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LETTER

Letter to the Editor Regarding "Surgical Management of Recurrent and Persistent Macular Holes: A Practical Approach"

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Key Summary Points

Why carry out this letter?

The review presented by Cao et al. discussed current approaches to manage recurrent or persistent macular holes, without mentioning in detail all surgical technique variations of human amniotic membrane use.

What was learned from the letter?

Human amniotic membrane can be either cryopreserved or lyophilized according to availability in various countries or surgeon personal practices.

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Human amniotic membrane has been increasingly used and reported as inlay (i.e., subretinally positioned inside/lying on the macular hole with the "chorion down"). Nevertheless, overlay (i.e., epiretinal position with "chorion up") should be considered as a valuable option: it provides encouraging anatomical and functional midterm results, while offering numerous advantages (safer, no additional trauma of the foveal area, shorter surgery, retinal layer organization respected, potential reversibility) compared to inlay.

Cao et al. have published "Surgical Management of Recurrent and Persistent Macular Holes: A Practical Approach" [1]. This relatively exhaustive review presents current options to manage complex macular holes (MHs) after primary failure, especially one of the most recent developments, human amniotic membrane (AM) transplantation.

However, it would be interesting to discuss surgical techniques using this adjuvant to close complex MHs. Indeed, three key points must be developed: the nature of AM, the position of AM, and the orientation of AM. Thus, we discuss additional references which could bring the readers a more precise overview of the issues when AM is used to promote MH closure.

Different techniques using cryopreserved AM (cAM), a widely available tissue, have provided encouraging results either used first as a plug transplanted into the subretinal space [2–6] or placed secondly in an epiretinal position [7]. Rizzo et al. [2–4] used cAM from a local eye bank (Lucca, Italy) and positioned the plug with "chorion down", facing the retinal pigment epithelium (RPE) (i.e., as an inlay [8]). Abouhussein et al. [5] used homemade cAM and Huang et al. [6] used cAM from AmnioGraft (Bio-Tissue, Miami, FL, USA) transplanted as inlay. This chorion-down orientation of the plug of cAM subretinally transplanted may ensure proper adhesion on the RPE, preventing secondary displacement. Moharram et al. [7] did not specify the source of their cAM, and were the only team who reported epiretinal use of cAM to close MH-associated rhegmatogenous retinal detachment (RRD) in highly myopic eyes: their rationale was to consider complex MH as a macular ulcer by analogy with persistent corneal ulcers. They positioned the cAM plug with the chorion down, facing the retina, therefore not as a "true" overlay as defined by Letko et al. [8] for corneal applications. Note that population samples in this series using cAM were small, and comparability was limited by lack of data regarding mean preoperative MH diameter or heterogeneous baseline characteristics and follow-up.

Lyophilized AM (lAM) was used for the first time in ophthalmology in 2004 [9], with similar physical, biological, and structural properties to cAM [10]. Compared to cAM, lAM presents several advantages: immediate availability in the operating room with simpler logistics [11]; long shelf life at room temperature; thinner and more transparent [6], which can help in integrating it when used as an inlay, or as a smart interface with less mask effect when used as an overlay; and easy to trephine before rehydration, with roll-up allowing a "no touch" technique [12] for lAM insertion thanks to a dedicated catheter.

We recently published [12] an interesting standardized surgical technique which combines the advantages of lAM and the epiretinal position with "chorion up" (i.e., lAM used as a "true" overlay [8]). We used sterile devitalized trephined discs of lAM (Visio Amtrix, TBF, Mions, France) with "chorion up" to cover the MH with ample overlap for easier handling and positioning. The rationale combines mutually nonexclusive hypotheses: (1) The overlay can play the same role as an inverted internal limiting membrane (ILM) flap [13], but will be larger, easier to position, and more stable. Like a biological bandage, it can act as a scaffold to promote healing, with centripetal migration of cells, stimulation of macrophage-like cells facilitating MH closure, and a more physiologic closure mechanism versus subretinal position [14]; besides, if complete closure is impossible, it acts as a patch and prevents MH-induced RRD. We hoped to obtain excellent functional results by analogy with those already obtained for ILM used as an epiretinal inverted flap versus insertion into the MH [15]: the epiretinal position resulted in significantly better recovery of photoreceptor layers, and therefore better visual recovery. (2) The overlay better respects the organization of all retinal layers, preventing induction of foveal gliosis by interposition of exogenous tissue (cAM or lAM) transplanted into the subretinal space, which must be integrated between the MH edges. (3) It seemed safer not to manipulate the MH edges, so as not to worsen the RPE and neuroretinal injuries, particularly during graft insertion [16]. (4) The overlay could prevent the parafoveal atrophy described after retraction of cAM or lAM used as inlays [17]. (5) Even considering the time taken to fully unfold the lAM for overlay, operating time can be shortened versus inlay, thus reducing light toxicity [18]. (6) If an adverse event occurs, the lAM can be removed, which is a key point for a new technique.

In our series of complex MH cases with no alternative [12] (minimum and maximum diameters, respectively 945 ± 330 and 1507 ± 717 μm; axial length 26.58 ± 3.38 mm; number of prior surgeries 1.4 ± 0.96), the overlaid epiretinal large disc of ILM blue-stained lAM with the chorion up seemed to promote anatomic success (80% of MH closed, 20% had reduced diameter, all MH-associated RRD reattached without recurrence) and functional recovery (mean logMAR BCVA improved from 1.92 ± 0.58 to 1.17 ± 0.57; $P < 0.001$), with

90% of eyes achieving ≥ 0.3 logMAR improvement) with 1-year follow-up. Thus, lAM used as overlay should be considered as a valuable, promising minimally invasive technique among the options to close recurrent or persistent MHs.

Indeed, large samples with homogeneous baseline characteristics and long follow-up must now be investigated, ideally in randomized multicentric studies that should compare these techniques to one another, for example lAM inlays with the chorion down and overlays with the chorion up, using our protocol.

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