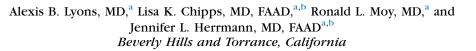
# Dehydrated human amnion/chorion membrane allograft as an aid for wound healing in patients with full-thickness scalp defects after Mohs micrographic surgery



*Key words:* dehydrated human amnion/chorion membrane allograft; Mohs micrographic surgery; non-melanoma skin cancer; wound care.

## **INTRODUCTION**

Large surgical defects after Mohs micrographic surgeries (MMS) often require rotation or advancement flaps, skin grafts, or delayed reconstruction after use of tissue expanders. For patients with limited tissue redundancy, wounds may also heal by secondary intention. Elderly patients undergoing MMS with full-thickness defects exposing bone pose a unique set of healing barriers, such as immunosuppression, increased infection risk, poor tolerance to bone chiseling for exposing pinpoint bleeding, and difficulty in reaching wounds to apply dressings successfully. Dehydrated human amnion/chorion membrane (dHACM) allografts are skin substitutes that can be placed in wound beds to accelerate wound healing and decrease pain without the need for meticulous wound care. These grafts are placed directly on bone weekly, integrate into the wound beds, and encourage rapid granulation without the need for dressing changes. We describe a case series of 5 elderly patients with large, full-thickness, surgical defects to the bone on the scalp/forehead after MMS who were treated with dHACM allografts (Epifix; MiMedx Group Inc, Marietta, GA) to facilitate timely wound bed granulation.

### **CASE SERIES**

Five elderly patients with full-thickness MMS defects to bone received weekly dHACM grafts to facilitate wound healing. Time until wound bed granulation was chosen as an endpoint, as patients

Abbreviations used:					
dHACM:	dehydrated human amnion/chorion membrane				
MMS:	Mohs micrographic surgeries				

were often released back to their referring provider at that time. For the patients who had complete epithelialization while under our care, we have included these times. After wound bed granulation, the wounds were allowed to heal via secondary intention. While using the dHACM, the graft was applied to the wound bed followed by petroleum jelly. Then, a nonstick dressing was applied with tape to cover the wound. The dressing was left in place for 1 week, and patients were instructed to keep the dressing dry during that period.

Patient demographics, wound sizes, graft application numbers, time until wound bed granulation, time until epithelialization (if known), and average reported pain over the course of treatment are delineated in Table I and Figs 1 and 2. None of the patients received preoperative or postoperative antibiotics or prescription pain medication. Patients 1, 2, 4, and 5 all had difficulty reaching their wounds and could not easily see the wound bed because of the location of the defect. Patient 2 subsequently had many squamous cell carcinomas of the scalp and is currently undergoing radiation therapy, which has slowed the healing of his wound. At the time of

From Moy, Fincher, Chipps Facial Plastics & Dermatology, Beverly Hills<sup>a</sup> and the Department of Dermatology, Harbor UCLA Medical Center, Torrance.<sup>b</sup>

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Correspondence to: Alexis B. Lyons, MD, 21 N Rodeo Dr #7, Beverly Hills, CA 90210. E-mail: alexisblyons@gmail.com.

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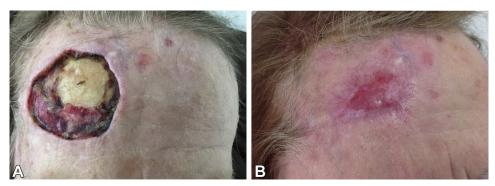
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### Table I. Patient demographics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender	М	М	F	М	М
Age	72	90	92	98	77
Comorbidities	CLL	None	HTN	Afib, CAD, HTN, CVA	Esophageal
					cancer, DM
MMS defect (cm <sup>2</sup> )	10.26	33.6	15.75	13.3	25
No. of weekly applications	4	6	4	9	7
Time until wound bed granulation (wks)	5	7	5	12	8
Time until epithelialization	7 wks	Still healing	11 wks	Still healing	21 wks
Reported pain	None	None	None	None	None

Afib, Atrial fibrillation; CAD, coronary artery disease; CLL, chronic lymphocytic leukemia; CVA, cerebrovascular accident; HTN, hypertension.



**Fig 1. A**, Patient 3 with MMS defect down to the bone. **B**, Patient 3 after 4 applications of dHACM allograft with complete healing at 2.5 months. Wound bed granulation occurred at 5 weeks.

submission of this report, his wound was still not epithelialized after 11 months.

### DISCUSSION

Elderly patients undergoing MMS with fullthickness defects exposing bone pose a unique set of healing barriers, such as increased infection risk, poor tolerance to bone chiseling for exposing pinpoint bleeding, and difficulty in reaching wounds to apply dressings successfully. The use of dHACM in patients with full-thickness MMS defects has several advantageous benefits compared with current standard of care of healing by secondary intention or methods to stimulate pinpoint bleeding like bone chiseling. One advantage is the ease of postprocedure wound care, which was appreciated by our cohort and their families. The use of dHACM allows for patients to come into the office only once per week for a dressing change with application of a new graft at that time compared with traditional healing by secondary intention, in which the wound would require daily cleansing and dressing changes and consistent attention by a caregiver or necessitates setting up home health. Another major advantage of using dHACM grafts to stimulate healing was the

paucity of postprocedure pain reported by our patients. Compared with frequent cleansing and dressing changes, which can be uncomfortable, none of our patients reported pain after dHACM allograft applications. None of our patients required narcotics, and fewer than 50% reported taking acetaminophen that we recommend to all of our post-Mohs surgery patients without contraindications. This absence of pain may be caused by the graft's antiinflammatory properties as well as the physical barrier covering nerve endings.<sup>1</sup> Third, the use of the dHACM also helps avoid invasive bone chiseling to stimulate pinpoint bleeding and subsequent granulation, as the graft contains cytokines and growth factors to facilitate healing less traumatically. In previous studies for full-thickness MMS wounds, chiseling, fenestration, or decortication of exposed bone was performed to promote granulation and allow for healing by secondary intention,<sup>2,3</sup> but this technique can be challenging for patients to tolerate.

The dHACM allograft is one of many treatment options available for full-thickness wounds. Human amniotic membrane with both amnion and chorion has been used for more than a century and has been found to promote healing, reduce localized pain,



**Fig 2. A**, Patient 5 with exposed periosteum and bone after MMS. **B**, Patient 5 after 7 applications of dHACM allograft with subsequent appropriate granulation tissue development.

provide a matrix for cellular migration and proliferation, and reduce inflammation; the dHACM also has antibacterial properties.<sup>4-7</sup> These allografts contain more than 50 cytokines and growth factors, which promote angiogenesis and specifically have been found to promote wound healing through the induction of fibroblast proliferation and upregulation of basic fibroblast growth factor, granulocyte stimulating factor, and placental growth factor biosynthesis.<sup>8,9</sup> The amnion is harvested from the placenta of healthy patients after cesarean sections and is cleaned and then dehydrated with a resultant allograft having a 5-year shelf-life.<sup>10</sup>

In several observational and randomized controlled trials, dHACM allografts were found to be superior when compared with standard wound care.<sup>10-12</sup> Most studies examined dHACM allografts primarily for the treatment of diabetic foot ulcers and venous stasis ulcers, whereas the literature for use after MMS is scant.<sup>11-13</sup> One prospective, randomized trial by Zelen et al<sup>11</sup> compared dHACM against the standard care for the treatment of diabetic foot ulcers and found that the overall healing rates at 6 weeks for dHACM allograft vs standard treatments were 92% and 8%, respectively.<sup>11</sup> Another study examining dHACM allograft with compression therapy against compression therapy alone for the treatment of venous leg ulcers found that 62% of the dHACM allograft group achieved 40% wound closure at 4 weeks, whereas only 32% of the control group achieved the same amount of closure.12 These allografts have also been used successfully in one study in the treatment of intractable pyoderma gangrenosum in which the application resulted in pain resolution and a decrease in the wound size of greater than 50% after three applications.<sup>14</sup>

In this case series, dHACM allografts were safe and well tolerated with no complications in elderly patients with full-thickness MMS defects for whom surgical repairs were declined or not possible and for whom daily or twice-daily wound care was challenging. All of our patients reported no pain after dHACM allograft application. Further studies are needed to compare the length of time for total resolution of full-thickness MMS defects to the bone using dHACM allografts versus secondary intention alone to determine if their use results in a significantly decreased healing time.

#### REFERENCES

- Hao Y, Ma DH, Hwang DG, Kim WS, Zhang F. Identification of antiangiogenic and anti-inflammatory proteins in human amniotic membrane. *Cornea*. 2000;19:348-352.
- Vanderveen EE, Stoner JG, Swanson NA. Chiseling of exposed bone to stimulate granulation tissue after Mohs surgery. J Dermatol Surg Oncol. 1983;9:925-928.
- Snow SN, Stiff MA, Bullen R, et al. Second-intention healing of exposed facial-scalp bone after Mohs surgery for skin cancer: review of ninety-one cases. J Am Acad Dermatol. 1994;31(3 pt 1):450-454.
- Mermet I, Pottier N, Sainhillier JM, et al. Use of amniotic membrane transplantation in the treatment of venous leg ulcers. Wound Repair Regen. 2007;15:459-464.
- Cornwell KG, Landsman A, James KS. Extracellular matrix biomaterials for soft tissue repair. *Clin Podiatr Med Surg.* 2009;26:507-523.
- 6. Talmi Y, Sigler U, Inge E, Finkelstein Y, Zohar Y. Antibacterial properties of human amniotic membranes. *Placenta*. 1991;12: 285-288.
- Fetterolf D, Istwan N, Stanziano G. An evaluation of healing metrics associated with commonly used advanced wound care products for the treatment of chronic diabetic foot ulcers. *Manag Care*. 2014;23:31-38.
- Koob TJ, Lim JJ, Masee M, Zabek N, Denoziere G. Properties of dehydrated human amnion/chorion composite grafts: Implications for wound repair and soft tissue regeneration. *J Biomed Mater Res B.* 2014;102(6):1353-1362.

- Koob TJ, Limm JJ, Massee M, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: therapeutic potential for soft tissue repair and regeneration. *Vasc Cell*. 2014;6:10.
- Zelen CM, Snyder RJ, Serena TE, Li WW. The use of human amnion/chorion membrane in the clinical setting for lower extremity repair: a review. *Clin Podiatr Med Surg.* 2015;32:135-146.
- Zelen CM, Serena TE, Denoziere G, Fetterolf DE. A prospective randomized comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. *Int Wound J.* 2013;10(5):502-507.
- 12. Serena TE, Carter MJ, Lam LT, Sabo MJ, DiMarco DT. A multicenter, randomized controlled clinical trial evaluating

the use of dehydrated human amnion/chorion membrane allografts and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. *Wound Repair Regen.* 2014;22:688-693.

- Park KK, Hagstrom E, Berrios R, Tung RC. A novel purse-string suture and dehydrated human amnion/chorion membrane allograft closure technique for the repair of defects following Mohs micrographic and excisional surgery. J Clin Invest Dermatol. 2016;4(1):3.
- 14. Snyder RJ, Ead J, Glick B, Cuffy C. Dehydrated human amnion/chorion membrane as adjunctive therapy in the multidisciplinary treatment of pyoderma gangrenosum: a case report. *Ostomy Wound Manage*. 2015;61:40-49.