Reconstruction of hand surgical wounds after pseudo-syndactyly correction or squamous cell carcinoma resection in patients affected from epidermolysis bullosa: a monocentric experience with a collagen-elastin dermal matrix substitute

Giulia Bernante,[1]* Alessandro Portoghese,[1]* Mario Lando,[2] Barbara Ferrari,[3] Camilla Reggiani,[3] Raimondo Feminò,[4] Chiara Fiorentini,[3]* Cristina Magnoni[3]*

[1]Division of Plastic Surgery, University of Modena and Reggio Emilia, Policlinico of Modena; [2]Department of Muscle-Skeletal Surgery Hand and Microsurgery, Modena University Hospital; [3]Division of Regenerative and Oncological Dermatological Surgery, Modena University Hospital; [4]Department of General and Specialist Surgeries, Anesthesia and Intensive Care Unit 2, University Hospital, Policlinico of Modena, Italy

*Shared first and senior authorship

Correspondence: Cristina Magnoni, Division of Regenerative and Oncological Dermatological Surgery, Modena University Hospital, via del Pozzo 71, 41125 Modena, Italy.
E-mail: magnoni.cristina@gmail.com

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Abstract

In patients with epidermolysis bullosa (EB), surgery may be required to remove squamous cell carcinoma (SCC) of the hands or to correct pseudo-syndactyly. Dermal substitutes may represent a suitable tool to promote the healing of surgical wounds in EB. We review our experience with a collagen-elastin dermal matrix to promote surgical wound healing due to hand surgery to correct pseudo-syndactyly or SCC resection in patients affected by EB.

Overall, 12 patients (mean age, 29±11 years, range 13-51; four females) with EB were considered, with a total of 25 different interventions (16 SCC removals; three amputations for recurrent infiltrating SCC; six pseudo-syndactyly corrections). All patients received a collagen-elastin dermal matrix sheet. Neodermis was achieved in all patients, and no adverse events potentially associated with the graft occurred. No SCC recurrence was reported at sites operated for either SCC resection or amputation. The opening of the first or second commissure appears to be maintained for over 1 year after the procedure, preserving digital function. We believe that the application of a dermal substitute, together with a close dressing protocol, may represent a suitable strategy for obtaining physiological tissue regeneration and maintaining proper hand function in patients with EB.

Introduction

Inherited epidermolysis bullosa (EB) is a group of rare (approximately 11/1,000,000 population) genetic disorders associated with skin fragility, leading to deformation of mucocutaneous blisters and erosions in response to minimal mechanical trauma, ultimately resulting in excruciating pain, functional impairment and a very poor quality of life.[1] Multiple subtypes of EB exist; nowadays, more than 30 variants of EB are recognized.[2]

All types of EB, particularly recessive dystrophic epidermolysis bullosa (RDEB), affect the hands. Notably, hands are particularly prone to repeated blistering, ulceration, and scarring.[2] Multiple hand injuries eventually lead to dermal fibrosis, finger atrophy, tendon shortening or fibrosis, and muscle contractures, causing permanent joint deformity, pseudo-syndactyly, and loss of motor manipulation.[2,3] Although the topic is still debated, most data bear out the effectiveness of hand surgery for the correction of pseudo-syndactyly in patients with RDEB. Recently, dedicated guidelines have been issued.[2] Prompt and proper healing of surgi-

cal wounds is crucial to ensure the best possible surgical outcomes, but consensus on optimal procedures has yet to be reached.[3,4] Ultimately, repeated hand injury also leads to the development of multiple, aggressive, and recurrent squamous cell carcinoma (SCC), which represents the main cause of death in patients with EB.[5] Wide local surgical excision is the standard of care for SCC of the hand in patients with EB.[6] Various approaches are used for wound reconstruction after SCC excision.[6,7] However, even in this case, there is no consensus on the best approach.[5] Given the rarity of EB, interventional studies with a large sample size are not always feasible; therefore, small case series play a valuable role as a source of evidence in this setting.[4] Dermal substitutes have been previously used to promote surgical wound healing in EB, with promising results.[4] Specifically, a collagen-elastin dermal matrix (MatriDerm®; MedSkin Solutions Dr. Suwelack AG, Hamburg, Germany; use of the trade name is for communication purposes only and does not imply endorsement) is a single-layer dermal substitute composed of type I, III, and V bovine collagen and elastin hydrolysate, used to cover a variety of skin injuries in adult and pediatric patients.[4,8-20] Our hospital (Policlinico of Modena, Italy) is a referral center for the treatment of EB in Italy. In our center, patients with this disease are followed by a multidisciplinary team coordinated by dermatologists, with more than 30 core members, including neonatologists, pediatricians, oncologists, pathologists, radiologists, anesthesiologists, palliative care experts, nurses, physiotherapists, and psychologists. Here, we review our experience with this collagen-elastin dermal matrix to promote surgical wound healing due to hand surgery for correction of pseudo-syndactyly or SCC resection in patients affected by RDEB.

Case Report

Design and ethical considerations

This was a retrospective case series with data collected from the archives of the Policlinico of Modena. The data examined were collected between 2017 and 2023. Patients or legal guardians provided their informed consent to use the data for research purposes, and the local ethics committee was informed of the preparation of this manuscript.

Patients and interventions

Overall, 12 patients (mean age, 29±11 years, range 13-51; four females) with RDEB were considered for this analysis, with a total of 25 different interventions. Among the different interventions, 16 were removals of cutaneous SCC after confirmation by biopsy and appropriate imaging, 3 were amputations for recurrent infiltrating SCC, and 6 were corrections of pseudo-syndactyly. All patients received grafts with the collagen-elastin dermal matrix. Patients and interventions are summarized in Supplementary Table 1. Figures 1-3 show some relevant cases and related images (patient #2, intervention 2; patient #3, intervention 12; and patient #11, intervention 24; one case of SCC removal, one case of amputation, and one case of pseudo-syndactyly correction, respectively).

Surgical procedures

All patients were treated by a single multidisciplinary team, including a hand surgeon, a dermatologic surgeon, a plastic surgeon, an anesthetist, nurses, and a physiotherapist.

Anesthesiologic procedures

All surgical interventions were performed in a single session, under sedation with midazolam+fentanyl or remifentanyl+propofol combined with loco-regional blocks. All regional blocks were performed with both electro-neural stimulation (ENS) 0.5mA+2Hz and ultrasound-guided technique in order to better define the plexus anatomy in the axillary region and optimize the amount of local anesthetics administered. Paracetamol and/or ketorolac were administered for postoperative analgesia to achieve satisfactory pain control.

Removal of squamous cell carcinoma or precancerous lesions

Wide local excision with 2 cm of safety margins with postoperative margin evaluation is the standard treatment for EB SCCs.[21] There is no consensus on the optimal reconstructive technique fol-

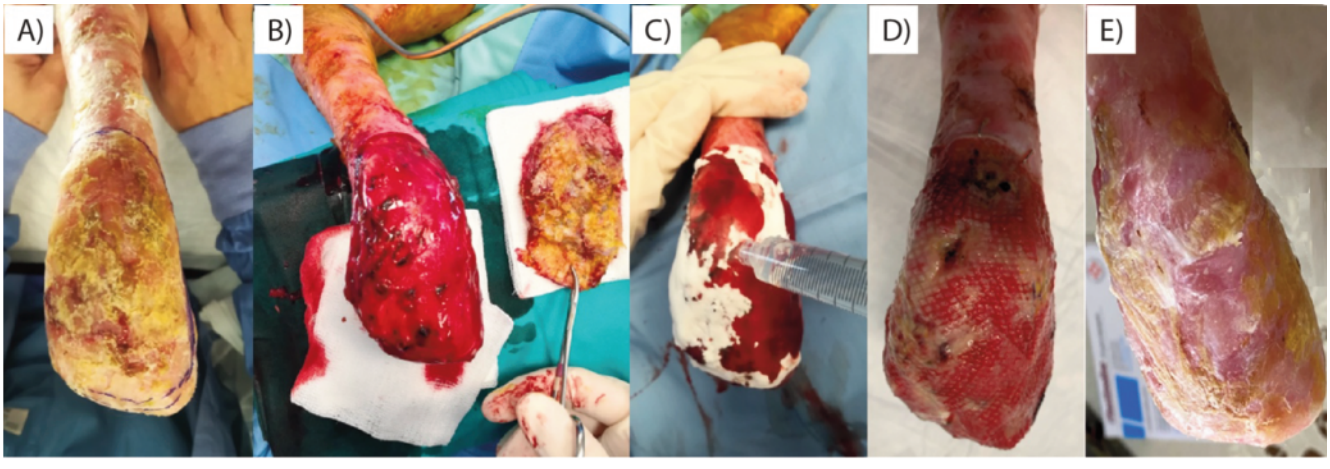

Figure 1. Example of squamous cell carcinoma (SCC) removal and application of the collagen-elastin dermal matrix (patient #2, intervention 2; see Supplementary Table 1 for further details). **A**) Pre-surgical status, showing a large SCC of the back of the right hand; **B**) wide excision of the tumor mass; **C**) rehydration of the dermal matrix after dry application; **D**) engraftment of the dermal matrix 20 days after placement; **E**) follow-up at 8 months.

lowing SCC excision. The choice of the closure technique depends on a combination of various factors, including defect size and location, patient preference, and preservation of function/range of motion. Reconstructive approaches include healing by secondary intention, full or split-thickness skin grafting, and dermal substitutes.[21] A sheet of the collagen-elastin dermal matrix was applied to the surgical wound (Figure 1), then trimmed to size and secured in place with surgical staples.

In cases of involvement of underlying structures such as vessels, nerves, or tendons, wide local excision was not possible, and more radical surgery (generally amputation) was required.

Amputation

Two amputations were performed below the elbow and one above. In order to perform the amputations, a volar and dorsal mirror incision of skin and superficial fascia was made at either the radiocarpal level or the humeral level. Then, we proceeded stepwise by isolating and protecting the vascular-nervous structures and cauterizing the sensory nerves with low-intensity bipolar for 2 minutes according to the Gosset technique. A double ligation of the radial and ulnar artery was performed. The muscles were transected, and the humerus or radius/ulna was cut at appropriate locations as determined by pre-surgical imaging. After careful

Figure 2. Example of the right arm below-elbow amputation due to infiltrating recurrent squamous cell carcinoma (SCC) of the hand and application of the collagen-elastin dermal matrix (patient #3, intervention 12; see Supplementary Table 1 for further details). **A**) Infiltrating recurrent SCC of the right hand; **B**) surgical wound after below-elbow amputation; **C**) application of the dermal matrix to the surgical defect; **D**) follow-up at 8 months.

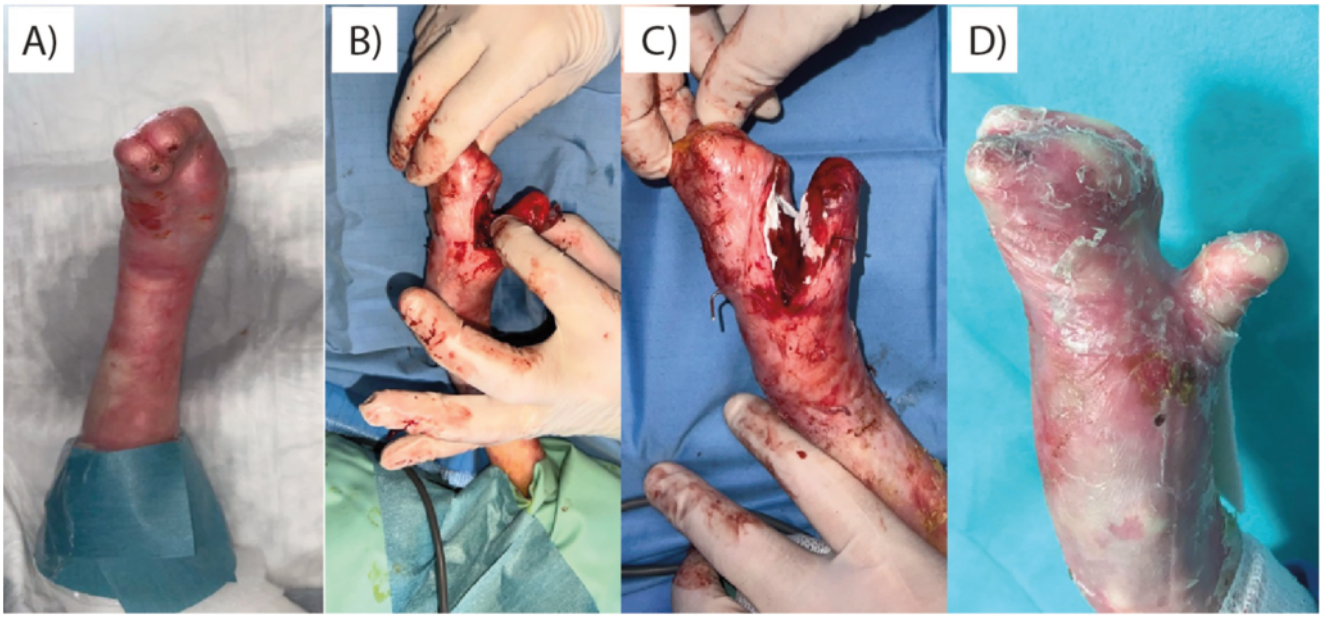

Figure 3. Example of pseudo-syndactyly correction and application of the collagen-elastin dermal matrix (patient #11, intervention 24; see Supplementary Table 1 for further details). **A**) Pseudo-syndactyly of the right hand; **B**) cutaneous incision at the first interdigital space; **C**) application of the dermal matrix to the surgical defect; **D**) follow-up at 12 months.

hemostasis, we placed the collagen-elastin dermal matrix on the surgical wound (Figure 2).

Correction of pseudo-syndactyly

The surgery was performed on one hand at a time to preserve the patient's autonomy as much as possible.

The release of the first commissure was obtained by performing a cutaneous incision starting at the dorsal aspect of the first interdigital space, between the first and second metacarpal bones, then extending to the base of the thenar region, reaching the proximal palmar crease. This was done by isolating and protecting the nervous vascular structures, releasing the fibrous and soft tissues of the thenar region, and incising the muscle fascia, consequently improving the opening of the first commissure. The surgical defect was then covered with the application of the collagen-elastin dermal matrix. With the aid of the fluoroscope, a 1-mm Kirschner wire was inserted lengthwise from the distal phalanx of the thumb to the first metacarpal while also locking it to the trapezium bone. A second 1-mm Kirschner wire was inserted crosswise between the first and second metacarpal bones. Thorough hemostasis was then performed, washing with a physiological solution. The release of the second commissure was performed by starting with a skin incision in the dorsal region between the second and third fingers and then dissecting by planes for the release of the first commissure. We then set up a rectangular dorsal flap to reconstruct the second commissure and opposing triangular flaps in the distal portion to correct pseudo-syndactyly. The donor area was then covered with the collagen-elastin dermal matrix (Figure 3).

Application and dressing of the dermal matrix

After washing with saline solution, a dry application of the matrix sheet was performed on the surgical wound. If the size of the defect was larger than a standard sheet, an additional sheet was used to fill the defect, with an overlap of approximately 2-3 mm on the first sheet. Then, the collagen-elastin dermal matrix was rehydrated on the wound bed using a saline solution; proper adherence to the wound bed was ensured. Sutures were performed by using surgical staples. Four to five layers of non-adherent paraffin-impregnated gauze were applied to the dermal matrix, and a light compression dressing of non-woven fabric was also placed. Perioperative prophylactic antibiotics were administered to all patients (single-dose cefazolin, 2 g IV) before the skin incision.

Postoperative follow-up

In the absence of complications, all patients were discharged the day after surgery. During the postoperative period, all patients were followed in an outpatient dermatologic clinic specifically dedicated to the management of EB. Patients were regularly medicated, and the dressing was replaced twice a week. After 2 weeks, staples were removed; Kirschner wires, when present, were removed 3 weeks after surgery under proper analgesia. All patients were followed twice a week until a neodermis was formed and re-epithelization was achieved (*Supplementary Table 1*). No cases of adverse events directly associated with the dermal matrix were reported.

Patients undergoing SCC resection were monitored every 3 months to assess any potential recurrence.

All patients undergoing pseudo-syndactyly correction underwent postoperative physiotherapy from 3 weeks after surgery. Physiotherapy included applying an elastomer in the operating room and keeping it in place for at least 24 hours a day for the first 2-4 months (after 4 months, only at night). Patients were instructed on the importance of keeping the elastomer in place as much as possible to maintain commissure opening. A qualified physiotherapist instructed the patients to perform pinching movements every 2-3 hours for 10-15 minutes (*e.g.*, using soft objects that do not cause discomfort to the skin, sometimes even fine objects such as straw or fork) together with a home exercise program in order to facilitate corticalization of the movement.

Outcomes

No cases of SCC recurrence at sites operated for either SCC resection or amputation were reported.

The opening of the first or second commissure appears to be maintained for over 1 year after the procedure, preserving digital function. However, patient monitoring was challenging to standardize due to poor compliance and because many patients did not reside in the same location as our hospital center.

Discussion and Conclusions

While remaining anecdotal evidence, the case series provides guidance and indications for surgical approaches in rare diseases such as EB.[4,22-25]

Our case series presents 25 interventions aimed at resecting SCC – either as wide local excision or amputation – or restoring function after pseudo-syndactyly in 12 patients with EB treated at our referral center. In all cases, the collagen-elastin dermal matrix was applied to promote tissue regeneration. We selected this particular dermal matrix since it is associated with a lower infectious risk compared with other matrices available on the market, and this feature is particularly important in challenging patients such as those with EB.[11]

Overall, 19 cases of SCC resection/amputation were considered in the present analysis: no cases of recurrence at the operated site were reported up to a maximum follow-up of 2 years. The application of the dermal matrix, together with a well-defined dressing protocol, was associated with complete tissue regeneration in all cases, with no local adverse events. The retrospective nature of the present analysis does not allow for comparisons of wound healing time with respect to other types of tissue regeneration, and this limitation should be kept in mind when interpreting our findings. However, we observed that the application of the dermal matrix allowed physiological tissue regeneration without needing skin transplantation from other donor sites. Moreover, our dressing protocol was quite easy to follow, and thus, after complete grafting, it could also be applied at the patient's home, with the support of their caregiver.

Our results also support the use of the collagen-elastin dermal matrix in tissue regeneration after the first or second commissure release. In our case series, postoperative functional improvement was reported in all six patients requiring release of the first or second commissure; they achieved good joint function and were able to follow rigorous postoperative rehabilitation.

The positive effect of surgery in this commissure release is not unequivocally accepted, and the risk of recurrence remains approximately 50%; however, most data to date support the surgical approach in patients with EB, even considering the psychological benefit of such intervention.[2,4] Following the results of our analysis, we believe that appropriate surgical technique, the use of a dermal substitute to promote wound healing, and rigorous rehabilitation associated with the overall interdisciplinary management of our patients with EB allowed us to succeed in optimizing their manual function and minimizing surgical risk.

Indeed, it is crucial to start physiotherapy sessions as early as possible and to continue them two or three times per week until improvement is evident to overcome postoperative rigidity. Furthermore, poor compliance with postoperative physiotherapy is associated with an increased risk of recurrence after surgery.[25]

Wound healing in patients with EB is always challenging because of their genetic alterations. Moreover, it can become even more challenging in the case of a large wound size or a particular anatomical area, such as the hand. Second-intention healing may not be a solution in all cases of hand surgery, as it may be associated with the risk of developing adherent scars between the fingers or at the wrist joint, which in turn may further diminish hand function and quality of life. Furthermore, using a skin graft in hand surgery is not always feasible, as it requires additional surgical wounds in the donor area. Therefore, we believe that the application of a dermal substitute, together with a close dressing protocol, may represent a suitable strategy to obtain physiological tissue regeneration and maintain proper hand function in patients with EB. Future analyses should also investigate the use of collagen-elastin dermal matrix combined with other approaches, such as keratinocytes suspension.[26]

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Online Supplementary Material:

Supplementary Table 1. Patient and intervention details.