The evolution of isolated neovascular tufts ("POPCORN") in the retinopathy of prematurity

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ABSTRACT

Purpose: To explore the natural evolution of isolated neovascular tufts ("popcorn") in retinopathy of prematurity (ROP) and its significance in the progression of acute ROP.

Methods: In this retrospective case series, 89 infants (89 eyes) in total having acute ROP were analyzed during serial retinal examinations with a RetCam III wide-angle fundus imaging system, among which 53 eyes were observed to have popcorn and 36 eyes did not. The clinical outcomes of the popcorn (+) group and the popcorn (-) group were compared.

Results: Popcorn was located only in Zone II, Stage 2 ROP, primarily in the temporal field (65%). It appeared at a mean postmenstrual age of (37.6 ± 1.3) weeks, disappeared at (41.0 ± 2.2) weeks, and lasted for (2.8 ± 1.1) weeks. The popcorn (+) group had a significantly higher natural regression incidence than the popcorn (-) group ($P < 0.05$). The laser-treated eyes in the popcorn (+) group had earlier presentations (36.4 ± 0.7 vs. 38.2 ± 1.3 weeks) and shorter existences (1.5 ± 0.5 vs. 3.2 ± 0.9 weeks) of popcorn than the regressed eyes ($P < 0.01$, respectively).

Conclusion: Popcorn is generally a "benign" indicator of the regression of ROP. The early presentation (<postmenstrual age 37 weeks) and short duration of popcorn require further observation.

Difference between pachychoroid and nonpachychoroid polypoidal vascular choroidal vasculopathy and their response to anti-vascular endothelial growth factor therapy

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ABSTRACT

Purpose: Recent investigations have found a biphasic pattern of choroidal thickness within polypoidal choroidal vasculopathy (PCV) patients. This study aims to investigate the relationship between choroidal thickness and the clinical features of PCV eyes.

Method: We investigated the correlation between various clinical features including subfoveal choroidal thickness (SFCT) and the response to 3-monthly anti-vascular endothelial growth factor (VEGF) treatments in 62 consecutive, treatment-naive PCV patients (66 eyes). After finding out SFCT as the only factor that was correlated with anti-VEGF treatment, we then set up to determine a best cutoff line for SFCT that could be used as a parameter to differentiate PCV patients into pachychoroid and nonpachychoroid groups using the Youden index for best combined specificity and sensitivity. We then compared the demographic features, clinical characteristics, and the response to anti-VEGF between both groups, to determine whether there is a difference between these two groups.

Results: Subfoveal choroidal thickness was the only significant factor for the treatment effect. The SFCT of 267.5 μm is the best cutoff line. The pachychoroid

group showed significant younger ages (64.1 ± 9.6 vs. 72.0 ± 8.2, P = 0.004), fewer age-related macular degeneration-like features (50.0 vs. 81.3%, P = 0.027), more central serous chorioretinopathy-like features (typical retinal pigment epithelial mottling [61.1 vs. 16.7%, P = 0.0014] and choroidal vascular hyperpermeability [88.9 vs. 37.5%, P = 0.0002]), and less response to 3-monthly anti-VEGF treatments (27.8 vs. 83.3%, P < 0.0001) as compared to the nonpachychoroid group.

Conclusion: Polypoidal choroidal vasculopathy patients could be subclassified into pachychoroid and nonpachychoroid groups. The pachychoroid subtype of PCV has significantly younger ages, fewer age-related macular degeneration-like features, more central serous chorioretinopathy-like features, and less response to anti-VEGF treatment.

Inverted internal limiting membrane flap techniques and outer retinal layer structures

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ABSTRACT

Purpose: To examine the influence of the inverted flap (IF) internal limiting membrane (ILM) technique in macular hole (MH) closure on outer retinal layers after MH surgery.

Methods: Retrospective study. Postoperative position of ILM, recovery rate of external limiting membrane and ellipsoid zone, and best-corrected visual acuity were evaluated. The Inserted group, where the IF is placed inside the hole, was compared with the Cover group, where the IF completely covers the hole.

Results: Sixty-two eyes of 58 patients who underwent vitrectomy and ILM peeling with the IF technique for large MHs (>400 µm) with successful MH closure and a follow-up of 12 months were evaluated. In the 24 eyes of the Inserted group, there was no regeneration of external limiting membrane or ellipsoid zone after 12 months. In the 38 eyes of Cover group, external limiting membrane recovered in 55.3% of patients 1 month after surgery, and in 86.1% after 12 months. The elipsoid zone layer was present in 58% of the patients.

Conclusion: Poorer anatomical and visual results were associated with the IF technique where ILM insertion occurs compared with ILM placed over the hole. These findings suggest that insertion of the ILM in the hole might prevent outer retinal layers realignment and visual recovery in MH surgery.

Use of choroidal vascularity index for choroidal structural evaluation in central serous chorioretinopathy with choroidal neovascularization

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ABSTRACT

Purpose: To evaluate choroidal vascular structure in eyes with central serous chorioretinopathy (CSC) by assessing the choroidal vascular index (CVI).

Methods: We retrospectively analyzed the medical records of 117 eyes with CSC. Subjects were divided into 4 groups according to clinical characteristics: 1) acute CSC (N = 29), 2) non-neovascularized chronic CSC without flat irregular pigment epithelial detachment (N = 49), 3) non-neovascularized chronic CSC with flat irregular pigment epithelial detachment (N = 21), and 4) chronic CSC with choroidal neovascularization (N = 18). Subfoveal choroidal area (1,500 mm) of swept source optical coherence tomography scans were divided into luminal and stromal areas by the image binarization technique. The CVI was defined as the ratio of the luminal to the total subfoveal choroidal area.

Results: The CVI was significantly lower in eyes of Group 4 than those of other groups (all $P < 0.05$). The subfoveal choroidal thickness was significantly lower in Group 4 than in Groups 1 and 2 ($P < 0.05$), but regression analysis showed no association with the CVI.

Conclusion: Decreased CVI may reflect choroidal vascular structure changes in eyes with choroidal neovascularization complicating CSC. These findings suggest

that the CVI could be useful for evaluating choroidal vascular changes in eyes with CSC.

INTERNAL LIMITING MEMBRANE PEELING VERSUS NONPEELING TO PREVENT EPIRETINAL MEMBRANE DEVELOPMENT IN PRIMARY RHEGMATOGENOUS RETINAL DETACHMENT: A Swept-Source Optical Coherence Tomography Study with a New Postoperative Classification System

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ABSTRACT

Purpose: To determine whether internal limiting membrane peeling in primary rhegmatogenous retinal detachment prevents epiretinal membrane (ERM) development. Secondarily, we propose a classification system for postoperative ERMs.

Methods: Retrospective, interventional, comparative case series. Consecutive eyes with primary rhegmatogenous retinal detachment (n = 140) treated by a single surgeon. The presence of postoperative ERMs was assessed with swept-source optical coherence tomography.

Results: An ERM was detected in 26 eyes (46.4%) in the nonpeeling group and in one eye (1.8%) in the internal limiting membrane peeling group ($P \leq 0.001$). The median visual acuity significantly improved in both groups ($P \leq 0.001$). Inner retinal dimples were observed in 41.1% of eyes in the internal limiting membrane peeling group versus 0% in the nonpeeling group ($P \leq 0.001$), and they were not

correlated with visual acuity (r = 0.011; P = 0.941). Based on swept-source optical coherence tomography findings, we identified three different types of ERMs: 7 (26.9%) were classified as Type 1, 12 (46.1%) as Type 2, and 7 (26.9%) as Type 3. Superficial retinal plexus deformations observed on optical coherence tomography angiography and en face images were detected in 100% of Type 3 ERMs, 41.6% of Type 2, and 0% of Type 1 (χ = 14.3; P = 0.001). Interestingly, all of the patients who presented these alterations also had metamorphopsia.

Conclusion: Internal limiting membrane peeling in primary rhegmatogenous retinal detachment seems to prevent postoperative ERM development. Swept-source optical coherence tomography analysis is helpful to define and classify different types of ERMs and to establish the surgical indication for their removal.

Brolucizumab: Evolution through Preclinical and Clinical Studies and the Implications for the Management of Neovascular Age-Related Macular Degeneration

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ABSTRACT

Improving or maintaining visual acuity is the main goal for the treatment of neovascular age-related macular degeneration (nAMD). Current nAMD standard of care dictates frequent intravitreal (IVT) anti-vascular endothelial growth factor (VEGF) injections, which places a substantial burden on patients, caregivers, and physicians. Brolucizumab, a newly developed anti-VEGF molecule for nAMD treatment, has demonstrated longer durability and improvement in visual and anatomic outcomes in clinical studies in a q12-week regimen, indicating its potential to reduce treatment burden as an important therapeutic tool in nAMD management. This review focuses on the development of brolucizumab and the preclinical and clinical studies evaluating its efficacy, tolerability, and safety. Brolucizumab (also known as "RTH258" and "ESBA1008") is a humanized, single-chain variable fragment (scFv) antibody with a molecular mass of approximately 26 kDa that inhibits VEGF-A. Preclinical studies show that brolucizumab readily penetrates the retina to reach the retinal pigment epithelium (RPE)/choroid with minimal subsequent systemic exposure. The safety, tolerability, and efficacy of a single IVT brolucizumab administration in patients with treatment-naïve nAMD were first demonstrated in the SEE Phase 1/2 study. The OSPREY Phase 2 study

showed brolucizumab to be as efficacious as aflibercept in a q8-week regimen with regard to best-corrected visual acuity (BCVA) and brolucizumab achieving greater fluid resolution. Brolucizumab-treated patients in the OSPREY study were subsequently challenged with a q12-week dosing interval, and the outcomes provided key information for the study design and end points of the Phase 3 studies. In the HAWK and HARRIER Phase 3 studies, after 3 monthly loading injections, brolucizumab treatment regimen (q12-week or q8-week) was guided by individual disease activity assessment using functional and anatomic parameters (central subfield thickness [CST], intraretinal fluid [IRF], or subretinal fluid [SRF]) versus aflibercept (q8-week). Fewer brolucizumab 6-mg treated eyes had disease activity versus aflibercept, and anatomic outcome results at weeks 16 and 48 demonstrate brolucizumab as a potent drying agent. Moreover, of patients treated with 6 mg brolucizumab, 55.6% and 51.0% maintained a q12-week dosing interval immediately after the loading phase until week 48 in HAWK and HARRIER, respectively. These Phase 3 studies demonstrated that the brolucizumab q12-week regimen maintains efficacy and safety while reducing treatment burden associated with regular IVT injections for patients with nAMD.

Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial

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ABSTRACT

Purpose: Injection of pharmacotherapy into the suprachoroidal space, between the sclera and choroid, is an alternative delivery technique developed with the rationale of providing higher drug concentrations to posterior ocular structures compared with other intraocular and periocular injection procedures. This study was conducted to evaluate the safety and efficacy of suprachoroidally injected triamcinolone acetonide formulation (CLS-TA), a suspension of triamcinolone acetonide, in improving vision among patients with noninfectious uveitis complicated by macular edema (ME).

Design: Phase 3 masked, randomized trial.

Participants: One hundred sixty patients with ME secondary to noninfectious uveitis. Patients were required to have a best-corrected visual acuity (BCVA) of 5 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent, 20/800) and 70 or fewer ETDRS letters read (Snellen equivalent, 20/40) in the study eye.

Methods: Patients were randomized 3:2 to suprachoroidally injected CLS-TA or sham treatment, with administrations at day 0 and week 12.

Main outcome measures: The primary end point was improvement from baseline of 15 or more ETDRS letters in BCVA at week 24. The secondary end point was reduction from baseline in central subfield thickness (CST) at week 24.

Results: In the CLS-TA arm, 47% of patients gained 15 or more ETDRS letters in BCVA versus 16% in the control arm ($P < 0.001$), meeting the primary end point. Mean reductions in CST from baseline were 153 µm versus 18 µm ($P < 0.001$). No serious adverse events (AEs) related to treatment were reported. Corticosteroid-associated AEs of elevated intraocular pressure occurred in 11.5% and 15.6% of the CLS-TA and control groups, respectively. Cataract AE rates were comparable (7.3% and 6.3%, respectively).

Conclusions: Patients in the CLS-TA study arm experienced clinically significant improvement in vision relative to the sham procedure, demonstrating the efficacy of suprachoroidal injection of CLS-TA for the treatment of ME in a vision-threatening disorder.

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