Use of a Permanent Acellular Dermal Allograft in Recessive Dystrophic Epidermolysis Bullosa Involving the Hands

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RECESSIVE DYSTROPHIC epidermolysis bullosa (RDEB) is characterized by blistering and scarring of the skin and mucous membranes. The hands are particularly vulnerable because of the contact and shearing forces of normal daily activity.

REPORT OF A CASE

An 11-year-old white boy presented with RDEB and extensive epidermal scarring around the hand that caused restrictive adduction of the thumbs and pseudosyndactyly. Repeated cycles of blistering and scarring resulted in gradual encasement of the hand in an epidermal “cocoon” (Figure 1). Functional impairments included loss of fine motor manipulation of objects commensurate with the loss of digital prehension.

THERAPEUTIC CHALLENGE

Our goal was to relieve the scar contractures associated with the epidermal encasement of the hand in a patient with RDEB, while minimizing donor site morbidity and graft hypertrophy.

SOLUTION

We used a permanent dermal transplant that was developed for full-thickness burn wounds (AlloDerm; LifeCell Corp, The Woodlands, Tex). Fresh human cadaveric allograft skin was procured from tissue banks following donor and serological screening in accordance with guidelines of the American Association of Tissue Banks and the Food and Drug Administration. Skin was transported, on ice, overnight in Rosewell Park Memorial Institute (RPMI) 1640 medium supplemented with antibiotics. The skin was then aseptically processed to remove the epidermal, fibroblast, and endothelial cells that are the targets for immune response, leaving a structurally intact (ie, retaining elastin, proteoglycans, and the basement membrane complex), freeze-dried, acellular, dermal allograft.

Preparation of Acellular Dermal Allograft

The permanent dermal transplant package was opened in the operating room, and the freeze-dried dermal matrix was washed twice in a minimum of 100 mL of lactated Ringer solution at room temperature and then rehydrated in 100 mL of normal saline solution or lactated Ringer solution for 10 minutes before application.

Surgical Procedure

The objective of the hand reconstruction in patients with RDEB is usually to reestablish elementary pinch and grasp. Accordingly, the highest priority was given to releasing the adduction contracture of the thumb (Figure 1). The thumb adduction contracture involves dermal and subdermal fibrosis, myofascial fibrosis, and shortening of the adductor pollicis and first dorsal interosseous muscles. Epithelial removal, as in “de-cocooning,” does not begin to correct the basic functional problems, which are deep fibrosis and scarring.

Figure 1. Characteristic thumb adduction contracture along with epidermal “cocoon” and pseudosyndactyly.
A complete release of the thumb contracture was accomplished by a generous incision extending from the base of the web at the level of the carpometacarpal joint dorsally, across the web to course volarly on the palm. To maintain abduction during the period of skin graft healing, skeletal stabilization of the thumb was performed by placement of nonparallel Kirschner wires between the first and second metacarpal bones. The allograft was applied. A 150-µm split-thickness skin graft was harvested from the anterior area of the thigh, which was free of blistering, and sewn into place with 6-0 ophthalmic catgut (Figure 2). The thigh donor site was covered with a single layer of scarlet red. A circumferential noncompressive dressing of cotton batting was placed around the hand, followed by volar and dorsal splints for immobilization.

After 1 week, the dressings were removed with the patient under a short general anesthetic (Figure 3). The Kirschner wires were removed at 4 weeks. An orthoplast splint was used to hold the thumb abducted and the fingers separated. An active range of motion exercises were then encouraged. Passive exercises were avoided for fear of frictional trauma. The patient was gradually weaned from the splint during waking hours. Night splinting was continued for several months.

There was 100% acceptance of the dermal allograft and epidermal autograft. The donor site reepithelialized within 4 days of surgery. The patient was gradually weaned from the splint over several months. A survey of the patient and parents at 6 weeks and 6 months after surgery indicated a high degree of satisfaction. They were particularly pleased with the virtual absence of donor site morbidity and the overall improvement in cosmesis and function (Figure 3).

**COMMENT**

A variety of operative approaches have been used to deal with the hands of children with RDEB, including the use of split-thickness autograft, human allografts, cross-linked porcine skin, and human cultured epithelial cells.6-10 These treatments cannot provide a permanent, durable dermal replacement, as they are rejected, do not revascularize, or do not withstand normal wear and tear. Cadaveric human allograft skin has proved effective as a short-term solution in massively burned patients.11 However, its use has not been documented in patients with RDEB. The most immunogenic components of transplanted allograft skin are the cellular elements of the epidermis and dermis. Thus, an allograft may vascularize within 3 days, but it is subsequently rejected in 2 or 3 weeks.

Acellular bone grafts have been routinely used in oral and orthopedic surgery for several years, lending credence to the claim that such tissues will maintain their structural integrity over time.12-14 In the skin, the epidermis contains most of the immunogenic components. If it is removed along with dermal cells, the remaining noncellular dermal tissue is relatively inert immunologically. Acellular dermal allografts may serve as a scaffold for ingrowth of host cellular elements, resulting in a normally organized tissue.15 Similarly, the use of allogenic dermis in combination with autogenous cultured epithelial cells that form a permanent coverage for full-thickness RDEB wounds has been explored.16-21 However, this technique requires excision of the upper dermis, with sacrifice of epithelial attachment mechanisms, perhaps explaining the fragility of the resulting coverage.

Despite the well-described liabilities of donor site morbidity and graft hypertrophy, split-thickness autografts remain the standard of care for resurfacing full-thickness defects associated with reconstructive procedures in patients with RDEB.5,22 Because of widespread involvement over a large total body surface area, surgeons are required to use thinner autografts than would be ideal in reconstruction because of the routine shortage of adequate donor sites in such patients. Potential donor site morbidity includes pain, delayed wound healing, infection, and hypertrophic scarring. The adverse aspects of split-thickness skin graft procurement are thought to be directly related to the thickness at which the donor skin is harvested. Hypertrophy of grafted skin is related inversely to the thickness of...
transplanted dermis. Both these liabilities might be lessened by the ready availability of a functioning, "off-the-shell" dermal substitute.

Biosynthetic dermal substitutes have been widely studied in animal models, but apart from their use in massively burned patients, they have gained little clinical acceptance in the treatment of skin injury or disease. The use of biosynthetic dermal substitutes is based on the premise that the matrix or mesh supporting the cultured fibroblasts will degrade in the wound healing process, leaving behind the fibroblasts and their secreted dermal proteins. Studies have shown, however, that only fetal fibroblasts in utero are capable of regenerating dermal extracellular matrix without scarring. Mature fibroblasts repair damaged or missing dermis through the formation of granulation tissue, which later matures into scar tissue. Mature fibroblasts do not regenerate the complex architecture of the epidermis and upper dermis. This observation has focused attention on the matrix deficit in full-thickness injury and has prompted the development of a structurally and biochemically intact acellular allograft dermal matrix that is intended to function as a template for dermal regeneration. A matrix template approach has been developed and has proved effective for allografts. The putative benefits of an acellular allograft are summarized in the Table.

A detailed comparison between the dermal graft used in this case and intact dermis indicates that the extracellular matrix of the basement membrane and the dermis of the acellular graft is essentially identical to that of skin, only without the cellular component. Since the basic skin architecture with its original underlying RDEB defect is unaltered by the operation, a gradual recurrence of the deformity is to be expected. One factor that appears to prevent recurrence of the interphalangeal joint contractures is prolonged use of splinting.

This case report indicates that cryopreserved acellular human dermis can engraft successfully and support engraftment of an overlying ultrathin autograft in patients with RDEB. With acellular dermal grafts, clinicians may now have an alternative to conventional autografting. While these initial results relating to the effectiveness of cryopreserved acellular human dermis in optimizing appearance and function are encouraging, longer follow-up is required before definitive conclusions can be made.

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REFERENCES

Clinicians, local and regional societies, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern and be submitted double-spaced and in triplicate. Photomicrographs and illustrations must be clear and submitted as positive color transparencies (35-mm slides) or black-and-white prints. Do not submit color prints unless accompanied by original transparencies. Material should be accompanied by the required copyright transfer statement, as noted in “Instructions for Authors.” Material for this section should be submitted to George J. Hruza, MD, Cutaneous Surgery Center, Suite 16411, 1 Barnes Hospital Plaza, St Louis, MO 63110. Reprints are not available.