Use of Viable Cryopreserved Placental Membrane as an Adjuvant to Facial Keloid Resection

Rishi J. Gupta, DDS, MD, MBA*†
Stephen T. Connelly, DDS, MD, PhD*†
Rebeka G. Silva, DMD*†
Nat R. Gwilliam, MD‡

INTRODUCTION

Normal wound healing proceeds through a well-defined cascade of hemostasis, inflammation, proliferation, and maturation phases that are characterized by complex cellular interactions and cytokine signaling pathways. Keloids occur due to dysregulation of fibroblast activity during the inflammatory phase, resulting in excess collagen deposition extending beyond the boundaries of the original wound.1,2 Treatments targeting fibroblasts and down-regulating inflammation—including steroids, radiation, and interferon—make up the majority of interventions for pathological scarring.2–4

Although surgical resection of the keloid removes scar tissue, surgery also triggers an inflammatory response, thus increasing risk of keloid recurrence. For that reason, surgery may be paired with anti-inflammatory agents, such as a series of postoperative steroid injections or irradiation. However, these modalities carry side effects that can be severe and systemic.1

Viable cryopreserved placental membrane (vCPM) retains all components and properties of fresh tissue, including anti-inflammatory, anti-fibrotic, and pro-angiogenic effects via paracrine signaling.5–8 These make vCPM a potential surgical adjunct in prevention of scar formation in keloid-prone patients. In this article, we present the first-reported case of viable cryopreserved placental membrane, with living mesenchymal stem cells, to treat a painful preauricular keloid in conjunction with surgical resection. (Plast Reconstr Surg Glob Open 2018;6:e1638; doi: 10.1097/GOX.0000000000001638; Published online 11 January 2018.)

CASE REPORT

The patient is a 62-year-old male with bilateral temporomandibular (TMJ) disorder, posttraumatic stress disorder, hypertension, and tobacco use who underwent bilateral TMJ arthroplasty. The arthroplasties were performed sequentially without complication. The patient subsequently returned to clinic with complaints of pain and discomfort along his left preauricular incision where a keloid had formed (Fig. 1). All other incisions had healed normally.

Twenty-one months after his left-sided TMJ arthroplasty, the patient underwent surgical resection of the keloid. An elliptical incision was made around the keloid with a #15 scalpel, with the deep portion of the scar removed sharply. The surgeon undermined surrounding skin with facelift scissors until the tissue could be approximated without tension. A strip of vCPM was then placed in the base of the wound (Fig. 2). The tissue was closed with a 4-0 absorbable monofilament in the deep dermis and a running continuous 5-0 nylon skin closure (Fig. 3). Dressing included bacitracin, nonadherent barrier, and Tegaderm.

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At follow-up 4 weeks later, the incision was clean, dry, and intact with no erythema or induration (Fig. 4). No keloid reformation occurred on subsequent 4- and 9-month follow-ups, at which point the scar was minimally visible and the patient pleased with the aesthetic results.

**DISCUSSION**

Pathological scars remain a challenge despite numerous treatment modalities. One reason is the complexity of the pathomechanism for which there is no animal model, limiting our ability to study effects of treatments. There are also few robust clinical studies assessing interventions. As a result, individual clinical experience has driven care.

First-line treatment in the United States is typically corticosteroids, which matches international expert guidelines. Monotherapy is often inadequate, however. Reported recurrence rates with steroids alone range from 9% to 50% but were found to decrease to 14.3% when combined with surgical resection. Similarly, improved results with multimodal therapy were found combining surgery and irradiation, steroids and fluorouracil (5-FU), and so on. Of note, many of these protocols require repeated interventions, such as monthly injections of steroids or botulinum toxin.

Ongoing research into the inflammatory mechanisms of keloid formation and clinical treatments has yet to find a durable solution. Within the literature and practice, there is an ongoing search for novel therapies with the hope of decreasing recurrence rates and ultimately preventing initial formation of keloids.

**CONCLUSIONS**

This case report is a proof of concept for use of vCPM in the treatment of fibroproliferative scar formation in conjunction with surgery. Though findings are limited as
3. Gauglitz GG, Korting HC, Pavić T, Ruzicka T, Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Mol Med*. 2011;17(1-2):115–125. doi:10.2119/molmed.2009.00153.

4. Ogawa R. Keloid and Hypertrophic Scars Are the Result of Chronic Inflammation in the Reticular Dermis. *Int J Mol Sci*. 2017;18(3). doi:10.3390/ijms18030666.

5. Johnson A, Gyurdieva A, Dhall S, Danilkovitch A, Duan-Arnold Y. Understanding the Impact of Preservation Methods on the Integrity and Functionality of Placental Allografts. *Ann Plast Surg*. 2017;79(2):203–213. doi:10.1097/SAP.0000000000001101.

6. Duan-Arnold Y, Gyurdieva A, Johnson A, Uveges TE, Jacobstein DA, Danilkovitch A. Retention of Endogenous Viable Cells Enhances the Anti-Inflammatory Activity of Cryopreserved Amnion. *Adv Wound Care*. 2015;4(9):523–533. doi:10.1089/wound.2015.0636.

7. Duan-Arnold Y, Uveges TE, Gyurdieva A, Johnson A, Danilkovitch A. Angiogenic Potential of Cryopreserved Amniotic Membrane Is Enhanced Through Retention of All Tissue Components in Their Native State. *Adv Wound Care*. 2015;4(9):513–522. doi:10.1089/wound.2015.0638.

8. Duan-Arnold Y, Gyurdieva A, Johnson A, Uveges TE, Jacobstein DA, Danilkovitch A. Retention of Endogenous Viable Cells Enhances the Anti-Inflammatory Activity of Cryopreserved Amnion. *Adv Wound Care*. 2015;4(9):523–533. doi:10.1089/wound.2015.0636.

9. Mustoe TA, Cooter RD, Gold MH, et al. International clinical recommendations on scar management. *Plast Reconstr Surg*. 2002;110(2):560–571. doi:10.1097/00006534-200208000-00031.

10. Gold MH, McGuire M, Mustoe TA, et al. Updated international clinical recommendations on scar management: part 2-algorithms for scar prevention and treatment. *Dermatol Surg*. 2014;40(8):825–831. doi:10.1111/dsu.12050.

11. Gold MH, Berman B, Clementoni MT, Gauglitz GG, Nahai F, Murcia C. Updated international clinical recommendations on scar management: part I—evaluating the evidence. *Dermatol Surg*. 2014;40(8):817–824. doi:10.1111/dsu.12182.

12. Davis SA, Feldman SR, McMichael AJ. Management of Keloids in the United States, 1990–2009: An Analysis of the National Ambulatory Medical Care Survey. *Dermatol Surg*. 2013;39(7):988–994. doi:10.1111/dss.12182.

13. Hayashi T, Furukawa H, Oyama A, et al. A New Uniform Protocol of Combined Corticosteroid Injections and Ointment Application Reduces Recurrence Rates After Surgical Keloid/ Hypertrophic Scar Excision. *Dermatol Surg*. 2012;38(6):893–897. doi:10.1111/j.1524-4725.2012.02345.x.

14. Bennett KG, Kung TA, Hayman JA. Brown DL. Treatment of Keloids With Excision and Adjuvant Radiation. *Ann Plast Surg*. 2017;78(2):157–161. doi:10.1097/SAP.0000000000000903.

15. Ramirez-Fort MK, Meier B, Feily A, Lange CS. Should adjuvant irradiation to prevent keloidal fibroproliferative growth, be standard of care? *Br J Dermatol*. July 2017. doi:10.1111/bjd.15667.