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Unique Usages of Dehydrated Human Amnion Chorion Membrane Allografts in Dermatology

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ABSTRACT

Dehydrated human amnion chorion membrane (dHACM) allografts are synthetic skin substitutes derived from placental tissue. dHACM allografts are used for replacing lost or damaged dermal tissue, as they contain many of the components found within the extracellular matrix that are beneficial in wound healing. Common uses of dHACM allografts include the healing of diabetic and non-diabetic foot and leg ulcers, decubitus ulcers, and wounds following debridement. While these grafts have been proven to be beneficial in other disciplines of medicine, their potential for use in the field of dermatology is emerging.

Current clinical cases and research have shown dHACM allografts to be beneficial in repairing damaged tissue due to dermatologic conditions. They could play a role in the treatment of conditions causing chronic wounds, including dermal scarring or loss, and the repair of fragile skin. Examples of dHACM allograft use in dermatology include cases of pyoderma gangrenosum, Netherton syndrome, and wound healing with Mohs micrographic surgery. This literature review explores the efficacy of using dHACM allografts for the treatment of healing wounds within the field of dermatology.

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INTRODUCTION

Dehydrated human amnion chorion membrane (dHACM) allografts, such as EpiFix and AmnioFix among others, are synthetic skin substitutes derived from placental tissue. Comprised of an epithelial layer and 2 fibrous connective tissue layers, dHACM allografts function to repair lost or damaged dermal tissue. Healthy dermal tissue typically contains the extracellular matrix (ECM), which is made up of collagen, fibroblasts, proteoglycans, elastin, hyaluronic acid, fibronectin, and other components, all of which play a role in wound healing. dHACM allografts, derived from sterilized and dehydrated placental tissue, contain many of the components found in the ECM of the dermis, which makes them beneficial for wound healing.[1]

dHACM allografts are harvested from donors following cesarean section and thoroughly screened for infectious or viral diseases. They are comprised of 3 layers, the amnion, the chorion, and the intermediate layer separating the 2. The amnion, the side typically facing the fetus, is comprised of an epithelial layer with a fibroblast layer that contains types I and III collagen, contributing to the tissue's strength.[2] The amnion also contains other components of the ECM, including laminin and fibronectin, which contribute to the stroma and basement membrane.[2] The intermediate layer separates the amnion from the chorion and contains many nutrients such as glycoproteins. Lastly, the chorion layer, the side that contacts maternal tissue, is comprised of multiple layers that contribute to both the strength of the tissue and have nutrients that promote cell growth.[3] Altogether, the amniotic membrane consists of an epithelial layer and 2 fibrous connective tissue layers that contain important components of the ECM including fibroblast growth factor, platelet-derived growth factor, transforming growth factor-beta 1, and multiple interleukins. These components contribute to the wound healing properties of the human amnion chorion membrane.

dHACM allografts have been shown to improve the healing of tissue of the skin, cornea, ligaments, and periodontal tissue, among others. Common uses of dHACM allografts include the healing of diabetic and non-diabetic foot and leg ulcers, decubitus ulcers, and wounds following debridement. Patients receiving dHACM allografts for chronic leg ulcers due to venous insufficiency or diabetic nervous system degeneration tend to have poor circulation. This lack of blood flow leads to decreased delivery of nutrients required for wound healing, increased scarring of tissue, and increased risk of infection.

Multiple studies have shown that dHACM allografts are superior to standard treatment of chronic wounds, including regular debridement, compression stocking and bandages, and regular dressing changes. One randomized controlled trial evaluating the use of the standard of care with or without dHACM allograft application for diabetic foot ulcers showed that 92% of patients with dHACM allograft application reported fully healed ulcers after 6 weeks, while only 8% of patients who did not receive dHACM allografts reported healing after 6 weeks.[4] Additionally, patients receiving dHACM allografts experienced significantly faster healing time and a 0% recurrence rate with 12 months of follow-up.[4] In addition to decreased time of wound healing, the use of dHACM allografts has been shown to decrease the pain associated with leg ulcers, as dHACM allografts contain anti-inflammatory properties.[5]

Another study comparing the application of dHACM allografts to compression therapy and leg elevation for the treatment of venous stasis ulcers showed significantly greater wound closure for patients receiving dHACM allografts.[6] In this study, 62% of patients receiving dHACM allografts versus 32% of patients treated conservatively with compression stockings experienced 40% wound closure 1 month following the initiation of treatment.[6] In addition to the use of dHACM allografts for skin ulcers, specialties such as ophthalmology have used these allografts for cornea repair, and orthopedic surgery has shown the benefits of using dHACM allografts for the repair of poorly vascularized tissue, such as tendons, ligaments, and cartilage.[6,7] The antimicrobial and anti-inflammatory nature of amniotic tissue has led to decreased scar tissue formation and decreased pain following tissue repair in orthopedic surgery.[7]

Multiple cases reporting the benefit of using dHACM allografts for healing dermatologic conditions exist; however, there is no comprehensive literature addressing the use of dHACM allografts within dermatology. The goal of this paper is to review the literature and state dermatologic conditions that could benefit from the application of dHACM allografts.

MATERIALS AND METHODS

Two reviewers independently searched PubMed and MEDLINE using the terms "dehydrated human amnion chorion membrane allograft" and "dermatology" for published articles and found 7 articles from the years 2015 to 2021, as no articles pertaining to this topic were published prior to 2015. Of the original 7 articles, 2 articles were excluded, as they did not address the use of dHACM allografts for the treatment of specific dermatologic conditions. Five articles were included, and 4 of the 5 are included in Table 1, as they addressed the use of dHACM allografts for the treatment of unique dermatologic conditions. One article was included in this manuscript, but not included in the table, as it addresses the function of dHACM allografts. Additionally, the *JAAD Case Reports* database was searched using the term "dehydrated human amnion chorion membrane allograft," and 3 additional cases, not found on PubMed, addressing dHACM use for healing dermatologic conditions were included. A total of 7 articles pertaining to dHACM allograft use for the treatment of dermatologic conditions are included in Table 1. No articles containing negative results, in which the treatment of dHACM allografts for healing chronic wounds failed, were found. After a search was completed, the 7 articles were analyzed for unique dermatologic conditions successfully treated with dHACM allografts. The main parameters were study design, anatomical location of condition, type of dermatologic condition treated, number of patients treated, and response to treatment.

TABLE 1.

Research Articles Addressing Dermatologic Conditions Successfully Treated With dHACM Allografts

First Author	Year of Publication	Type of Study	Anatomic Location	Condition Treated	# of Patients	Time to Re-epithelialization
Kempton[9]	2018	Case Report	Scalp	Erosive Pustular Dermatosis, superimposed on Lamellar Ichthyosis	1	12 weeks
Lyons[10]	2018	Case Series	Scalp	Full-thickness defects following Mohs micrographic surgery	5	7, 11, and 21 weeks 2 patients still healing at time of reporting
Wisco[11]	2016	Case Series	Lower eyelid	Eyelid defects following Mohs micrographic surgery	3	6.5, 2, and 2.5 weeks
Bacik[12]	2018	Case Report	Lower face and neck	Ulcerated Hemangioma	1	5 weeks
Snyder[13]	2015	Case Report	Leg	Pyoderma Gangrenosum	1	8 weeks
Frigerio[14]	2019	Case Report	Scalp, trunk, extremities	Netherton Syndrome	1	2.6 weeks
Toman[8]	2022	Retrospective Case-Control Study	Face, head, and neck	Defects following Mohs micrographic surgery	143	4.4 weeks

RESULTS

Results of our literature review showed that multiple dermatologic conditions could benefit from the use of dHACM allografts for wound treatment. One retrospective case control study reporting the efficacy of treating skin defects following Mohs micrographic surgery (MMS) found treatment of defects with dHACM allograft led to significantly lower risk of infection (P=0.004), improved scar cosmesis (P<0.0001), lower rates of scar revision (P<0.0001), and less reoperation (P=0.0007) as compared to patients who received repair using autologous tissue.[8] MMS of the scalp, lower eyelids, and other locations on the head and neck also resulted in improved wound healing following dHACM allograft treatment.[10,11] The treatment of full thickness scalp and forehead defects with exposed calvarium in 5 patients following MMS with dHACM allograft repair showed improved healing time, preferable cosmetic results, and decreased pain as compared to healing via secondary intention.[10]

In a case of pyoderma gangrenosum refractory to 3 months of immunosuppression and wound care, the application of dHACM allografts showed promising results with a decrease in wound size by more than half within 2 months, a decrease in pain by half within hours of application, and a complete absence of pain within 4 days.[13] Another favorable result from the application of dHACM allograft was observed among a patient with a 7-year history of erosive pustular dermatosis superimposed on lamella ichthyosis, refractory to antibiotics, antifungals, intralesional corticosteroid, and antihistamines.[9] Within 12 weeks of dHACM allograft application, the lesion had completely healed with no recurrence at five month follow-up.[9] While no comprehensive literature exists, multiple case studies and case series have reported dHACM allografts to be successful in treating wounds caused by erosive pustular dermatosis, pyoderma gangrenosum, ulcerated hemangioma, Netherton syndrome, and defects following MMS. Table 1 includes a comprehensive list of unique dermatologic conditions successfully treated with dHACM allografts.

DISCUSSION

dHACM allografts are beneficial as wound healing adjuncts for both acute and chronic wounds in dermatology. Acute wounds induced via MMS have shown promising results in terms of healing with the application of dHACM allografts. Patients and families report increased ease of post-operative wound care, as dHACM allografts require once weekly dressing changes, while standard wound dressings require daily changes. This advantage is multiplied when it comes to wounds located in difficult to reach or see places such as the head, neck, and back. Additionally, as patients receiving MMS are typically of older age, ease of wound care is particularly important for both patients and their caregivers.

dHACM allografts could also play a role in the treatment of conditions causing chronic wounds, including dermal scarring or loss and the repair of fragile skin. Cases reporting successful treatment of chronic wounds on an infant with Netherton syndrome with subsequent protein and electrolyte loss due to skin fragility, and an infant with a chronically ulcerated hemangioma of the chin and neck refractory to propranolol, suggest the use of dHACM for the treatment of refractory skin conditions due to fragility.[12,14] As early treatment of infantile hemangiomas is vital to stop further progression and reduce the risk of ulceration and infection, dHACM should be considered early in refractory infantile hemangiomas.[12] The success of dHACM allografts in treating refractory pyoderma gangrenosum and erosive pustular dermatosis also demonstrates its ability to aid in the healing of chronic wounds.

While dHACM allografts are effective for the treatment of both dermatologic and non-dermatologic conditions, limitations in regard to the cost of treatment exist. Currently, amniotic membrane grafts remain expensive and range in price from US $2000 to $10 000.[15] In the study by Zelen et al, the average cost of application of allografting was US $2798.[4,16] It has been suggested that further studies are warranted regarding quality of life after treatment to justify use of the expensive biomaterials.[16] However, in the management of diabetic foot ulcers, dHACM usage in a cohort of Medicare patients was cost-effective by reducing major amputations, emergency department visits, inpatient admissions, and readmissions.[17] The cost of dermatologic conditions could potentially decrease with the use of dHACM allografts by avoiding further medical expenses, especially in the setting of chronic or refractory disease.

This article highlights the importance of considering the use of dHACM allografts for the treatment of multiple dermatologic conditions. dHACM allografts have been shown to decrease the time of wound healing, decrease pain involved with wounds, improve the convenience of dressing wounds, decrease the risk of infection, and heal lesions refractory to standardized therapy. Conditions described in this paper as well as other dermatologic conditions causing both acute and chronic wounds could benefit from the use of dHACM allografts in everyday clinical practice.

DISCLOSURES

The authors have no conflicts of interest to declare.

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