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CASE REPORT
Reconstructive

Skin Allograft after Bone Marrow Transplantation of Patient with Recessive Dystrophic Epidermolysis Bullosa

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Summary: In this study, we present a 26-year-old woman with case presentation of recessive dystrophic epidermolysis bullosa who had developed squamous cell carcinoma. The patient underwent bone marrow transplant and skin grafting with the same bone marrow donor. After excision of squamous cell carcinoma and skin grafting, no tumor was observed; thus, chemotherapy and radiation were no longer needed. *(Plast Reconstr Surg Glob Open 2023; 11:e5389; doi: 10.1097/GOX.0000000000005389; Published online 9 November 2023.)*

Epidermolysis bullosa (EB) is a term used to describe a set of hereditary mechanobullous disorders associated with mutations in genes responsible for protein aggregates in the skin. It consists four major subtypes, including EB simplex (EBS), junctional EB (JEB), and dystrophic EB (DEB), and recently, the reclassified Kindler syndrome. Recessive dystrophic epidermolysis bullosa (RDEB), a subtype of DEB, is an incurable disease characterized by skin blistering due to the lack of type VII collagen (C7) protein. Type VII collagen is the primary component of anchoring fibrils.[1]

Patients with RDEB have large and painful blisters that lead to open wounds. Those who have larger wounds experienced more pain and itch.[1] As of today, RDEB is managed only with supportive care. However, therapies including gene therapy, cell therapy, and protein-based therapy have been reported to be promising as RDEB treatment.[2] Gene therapy is one of the advanced treatments for RDEB. The most popular type of gene therapy for treating genetic problems uses viral vectors. For RDEB gene therapy, retroviral, lentiviral, and adenoviral vectors have been created.[3,4] One study showed that bone marrow transplant has been suggested to enhance quality of life of some patients with the recessive dystrophic subtype of EB.[5]

Various options for wound closure after excision of EB squamous cell carcinoma (SCC) have been used. One of the options is a skin graft, wherein a patch of healthy skin was transferred from one area to an open wound.[6] This graft can be classified either as split- or full-thickness. Split-thickness encompasses the epidermis with a dermis portion, whereas full-thickness consists of both the epidermis and dermis.[7] In regard to donor sites, skin grafts are classified as autograft (same individual), isograft (tissue extracted from one person and surgically grafted onto another genetically identical person, which could be an identical twin), allograft (obtained from another person), and xenograft (skin from other species).[8] Skin grafts can be performed when the skin of an RDEB patient is intact. When this is not possible, skin can be harvested from a matching relative.

In this case, we aimed to perform skin allograft in a patient who was diagnosed with RDEB who also developed SCC.

CASE STUDY

We present the case of a 26-year-old woman who was diagnosed with RDEB. A bone marrow transplant was performed in 2019 on the patient, and her matched sister served as the donor; the match was 100% between the two sisters. The patient underwent several procedures and has seen multiple physicians for 6 years after the diagnosis. Because of persistent ulceration in the right leg, she underwent an incisional biopsy in 2019. It was found out that the patient developed SCC. The patient is not a good candidate for local excision and coverage by flap because all her skin is affected by her disease, causing skin ulceration and poor wound healing, and the only valid option was amputation.

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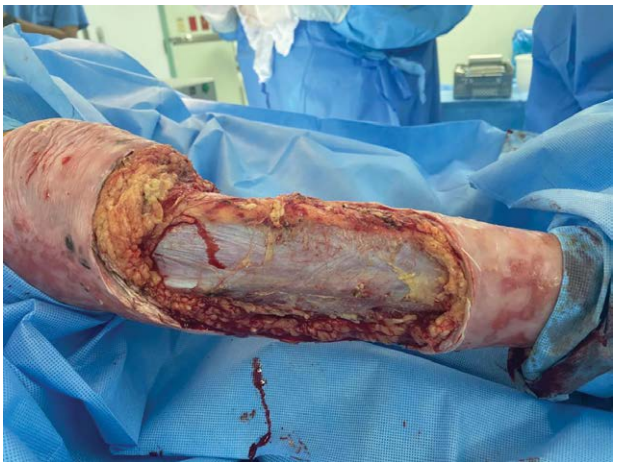

Fig. 1. Intraoperative picture showing defect post excision of tumor.

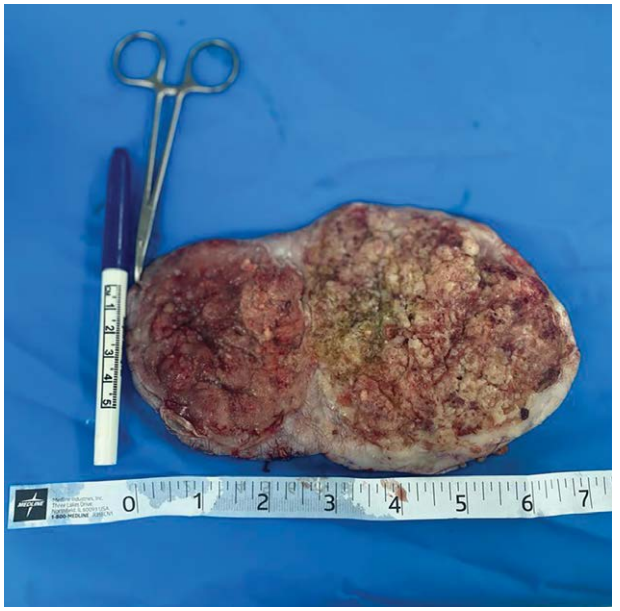

Fig. 2. Excised SCC.

Because the patient refused amputation, skin allograft became an option. The skin was harvested from her sister, because the patient lacked intact skin to cover the wound. The patient underwent SCC excision on the right leg, followed by skin grafting; no preoperative or postoperative medications were used (Figs. 1–3). After 1 year of follow-up, her skin graft healed well with no complications (Fig. 4).

DISCUSSION

The patient in this study was diagnosed with RDEB, and she underwent bone marrow transplant as a treatment. RDEB is a type of dystrophic epidermolysis bullosa and is characterized by widespread blistering caused by collagen deficiency in the skin. Severe blistering may lead to serious

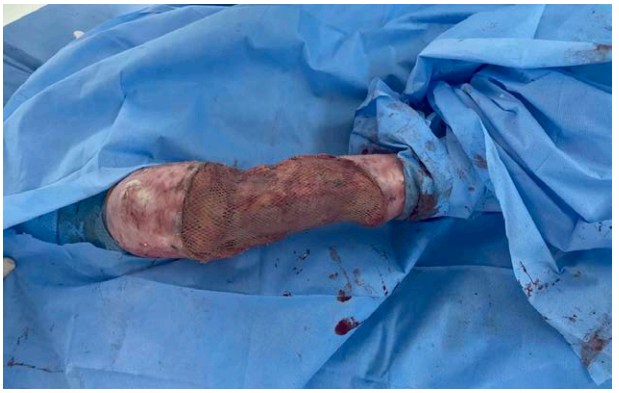

Fig. 3. Defect post coverage with skin graft harvested from the patient's sister.

Fig. 4. Follow-up after 1 year shows healed skin graft.

medical problems such as pseudosyndactyly, impaired vision, joint contractures, and scarring.[9] According to the literature, one of the risks of having severe generalized RDEB, a common form of RDEB, is developing SCC.[1] Based on the US National EB registry, risk of SCC development in severe generalized EB patients aged 20 years is 7.5% and increases to 67.8% by the age of 35 years.[10] Studies showed that SCC in patients with recessive RDEB is frequently more aggressive than in other forms of EB. For patients with RDEB, bone marrow transplantation[11] and skin substitutes[12] have already shown variable efficacy and safety.

As of today, RDEB is incurable, but progress has been made in developing treatments such as bone marrow,

protein therapy, stem cell therapy, gene therapy, and fibroblast cell therapy. The patient in this study was treated with bone marrow stem cell therapy, in which her matched sister served as a donor. In the study by Wagner et al,[11] allogeneic bone marrow transplant performed in RDEB patients showed partial correction of C7 deficiency and mucosal integrity. One study reported that after the transplant, de novo C7 was produced and wound healing improved.[2]

Because the patient was not fit for local excision, skin grafting was recommended. After right-leg SCC excision followed by skin grafting, histopathology results showed margin-free tumor; thus, the patient did not need to undergo chemotherapy or radiation.

Different skin grafting approaches are currently being used in treating ulcers in RDEB. RDEB patients cannot receive grafts from themselves due to lack of skin integrity. Also, grafts from donors were not always successful because the immune system of the host often rejected the transplanted tissue. Immune response to grafted tissues became a barrier in the success of skin graft. Because the skin was harvested from a relative, rejection is possible. Rejection happens when the immune system of the receiver recognizes the donor tissue as foreign. This could trigger an immune response that could destroy the donor cells leading to the graft rejection.

Skin allograft was the method used in this case because of its potential to help RDEB patients' skin with skin adhesion and in increasing the amount of type VII collagen.[11,13] Ebens and colleagues[14] approached this problem by harvesting epidermal grafts from the donor of the bone marrow, using an epidermal harvesting system. This method could give the RDEB patients with two sets of blood stem cells (chimerism) generating immune cells, allowing them to receive grafts from their bone marrow donor. Furthermore, Ebens et al[14] report that bone-marrow-derived epithelial cells could help in healing of wounds because they were recruited in the grafted site.

Benichou et al[15] concluded that introduction of chimerism followed by bone marrow transplant is the most reliable method for the success of allogeneic skin grafts.

This study showed the effectiveness of using a biological skin substitute in a patient with RDEB. Studies reported that biological skin grafts have a more preserved and native extracellular matrix structure, potentially allowing for the formation of a more natural dermis. Because of the presence of a basement membrane, they also have excellent re-epithelialization characteristics.[16,17]

Because this is a case report, the results cannot be generalized, and cause-and-effect relationship cannot be established. Nevertheless, the researchers were able to present a complicated case of RDEB and showed the effectiveness of skin allograft performed in a patient who developed SCC.

CONCLUSIONS

The patient underwent bone marrow transplant before skin grafting with the same donor. The patient developed immune cells allowing the skin graft. After excision of SCC and skin grafting, histopathology results showed a margin-free tumor.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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This case report conforms to the Declaration of Helsinki.

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