Clinical Experience

Using Dehydrated Human Amnion/Chorion Membrane Allografts for Acute and Reconstructive Burn Care

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Abstract: Amniotic membrane is immunologically privileged and is a reservoir of growth factors and cytokines known to modulate inflammation and enhance the healing process, while also possessing antimicrobial, anti-fibrosis, and anti-scarring properties. These properties establish a strong argument for using amniotic membrane derived products as a treatment for burns. The purpose of this article is to describe the use of commercially available dehydrated human amnion/chorion membrane allografts in patients with partial-thickness and full-thickness burns.

Key Words: amniotic membrane, dehydrated human amnion/chorion membrane, full-thickness burns, partial-thickness burns

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H uman amniotic membrane is a reproductive tissue composed of both amnion and chorion that holds the amniotic fluid which protects the fetus in the uterus. The amniotic membrane is immunologically privileged and is a reservoir of growth factors and cytokines known to modulate inflammation and enhance the healing process, while also possessing anti-microbial, anti-fibrosis, and anti-scarring properties.1 If the premise of using products derived from human amniotic membrane is to stimulate native cytokines to heal a wound, then what better population than the burn injured patient to foster the art of scarless healing.

During a 10-year period between 2006 and 2015, over three quarters of patients admitted to North American Burn Centers had a burn size under 10% total body surface area. Ninety percent of admitted patients had a burn surface area of 20% or less, and only 2% of cases had a total surface burn area greater than 50%. There is an abundance of data collected and collated on burn center inpatients, yet approximately 75% of patients with burns are never actually admitted, but are treated as an outpatient—whether full-thickness or partial-thickness skin injury exists.3 This is the ideal population in which to maximize quick times to healing thus minimizing pain, social disruption, and long-term scar consequences. However, neither total percent body surface area burned nor the age of the patient should be considered an exclusion for use of amniotic membrane products.

Using amniotic membrane to cover and treat wounds has been reported in the literature for over a century, though obstacles including obtaining and storing the membrane and the potential for disease transmission preclude its use in native form.4 Dehydrated human amnion/chorion membrane (dHACM) allografts (EpiFix, AmnioFix, EpiBurn; MiMedx Group Inc., Marietta, Ga) eliminates the obstacles associated with use of fresh amniotic membrane. The dHACM allograft is created through a proprietary PURION Process that gently washes the membranes to reduce bioburden with minimal manipulation while maintaining structural integrity of the tissue. The dehydrated allograft, available in both multiple sized sheet and micronized configurations, allows for off-the-shelf use for a number of clinical applications for homologous use. Growth factors, cytokines, and chemokines that enhance healing remain in PURION Processed dHACM allografts5,6 which have been shown to be effective in the treatment of many types of wounds.7–9 The purpose of this article is to describe the use of dHACM in patients with partial-thickness and full-thickness burns.

METHODS

Using Amniotic Membrane Allografts for Treatment of Partial-Thickness Burns

Areas, such as the hands and faces, seem to be ideal surface areas for treatment with amniotic membrane allografts, such as dHACM, for cosmesis as well as return to function.10 Debriding all eschar down to a bleeding viable dermal layer is basic to any start of burn care. When dermal elements sufficient to heal a burn are present (as determined clinically or by histologic analysis) then initially grafting with an amniotic membrane allograft may help to stimulate cytokine migration into the wound, stimulate cell proliferation, and speed the time to wound reepithelialization. In cosmetic areas of the face and hands, the various sizes of the dHACM allograft available are ideal for application. Larger dHACM grafts can easily cover nearly an entire face of a child, the forehead and nose/forehead of an adult or the midface nose and cheeks. The graft is applied as a sheet or piecemeal to cover the areas where wound healing is desired. It is protected for several days with moist retaining dressings and changed only as needed for exudate control. In many cases, the dHACM will adhere to the wound and be visible for several dressing changes. It is not removed and only gently cleansed and redressed. In cases where there is a higher exudate, the dHACM may “melt” into the wound bed quicker but care should be taken not to aggressively wash/debride the wound for several days until cytokine release is completed. Follow-up wound care is again gentle with dressings not known to impair keratinocyte activity (eg, avoid topical antibiotics and cleansers known to be more cytotoxic to multiple cell types).

Deeper partial-thickness wounds also should be considered for staged dHACM treatment. Deeper dermal injuries benefit from tangential excision of the eschar which then allows for topical wound care treatments to directly affect the residual dermal elements. Placing
dHACM on these wounds may affect wound healing to a complete degree or may stimulate the wound bed with angiogenesis so that a subsequent split thickness (perhaps even a thin graft) can be applied. Again, by stimulating the initial cytokine response to injury, the final scar outcome is felt to be superior to 1-stage excision and grafting.

Using Amniotic Membrane Allografts for Treatment of Full-Thickness Burns

Full-thickness burns larger than 1% total body surface area are traditionally considered for grafting. Using a staged technique, dHACM may be applied at the time of excision to truly viable deep tissues. Underlying subcutaneous or muscle tissue retains enough vascularity for incorporation of the allograft tissue and benefit from the release of mediators of wound healing into the excised areas. This may take more than 1 debridement depending on the mechanism of injury (chemical or electrical). Once the wound bed is free of necrotic tissue and has adequate vascularity, an autograft can be applied—“take” of this graft is not impeded by the preapplication of dHACM.

Amniotic membrane allograft, such as dHACM, is not indicated as the sole treatment option for burn wounds that are full thickness to subcutaneous tissue or deeper structures. These wounds need coverage with autologous tissue. The dHACM tissue can be used as a bridge between debridement and the formation of an adequately vascularized tissue bed for engraftment.

Using Amniotic Membrane Allografts for Treatment of Other Types of Thermal Injury

Frostbite Thermal Injuries

This patient population is unique in that the depth of the injury is not often known. Factors, such as temperature and humidity, may affect how densely the tissues are frozen and damaged. Initial treatment of the wounds is conservative, allowing ample time for “demarcation” of the truly devitalized tissues. When gentle debridement is indicated, the exposed tissues are prone to desiccation if not treated with moist wound care. As the underlying vascularity is compromised, all wound care treatments seek to optimize and promote angiogenesis. Serial applications of amnion on appropriately debrided wounds can help achieve healing and decrease level of amputations. Although there is no current literature available on PubMed regarding the use of amniotic membrane allografts in cold thermal injury, this author (D.A.R.) has preliminary experience showing the positive influence of amniotic tissue topical treatment on debrided frostbite toe injuries.

Corneal Grafts

The cornea is often injured in severe facial burns. The sequelae of an ocular burn can be severe and particularly challenging to manage including significant decrease in visual acuity. Amniotic membrane transplantation may stop ulceration and promote corneal epithelialization in the majority of patients with the most severe chemical or thermal eye injuries.11 The cornea is also sloughed in patients suffering from toxic epidermal necrolysis. In both cases, the loss of the protective squamous cell covering of the eye leads to excess scarring and the future early need for cataract intervention surgery. Amniotic membrane has long been used as a topical wound covering to restore corneal epithelial integrity in eyes with both corneal and conjunctival ulceration.12,13 Although healing may still take up to 24 days to complete, final visual acuity is better in patients who have had corneal protection during the healing phase.

Tissue Rearrangement and Flap Reconstruction

Difficult wound beds, to include those with exposed deep structures, such as bone/joint/tendon/vessels, are often covered with a variety of soft tissue flaps. These flaps can be simple advancement of local tissues, regional rotation of similar tissues, or the free tissue transfer of remote tissues. Even the most robust flap however is not successful unless the underlying wound bed is free of infection/necrosis and is adequately vascularized. Amniotic membrane has been described in the single-stage closure of neural tube birth defects under pedicle flaps.14 Its presumptive mechanism of action is again to stimulate angiogenesis and enhance the “take” of the flap.15,16

Extrapolating to other types of wounds, it is conceptually easy to engineer composite tissue reconstruction techniques starting with amniotic tissue allografts over the wound bed with a well-vascularized 3-dimensional soft tissue overlay.

CLINICAL CASES TREATED WITH DEHYDRATED HUMAN AMNION/CHORION MEMBRANE (dHACM) ALLOGRAFTS (EpiBurn)

Examples of hand burns treated with dHACM (EpiBurn)

CASE 1

Patient D is a 67 year old left hand dominant female who experienced a scalding injury to her left (L) hand, primarily the first digit, dorsal aspect, caused by exposure to hot grease. She was initially seen in her local hospital emergency department and treated with conservative care, including use of Silvadene topically. She was referred to our outpatient burn clinic for follow-up care. Her medical history included hypothyroidism, GERD, hypercholesterolism, and asthma (Fig. 1). Important surgical procedures include subtotal thyroidectomy, mastectomy, and hysterectomy. She was taking multiple medications and was allergic to sulfonamide drugs. When seen for her first burn clinic visit, she was noted to have a less than 1% surface area mixed depth partial-thickness (deep and superficial) burn to her left hand, located on the volar proximal palm, thenar surface, and first digit distally. There was no evidence of infection. Portions of the wound blanched and were moist. A significant central area of the wound was observed to be pale and to have decreased sensation.

Treatment

The wound was cleaned with saline, and the first EpiBurn graft was applied and covered with Adaptic and a dry sterile dressing (DSD). Total graft size applied was 9 × 3 cm. The patient was instructed to keep the dressing in place for 48 hours, then start daily dressings with Adaptic and DSD. When seen at the first follow-up visit 1 week later, significant evidence of healing was observed with the only remaining open area present over the dorsum of the first digit. A second application of EpiBurn, identical to the first, with similar instructions, was performed.

Follow-Up

Her third burn clinic visit occurred 8 days later. At this visit, the burn was 99% healed, remained hyperemic, and a full range of motion of the hand and fingers was noted.

CASE 2

Patient M is a 30-year-old right (R) hand-dominant man with no significant medical history. He presented after burning his R hand, spilling butter and boiling water on it. He went to a local hospital where the burn was debrided and dressed. He was discharged and referred to our outpatient burn clinic for follow-up care. He presented to the burn service and was admitted for treatment (discharged 2 days later) (Fig. 2).

Follow-Up

At this time, he reported numbness to the dorsum of the thumb and mild pain, particularly along the palmar aspect. Examination revealed a 1.5% surface area deep second degree burn to the dorsum of the hand along the lateral aspect. In addition, a superficial burn was noted on the palmar aspect of the hand. The wound was treated with Santyl and DSD, and this was to be continued as an outpatient.

Five days after discharge, he was seen for his first burn clinic visit. Areas of superficial second and a larger central area of deep second-degree burn were noted. Some blanching and decreased sensation to light touch were described. There was no evidence of infection. An initial application of a 7 × 15 cm EpiBurn graft was made, and the wound dressed with Adaptic and DSD. The dressing was to be left on for 48 hours, to be followed by daily dressing changes with Adaptic and DSD.

The patient was seen again 4 days later for a second EpiBurn application. At this visit, a total of 6 × 15 cm was used for the graft and dressing orders were identical to the previous visit.

Follow-Up

By the third clinic visit, 1 week after the second EpiBurn application, the burn was almost completely healed. Again, the wound was cleaned, EpiBurn applied (5 × 5 cm sheet), and the wound dressed, with daily Santyl to be added after 48 hours after EpiBurn integrated. Ten

FIGURE 2. Case 2: A 30-year-old man with scald burn to R hand. A, First ED visit. B, First EpiBurn application in outpatient burn clinic at 5 days posthospital discharge. C, Second EpiBurn application. 9 days postdischarge. D, Third EpiBurn application. 7 days later. E, Healed at fourth outpatient clinic visit, 10 days later. F, Final clinic visit—full ROM.

days later, the burn had healed with 1 small area of unstable scar remaining; this had healed over to form a scab within 30 days. The patient had a full ROM of the hand at this last visit.

CASE 3

Patient T is a 24-year-old R hand dominant man who was installing AstroTurf at work using a hot adhesive. A significant amount of this adhesive made contact with his R hand. He presented immediately to a local hospital where some of the glue was removed with mineral oil. He was subsequently transferred to our burn service for burn management (Fig. 3).

Treatment

He was initially seen in the emergency department, and it was noted that his R hand had a deep second-degree burn involving 1% of his surface area. It was covered in adhesive. There were strong radial and ulnar pulses, and some areas of blanching were observed. The injury was relatively painless to touch. He was treated with debridement, Bacitracin, Adaptic, and DSD, to be applied daily with outpatient follow-up.

Four days later, the patient was seen in the burn clinic. The R hand and fingers were noted to have a deep partial-thickness burn, with edema, erythema on the dorsum of the hand, sluggish blanching, and decreased sensation. The overall appearance was cherry red. The wound was cleaned with saline and gauze and a 7 x 15 cm sheet of EpiBurn applied. It was covered with Adaptic and DSD, to be kept in place until the next visit in 3 days.

At the return visit 3 days later, the burn was starting to heal, though areas of superficial and deep partial-thickness injury were still present. The erythema was improved. The wound was again cleaned, and a 6 x 10 cm EpiBurn graft was applied, with a similar dressing. Instructions were to leave this in place for 48 hours, then begin daily washing and applications of Santyl and Adaptic with DSD.

Follow-Up

By a visit 5 days later, the wound continued to improve, though some areas of adherent fibrinous exudate remained. The cellulitis was completely resolved 2 days after EpiBurn. Daily dressing changes with Santyl were continued. By the fourth clinic visit 8 days later, the wound was 90% healed and was completely healed by the fifth visit 4 days later. Long-term follow-up results were considered very satisfactory.


CASE 4

Patient M is a 55 year old male with hypothyroidism and hypercholesterolemia who was at work drilling into a fuel tank when the tank caught on fire. He sustained a flash burn from the flame to the left side of his face and a contact fuel burn to his left hand. He was then brought promptly to our burn center (Fig. 4).

Treatment

Examination in the emergency department revealed areas of superficial and deep second-degree burns to the dorsum of the hand and a not-yet debrided burn blister. The deep second-degree burn area appeared white, pale, dry, and nonblanching. No surrounding erythema or infection was noted. The wound was debrided and cleaned with sterile saline and a DSD with bacitracin and Adaptic was applied. The patient was referred to the wound care clinic.

The patient was seen for his first wound care visit 4 days later. At that visit, no surrounding erythema or infection was observed. The burn had a cherry red appearance. It was still described as a mixed depth wound with areas of blanching and some areas of nonblanching. The first EpiBurn graft, a 7 x 15 cm sheet, was applied and covered with Adaptic and DSD. The patient was instructed to keep the dressing in place for 48 hours, then wash hand with soap and water, and continue daily bacitracin, Adaptic, and DSD. He returned for a second visit 3 days later. Significant reepithelialization was noted, the patient’s wound was again cleaned and a second EpiBurn graft, 5 x 5 cm, was applied with similar directions for postapplication care.

Follow-Up

Eight days later, the wound was mostly healed, with only small open areas remaining. Adaptic and DSD were continued. Six days later, the burn was completely healed, with only small residual scabs remaining, and the hand had a full range of motion.

CASE 5

A 33-year-old man with electrical injury to both hands, with fourth degree injury to left first web and thumb (Fig. 5).

Treatment

Although other wounds were healing, serial debridement was performed on the hand wound. EpiFix was applied to protect the wound
and enhance healing on an interim basis to foster healing until a split-thickness skin graft could be applied.

Follow-Up

Full healing was achieved with limited first web space total active motion. Adjunctive occupations therapy splinting and scar massage adjunctive resulted in limited help with ROM, but scar remained stable.

Examples of Burns of the Genitalia Treated With dHACM

CASE 6

A 14-year-old boy spilled hot noodles in his lap resulting in deep partial-thickness burns of his suprapubic area, penis, and scrotum (Fig. 6).

Treatment

The EpiBurn allograft was applied to penile burns in the OR on postburn day 2. Dermabond was also used. Dressing changes were conducted daily with xeroform and DSD.

Follow-Up

Full healing occurred by day 10. No scarring was observed in EpiBurn-treated areas.

CASE 7

A small child mistreated by dipping his lower extremities and pelvis in boiling water; extensive burns including penile burns were incurred (Fig. 7).


Treatment
His penis and scrotum were treated with EpiBurn (dHACM) to cover and assist in the healing process.

Follow-Up
In the final image, the patient had good healing and preserved function. This represents a successful use of a dHACM in lieu of skin graft.

Examples of Facial Burns Treated With dHACM

CASE 8
This 12-year-old boy sustained second-degree burns to the face, neck, chest, and upper extremities from a blast of an aerosol can in a bonfire. Facial swelling required intubation for 6 days until resolution of swelling relieved airway compromise (Fig. 8).

Treatment
Management of the facial burns included removal of superficial damaged tissue. Allograft was applied to the forehead, midface, and lower face, and dHACM was used to cover the eyelids within the orbital contours.

Follow-Up
Three months after discharge, all areas of the facial injury were healed without complication.

CASE 9
A 28-year-old white woman with facial burn injuries from a motor vehicle accident (Fig. 9).

Treatment
Skin grafting was recommended to the patient, but she refused. Local wound care was provided for 3 weeks, yet the wound failed to heal. After 4 weeks of local wound care, she continued to refuse split-thickness skin grafting (STSG), but allowed for debridement and application of the EpiFix allograft.

Follow-Up
Facial wounds went on to heal with mild hypertrophic scarring, but without itch or pain. At 6-month follow-up, she continued to use a silicone compression mask 8 hours per day.

CASE 10
A 28-year-old man with facial burns from a workplace explosion (Fig. 10).


Treatment

After light abrasion in the operating room, an EpiFix allograft sheet was applied to his forehead and a second allograft sheet was trimmed to fit nose and cheek wounds. Petroleum dressings were changed every other day until healed at 2 weeks. After petroleum dressings were discontinued, he continued to treat the healed areas with lotion.

Follow-Up

After 7 months, there was minimal hypertrophic scar on dorsum of nose.

CONCLUSIONS

The treatment goal when using an amniotic membrane allograft, such as dHACM (EpiBurn or EpiFix), is to protect the wound while promoting vascular angiogenesis and healing. Always looking to the ideal of how we can enhance the speed at which a wound achieves successful closure, thus limiting the inflammatory process that otherwise inhibits healing and leads to excess scar formation, allografts with bioactive properties such as dHACM present an exciting opportunity for the treatment of burns in either the inpatient or outpatient setting.

The dHACM allograft is available in a variety of forms and sizes for homologous use, including sheet, mesh, particulate and powder, which can be suspended in saline for injection. For each of these formulations, there is an endless opportunity to place these products into or onto wounds under standard wound coverings. The clinician can choose the appropriate form and size of allograft according to the individual needs of the patient and wound characteristics while minimizing waste of graft material. The PURION Process gently cleanses and washes the amniotic membrane tissue to reduce bioburden with minimal manipulation while maintaining structural integrity of the tissue, results in a commercially available dHACM allograft with a 5-year shelf life under ambient conditions. Screening and testing of placenta donors and terminat sterilization of the allograft helps to ensure added safety.

The cases presented illustrate our experience in using the amniotic membrane product dHACM to treat partial-thickness and full-thickness burns of the hand, genitalia and face, yet its use is not limited solely to those types of injuries. The dHACM allograft allows for contemporary use of a tissue recognized for centuries as having protective and healing properties.

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