithelium, mainly due to the presence of growth factors on the chorionic side of the amnion. The second reason is the discrete rolling of the plug where the chorionic side is located precisely in the concavity of the membrane, and such a shape of the transplant lifts the edges of the macular hole, making it impossible to close it completely [14] (Figure 3B).

Our results are not quite consistent with Valldeperas and Wong, who found that, in their patient group, recurrent MH surgery led to improved visual acuity, and their closure rate was 100 % of cases [17]. The reoperations of persistent MH in our group of patients resulted in a lower anatomic closure rate and relatively poor visual acuity. Preoperatively, all three patients had edematous retinal neuroepithelium on the edge of the MH, but only the first two had their edges elevated concurrently. In the third patient, the edges were attached to the RPE. We can assume that it is precisely the lifting of the edges of MH that can be a favorable sign of its resulting postoperative closure. To date, our experience suggests that it is recommended to fill the vitreous cavity tamponade by perfluorocarbon (C3F8) over SF6, to orient the basal membrane of the amnion upwards and the chorionic side towards the RPE due to growth factors, but also towards the retinal pigment

Table 1. Preoperative monitored parameters

patient number	characteristics of macular hole	number of previous PPVs	interval between PPV-rePPV	patient's age	gender	lens condition at reoperation	pre-operative BCVA
1.	Primary	1	3 months	70	woman	IOL	0,20 partly
2.	after CRVO	1	4 months	50	woman	surgery at last PPV	hand movement
3.	RPE atrophy	2	11 years	77	woman	IOL	0,10

BCVA – best corrected visual acuity, IOL – intraocular lens, CRVO – central retinal vein occlusion

Table 2. Postoperative parameters

patient number	BCVA after surgery	min / max macular hole size	postoperative monitoring	laterality	complication
1.	0,20	306/1318 μm	102 weeks	R	postoperative peripheral retinal tear at No. 11 - treated with laser coagulation
2.	0,15	810/1910 μm	98 weeks	L	-
3.	0,15	581/1295 μm	64 weeks	L	-

R – right eye, L – left eye, BCVA – best corrected visual acuity

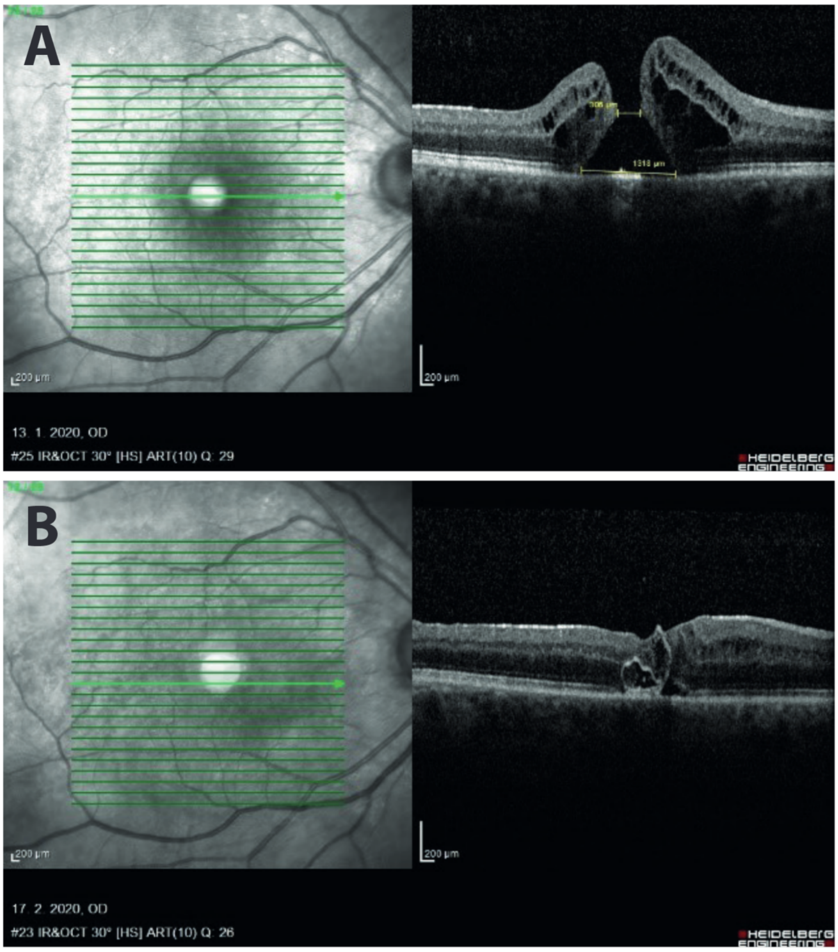

Figure 1. (**A**) SD-OCT before surgery of patient No. 1 shows the elevation and edema of the macular hole edges. (**B**) SD-OCT after surgery in patient No.1 shows not a linear shape, but the rolling of the amniotic membrane plug due to its orientation by the chorionic side to the neuroepithelium

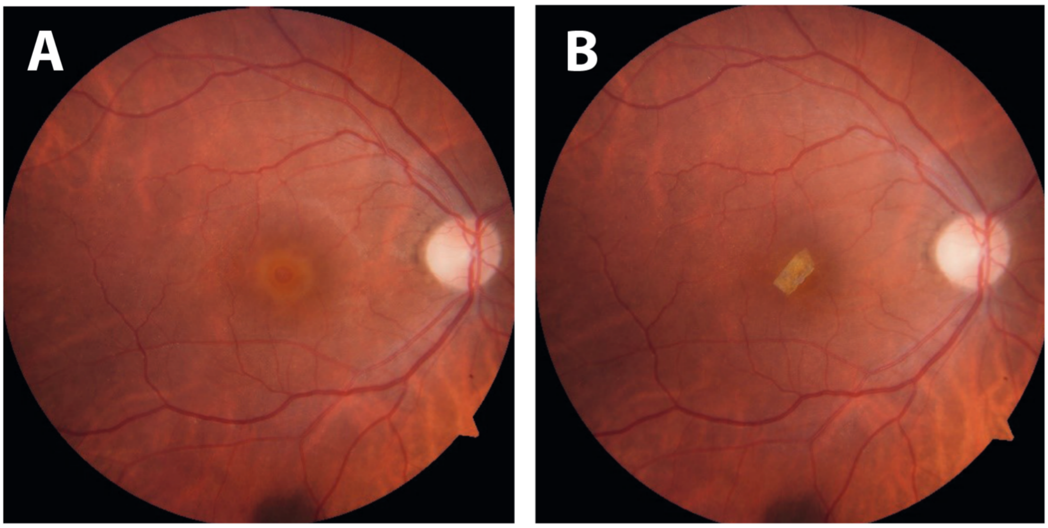

Figure 2. (**A**) preoperative finding. (**B**) postoperative finding of patient No. 1, the optic disc is pale, atrophic, the subretinal plug from the amniotic membrane persists postoperatively

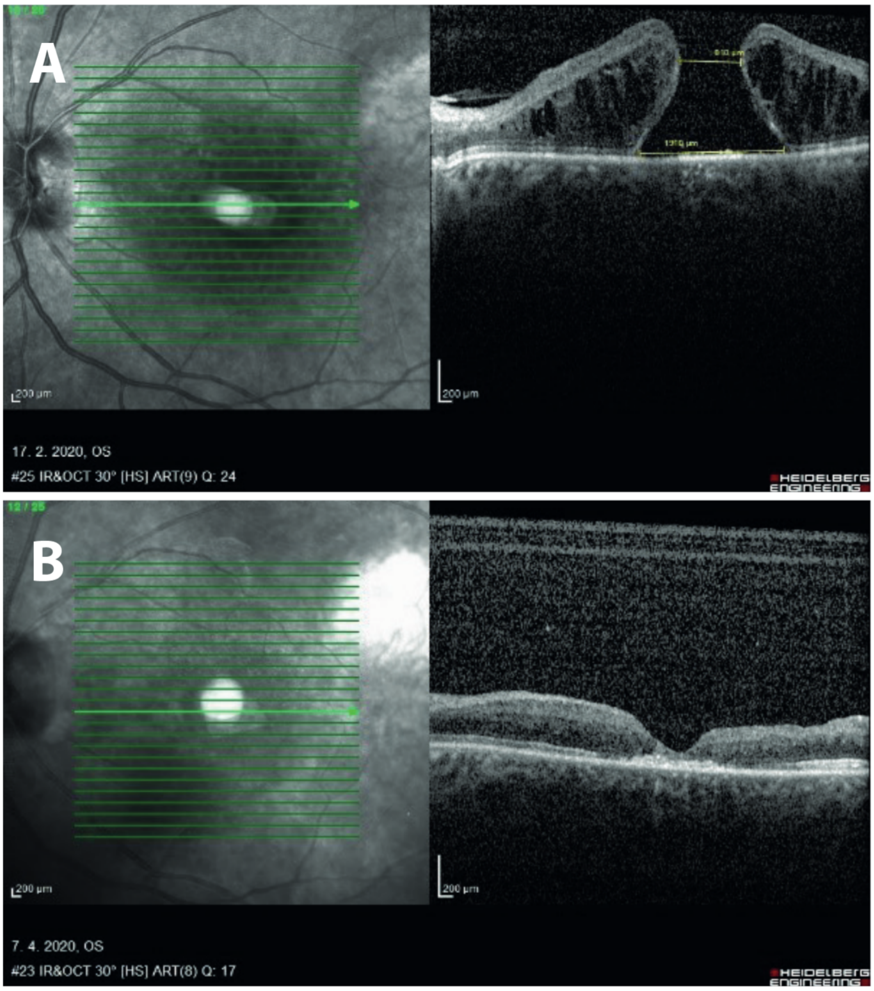

Figure 3. (**A**) preoperative SD OCT finding of macular hole in patient No. 2 after the previous central retinal vein occlusion with macular edema. (**B**) postoperative SD OCT finding in patient No. 2 shows closed macular hole; in place of original macular hole is displayed the linear hyperreflective strip of amniotic membrane plug; neuroepithelial layer is thinned below 300 µm

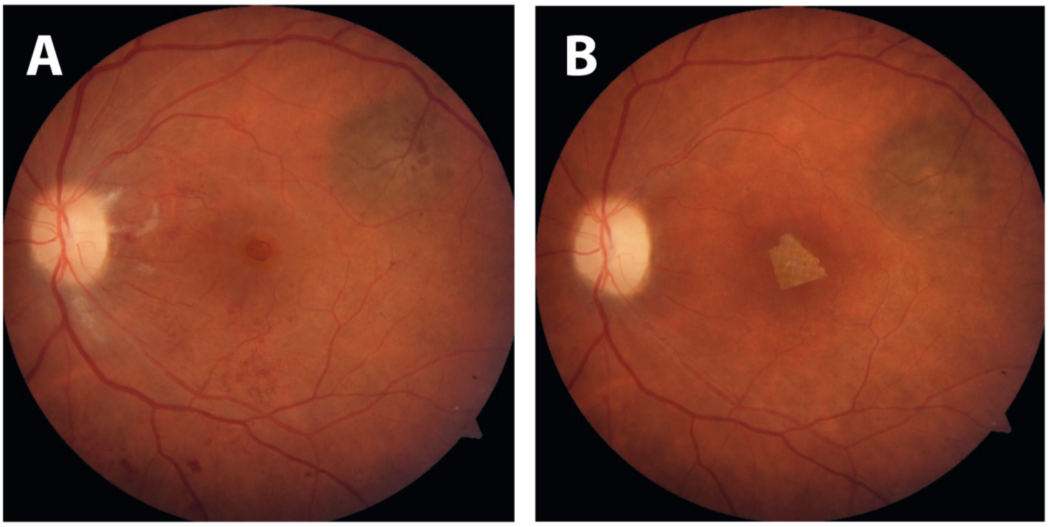

Figure 4. (**A**) patient No. 2 with residual intraretinal hemorrhages after central retinal vein occlusion, there is a choroidal nevus located temporally above the macula. (**B**) amnion membrane plug under neuroepithelium in central region in patient No. 2 postoperatively

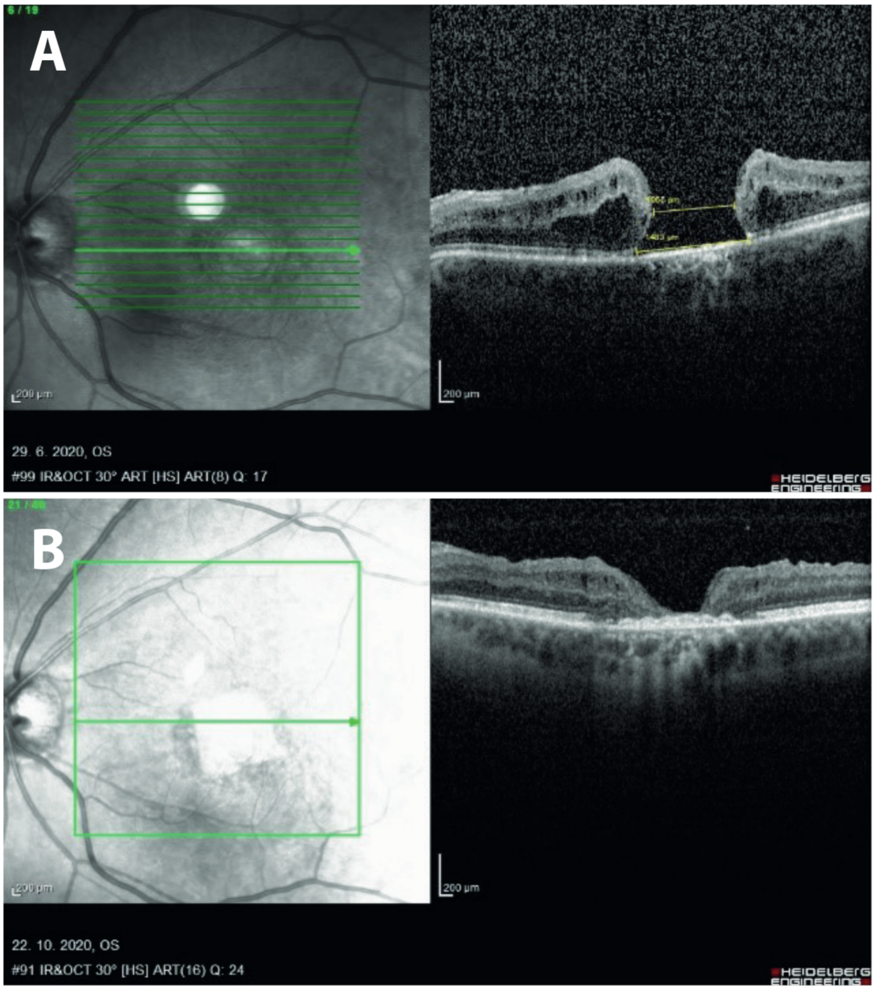

Figure 5. (**A**) preoperative SD OCT of patient No. 3 with macular hole; increased choroidal hyperreflectivity is present, due to RPE atrophy. (**B**) postoperative finding of linear hyperreflective subretinal line on SD OCT; margins of macular hole are without edema, attached, but macular hole in patient No. 3 remains unclosed

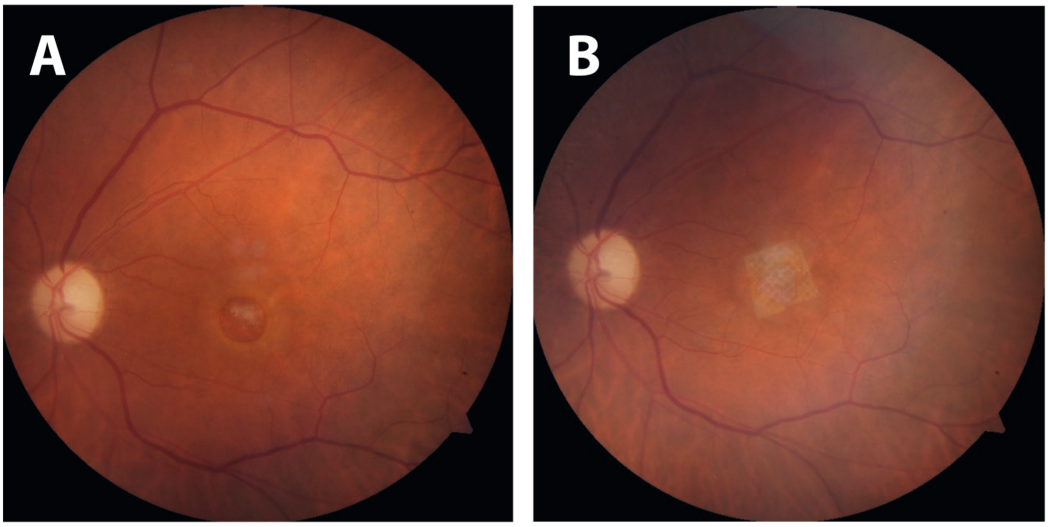

Figure 6. (**A**) preoperative yellowish spots on the bottom of macular hole in patient No. 3. (**B**) postoperative finding of subretinal amnion membrane plug in central region of patient No. 3

epithelium due to the hAM plug concavity. Furthermore, based on our experience, it can be assumed that it is not recommended to wait for the reoperation of a persistent MH longer than 3–4 months after the primary vitrectomy. As after any vitrectomy, we consider it important to monitor postoperatively the periphery of the retina. The possible appearance of a retinal tear and its laser treatment will prevent the development of retinal detachment.

Given the epidemiological situation of COVID-19, most elective surgeries are still performed today. This is the reason why the reoperation of persistent MH with hAM plug is postponed and has so far only been performed in a small number of patients.

CONCLUSION

Clinical trials currently underway [20] will soon report on the efficacy of the treatment of persistent and recurrent MHs using a plug from the human amniotic membrane.

Our experience shows that the surgical solution of a persistent and recurrent hole using the amniotic membrane is a hope for patients with recurrent MH.

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