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CRYOPRESERVED AMNIOTIC MEMBRANE (PROKERA®) TREATMENT OF ANTERIOR STROMAL HAZE SECONDARY TO HSV KERATITIS

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ABSTRACT

Purpose

To review the efficacy of cryopreserved amniotic membrane (CAM) to reduce stromal scarring in a case of refractory anterior stromal haze related to herpes simplex keratitis (HSK). The initial treatment course of conventional topical steroid and oral antiviral was completed followed by the addition of CAM to further address scarring.

Methods

Clinical presentation of a cornea with stromal haze that was refractory to previous steroid and topical and oral antiviral therapy were documented with anterior segment smartphone capture. Best corrected visual acuity was documented to contrast clinical observations. Use of the CAM Prokera® Slim was successful in reducing anterior stromal haze and improving best-corrected acuity.

Conclusions

CAM treatments may provide an additional therapeutic agent in the management of anterior stroma infiltration and scarring secondary to HSK. As demonstrated in this case, patients with visually significant stromal haze that is non-responsive to topical therapy may benefit from non-surgical placement of CAM. Due to the accessibility of CAM in private clinical settings, it should be considered as a viable new option for patients who have exhausted other traditional treatments and perhaps be considered in early infectious corneal disease states.

Keywords: Herpes Simplex Keratitis, Cryopreserved Amniotic Membrane

BACKGROUND

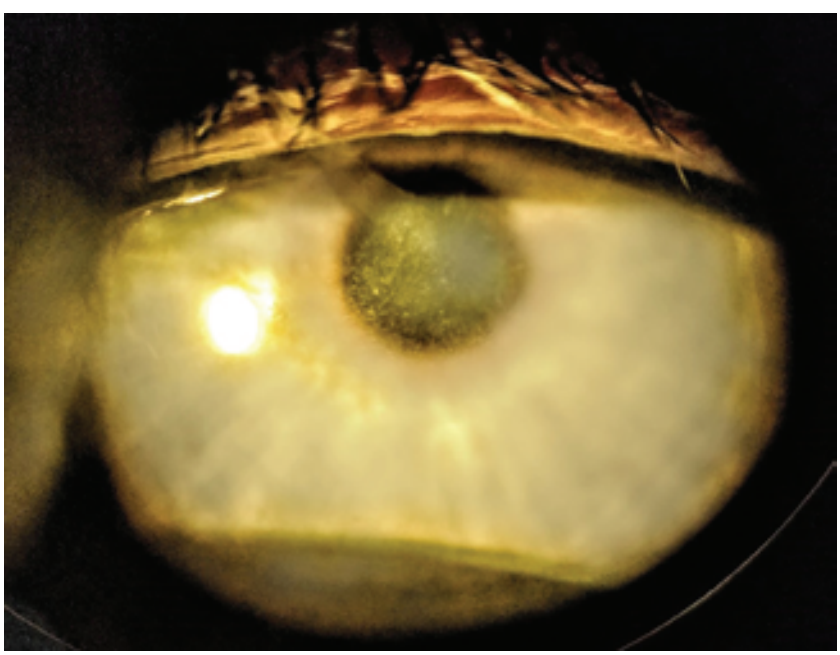
Herpes simplex keratitis (HSK) is known to be the great masquerader when it comes to corneal disease.[1] Despite our collective experience with it, it is still a poorly understood disease entity, particularly when HSK impacts the anterior stroma. Viral replication is intracellular so it would make sense that keratocyte density in the cornea would influence the spread and presentation of this disease entity.[2] Because keratocyte density is highest in the deep epithelium and anterior 10% stroma, it may be less likely that viral infection is responsible for stromal hazing that we observe clinically, rather the immune-mediated inflammation that is primarily T-cell driven (2) (3).[2,3] The applications of cryopreserved amniotic membrane (CAM) to manage infectious keratitis have been established in the literature.[4] It has been shown to be specifically effective in re-epithelialization and in reduction in stromal inflammation associated with other forms of infectious keratitis (5).[5] The case below describes the successful use of CAM in amniotic membrane transfer (AMT) in a case of HSK with stromal haze that was refractory to conventional therapy.

CASE

A 66-year-old South Asian male had been referred for an assessment of recurrent HSK OS with increasing stromal haze. He reported visual blur and fogginess of his left eye worsening over the previous year. The initial diagnosis of HSK was more than one year prior to this referral and he had been treated over the course of the year on 3 separate occasions with oral Valtrex 500 mg TID for 10 days (Valtrex, GlaxoSmithKline plc) in addition to topical Lotemax® gel (loteprednol etabonate ophthalmic 0.5%, Bausch and Lomb) QID OS tapered down over one month during the same periods. Endotheliitis was reported as part of his initial presentation by his ophthalmologist however was not mentioned as part of diagnoses in his repeated visits over the year. This patient was currently using Refresh® Endura (Allergan, Inc.) PRN and had was taking Valtrex 500 mg daily prophylactically on the recommendation of his primary care practitioner.

Best-corrected vision was 20/20 OD and 20/30 OS which improved to 20/25-2 on pinhole. Slit lamp examination revealed trace diffuse punctate epitheliopathy inferiorly OU and central 2+ anterior 1/3 stromal haze (Figure 1). The patient had inferior scleral show OU secondary to

FIG. 1 HSK with 2+ anterior stromal haze OS on presentation.



lower lid laxity due to midface hypotonicity and incomplete blinking associated with microlagophthalmos on Korb light test. No dendritic ulceration was noted on rose bengal staining and epithelium was otherwise intact. Anterior chambers were deep and quiet OU. Intraocular pressures (IOP) were measured by Goldmann applanation tonometry at 14 mmHg OD and OS.

HSK (stromal) with intact epithelium was diagnosed at this stage and the patient was prescribed Valtrex 500 mg PO TID for 10 days, followed by a prophylactic dose of 500 mg PO QD. Topically he was prescribed Pred Forte 1% QID (Allergan, Inc) for 2 weeks then tapered for an additional 2 weeks based on HEDS-1.[6] Topical non-preserved Hylo 1% (Hyaluronate, CandorVision Inc) was initiated at this time QID OU. Due to the longer presentation and refractory nature of his case, he was made aware that his vision was not expected to improve dramatically. He was followed during the course of the month for IOP response and epithelial integrity due to topical steroid use and no response was noted.

One-month post-treatment, the stromal haze had decreased to 1+ (Figure 2); however, corrected acuity had remained unchanged OS at 20/30. At this stage, we discussed moving forward with an off-label approach of using AMT by way of ProKera® Slim CAM (Bio-Tissue Inc, Miami FL) to attempt to manage the immune-mediated inflammatory response that was occurring in the anterior stroma. A guarded prognosis was given; however, the patient opted to proceed with this treatment plan. Through aseptic technique, a Prokera® Slim amniotic membrane was inserted into the left eye without incident. He was to continue using his non-preserved topical hyaluronate while maintaining Valtrex 500 mg PO QD as prescribed. The amnion had dissolved by day 5 and the carrier ring was successfully removed without incident.

Anterior stroma was markedly improved with trace haze and best-corrected acuity had improved to 20/20 (Figure 3). Prophylactic Valtrex 500 mg PO QD was continued as was his topical hyaluronate and he continues to follow up every 3–6 months. The cornea continues to maintain clarity to date at 9-months post-treatment.

FIG. 2 HSK with anterior 1+ stromal haze: 1-month post topical and oral therapy.

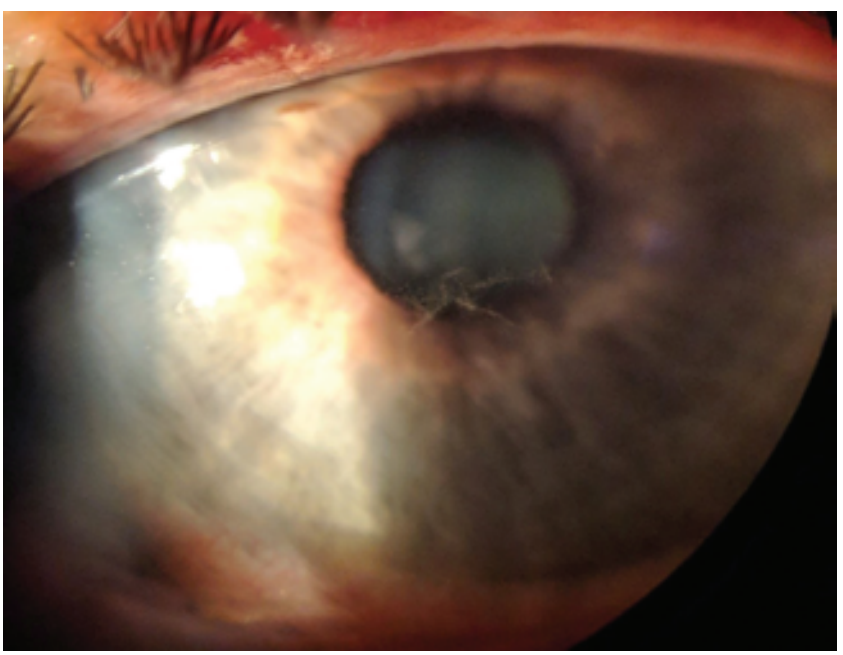
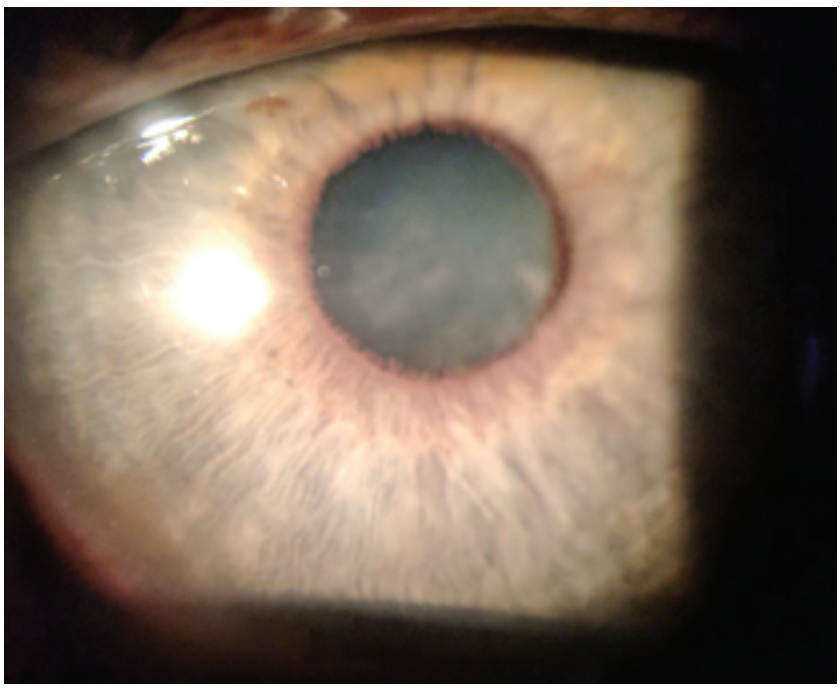


FIG. 3 HSK resolved anterior stromal haze 2-weeks post-Prokera® OS.



DISCUSSION

Immune-mediated inflammation in the HSK patient is, in part, a T-cell driven response to HSV antigens within the stroma (6).[6] Given this response, the anti-inflammatory properties exerted by CAM may play a significant role in countering this while assisting with its antimicrobial and, more specifically, antiviral action (7).[7] The Heavy Chain-Hyaluronan/Pentraxin-3 (HC-HA/PTX3) found in cryopreserved amnion is known to assist in the antiviral activity and also provides additional anti-scarring action.[7,8] This purified complex also aids in adaptive immune responses, notably suppressing the activation of Th1, Th17 lymphocytic pathways which are components of the corneal HSV immunopathological response(9).[9]

While the exact mechanism of how CAM affects the pathogenesis of HSK and associated stromal infiltration and subsequent scarring remains unclear, the above-mentioned pathways certainly suggest it does target the known components that make treating HSK challenging. This case reveals that AMT using CAM should be considered as an adjunctive treatment option that, when presented earlier on in the disease process, may result in rapid resolution of both signs and symptoms associated with HSK. It may also prevent vision loss associated with stromal scarring which at present has limited treatment options available for clinicians to address.

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