Case Series

The Effectiveness of a Novel Skin Barrier Protectant in the Management of Acute Radiation Dermatitis: A Case Series

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ABSTRACT

Objective: Acute radiation dermatitis (ARD) is a frequent adverse effect in patients with cancer undergoing radiotherapy (RT). The aim of this case series is to evaluate the effect of a novel skin barrier protectant in patients with ARD.

Methods: The skin barrier protectant was used in four patients with different cancer types undergoing RT at two clinical sites. All patients received the standard institutional skincare alongside the novel skin barrier protectant. The skin reactions were evaluated by an RT nurse using the modified version of the Radiation Therapy Oncology Group criteria.

Results: At the final RT session, three of four patients developed erythema with or without dry desquamation. One patient presented only a minor patchy moist wound. Overall, the pain and pruritus due to ARD was low or nonexistent. No adverse events related to the skin barrier protectant were reported.

Conclusions: This case series demonstrates the beneficial effects and safety of the novel skin barrier protectant in the management of ARD in patients with cancer of different etiologies. These results lay the foundation for future studies with larger, more homogeneous patient populations; a well-defined application scheme; and a stricter study design.

Keywords: oncology, radiation dermatitis, radiotherapy, skin barrier protectant, supportive care, wound care

ADV SKIN WOUND CARE 2022;35:1–6.

DOI: 10.1097/01.ASW.0000826824.10120.fe

INTRODUCTION

Radiation dermatitis is a common adverse effect of radiotherapy (RT), occurring in up to 95% of patients. These RT-induced skin reactions can be classified as acute, appearing within the first weeks after starting treatment, and chronic, still occurring months to years after the final RT session. This case series focuses on acute radiation dermatitis (ARD), an early inflammatory skin reaction due to ionizing radiation.[1]

The skin is a radiosensitive organ due to its high proliferation rate. The basal keratinocytes of the epidermis have a high turnover rate in particular. Radiotherapy causes an inflammatory reaction accompanied by local blood vessel damage, resulting in an erythematous reaction. Further, ionizing radiation causes indirect DNA damage via the generation of short-lived free radicals due to the ionization of cellular water molecules. Damage to the basal keratinocytes will disrupt the normal self-renewing process of the skin. During RT, repeated exposure of the skin cells to ionizing radiation prevents basal skin cells from maintaining optimal renewal of the epidermis. Dry desquamation occurs if new cells' production is faster than the shedding of the dead cells at the stratum corneum. If the basal stem cells become depleted, moist desquamation arises. Moreover, RT also impairs the skin barrier function, leading to increased water loss and skin dehydration. Because of the affected barrier function, the skin has a higher vulnerability to external chemical factors, allergens, and UV radiation.[2–4]

The severity of ARD depends on both patient- and treatment-related factors. Patient-related risk factors include the treated body site (eg, neck, face, extremities, pelvis, breast), obesity, age, smoking status, nutrition status, preexisting skin conditions, and genetic susceptibility. Regarding treatment-related factors, the dose per fraction, the total dose, the volume of the irradiated area, the use of bolus material, the fractionation regimen, and concurrent cancer therapies (eg, chemotherapy, targeted

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therapy) influence the risk of ARD.[5,6] The physical symptoms of ARD—which can include irritation, burning sensations, and/or pain—can impair patients' daily lives, leading to a diminished quality of life.[7]

Acute radiation dermatitis develops gradually along the RT course. It can range from erythema and edema to dry desquamation and, in some cases, moist desquamation. The skin toxicity reaches its peak at approximately 10 to 14 days after the completion of RT. After the peak, the healing process steadily starts. The criteria of the National Cancer Institute Common Terminology Criteria for Adverse Events or the Radiation Therapy Oncology Group can be used to evaluate ARD clinically.[8–10]

Prevention is based on a combination of general skincare and hygienic measures to reduce irritation and friction. On the other hand, ARD management is dictated by the severity of skin reactions during RT and needs to be maintained for up to 4 weeks after the final RT session. Proper patient education regarding skincare and efficient follow-up by the wound care specialist and radiotherapist are essential to reduce discomfort and stimulate wound healing. To date, no consensus on the prevention and management of ARD exists. Although the Multinational Association for Supportive Cancer Care developed guidelines in 2013 for how to prevent and manage ARD,[11] extensive scientific evidence is lacking for several preventive and treatment options. Therefore, individual RT departments often develop their own skincare protocol based on the available evidence and clinical experience.[2,4,12–15]

Because of friction with clothing or skin-to-skin contact, the skin may abrade, enhancing the risk of ARD. A skin barrier product can offer a solution to this problem, keeping the skin barrier function intact by hindering the desquamation of superficial keratinocytes at the stratum corneum. Further, it can protect both healthy and wounded skin against external insults such as friction, shear, allergens, chemicals, body fluids, and adhesives.[16–18] A novel skin protectant that combines a proprietary acrylic tetra polymer with 2-octyl cyanoacrylate has been developed for the management of incontinence-associated dermatitis (IAD). The polymer forms a long-lasting, waterproof, highly robust, elastomeric film barrier that is more durable than pure cyanoacrylate solutions. The protectant can be applied to all types of wounds, both wet and dry, whereas other skin barrier products can be used only on dry wounds. The skin barrier protectant lays a transparent film over the skin that acts as a physical barrier against moisture, irritants, and abrasion and creates an optimal wound-healing environment.[19,20]

The first clinical evidence of the novel skin barrier was in IAD. Incontinence-associated dermatitis is a specific type of irritant contact dermatitis caused by extended skin contact with urine or feces and friction. The mechanism of skin injury involves both chemical and physical irritation that leads to disruption of the epidermal barrier and increased skin permeability, inflammatory changes, skin breakdown, and increased risk of bacterial colonization and secondary infection. The clinical characteristics of IAD resemble those of ARD: persistent erythema and edema of the skin, and in more severe cases, vesicles, bullae, and erosions may develop. The first clinical study with the novel skin barrier product was a prospective study with 16 patients with IAD. Results demonstrated a significant reduction in IAD scores in 81% of the patients and significantly decreased pain scores in all nine patients who had reported pain at enrollment.[20] The researchers evaluated the efficacy of the novel skin barrier protectant in a patient with vulvar ARD. The case report demonstrated a beneficial effect of the skin barrier protectant on the wound healing process and the pain.[21] The present case series will provide more evidence in the use of the skin barrier protectant in patients with ARD.

This case series aims to evaluate the use of the novel skin barrier protectant in managing ARD in patients with cancers of different etiologies. Cases 1 and 2 are both patients with skin cancer, case 3 is a patient with head and neck cancer, and case 4 is a patient with a liposarcoma.

METHODS

Study Design

A case series study was performed with four patients with cancers of different etiologies who underwent RT at two clinical sites between 2017 and 2019. Case reporting guidelines were followed,[22] and patients provided written informed consent for the processing of personal data and a waiver for the use of photographs. The study complied with the Helsinki Declaration guidelines on clinical research and legislation on the protection of privacy.

Institutional Topical Skincare Treatment

Each patient was individually advised to follow the institutional skincare guidelines based on the local guidelines of the Flemish Association for Radiotherapy and Oncology Nurses (eg, wear loose-fitting clothing, gentle washing with or without mild soap, patting dry with a soft towel instead of rubbing).[15] Further, the patients were instructed to apply a topical hydrocolloid gel (Flamigel; Flen Pharma, Kontich, Belgium) three times daily, beginning the first day of RT. For painful skin reactions and/or to prevent friction from clothing or skin, a foam, absorbent, self-adhesive silicone dressing (Mepilex; Mölnlycke Health Care, Gothenburg, Sweden) was applied.

Skin Barrier Protectant

The skin was cleaned with a wound cleanser before the first application of the skin barrier protectant (Cavilon Advanced Skin Protectant; 3M Health Care, St Paul,

Minnesota). An experienced nurse applied the new skin protectant twice weekly on the irradiated area. The product is applied as a liquid, and it polymerizes as a film in 30 seconds. The skin protectant consists of a combination of two chemicals, an acrylic tetrapolymer and a 2-octyl cyanoacrylate, to create a durable film that adheres to both intact and moist-wet wounds and protects the skin from irritants, moisture, and friction. The skin protectant was tested for cytotoxicity, irritation, sensitization, genotoxicity, and systemic toxicity based on the criteria of expected use (>30 days in contact with a breached skin barrier) and guidance covering the biologic evaluation of medical devices outlined in EN ISO 10993-1:2009 before being applied on humans. The test results (not shown) demonstrated that the product is safe for its intended use.[20] The bolus effect of the skin protectant combined with external beam RT was evaluated by an experienced physicist. The skin protectant did not cause any significant dose buildup or water equivalent properties when applied to six layers when measured on water equivalent phantom material.

Outcome Measures

Clinical information regarding patients' personal, disease-related, and treatment-related characteristics was collected via the patients' medical charts. The severity of ARD was evaluated using the modified version of the criteria of the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer.[8] Pain and pruritus were evaluated using a visual analog scale with a scoring grid ranging from 0 (no pain/pruritus) to 10 (worst imaginable pain/pruritus).

RESULTS

Four cases were selected by the treating radiotherapist and wound care nurse based on their high risk of developing severe ARD. The main risk factors for ARD related to these cases were the applied daily RT dose, the use of bolus material, and the anatomic location of the tumor consisting of skin folds hindering proper wound care. Via these cases, the researchers show that the novel skin barrier protectant can be applied to different skin regions under distinct RT modalities.

Case 1

The patient is an 86-year-old man with no known history of skin diseases. In 2009, he was diagnosed with bladder cancer (T3 N0 M0). On October 20, 2017, he was diagnosed with a spinocellular epithelioma on his left nostril with a penetration depth of at least 2 cm. The tumor was surgically removed, followed by a reconstruction via a nasolabial flap. Adjuvant RT was applied on the tumor between December 27, 2017, and January 4, 2018. The RT regimen consisted of 20 fractions of 2.5 Gy followed by a boost of 6 fractions of 2.5 Gy, resulting in a total of 26 fractions with a total dose of 65 Gy using photon beams. As bolus material, wet compresses were placed inside both nostrils and on top of the nose bridge to make up for missing tissue and to provide buildup of dose to the skin surface.

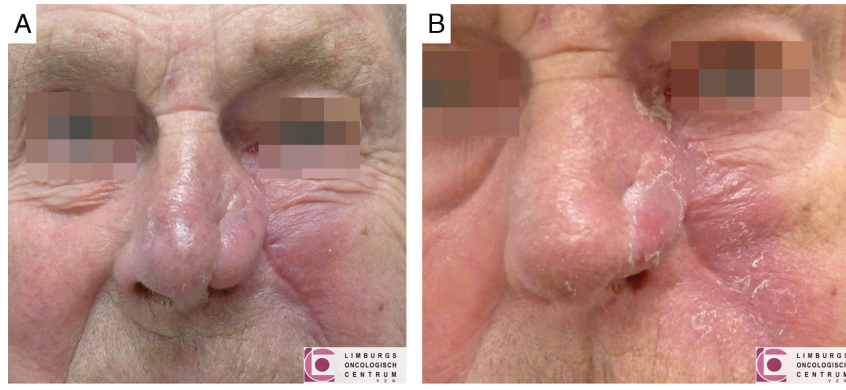
The patient received standard institutional skincare from the start of RT, including the application of hydrocolloid gel (three times a day). The skin barrier protectant was applied from fraction 8 when the patient presented a grade 1 skin reaction (Figure 1A). At the end of RT, the patient presented a grade 2A skin reaction comprising erythema and dry desquamation in the treated area (Figure 1B). The skin around the eye was irritated. He gave a score of 0 out of 10 for pain and 2 out of 10 for pruritus. The patient did not develop adverse events related to the skin barrier protectant.

Case 2

The patient is a 71-year-old man with no comorbidities or previous skin conditions. He was diagnosed with a

Figure 1. CLINICAL PHOTOGRAPHS OF A PATIENT WITH ACUTE RADIODERMATITIS ON HIS LEFT NOSTRIL

A, At the first application of the skin barrier protectant, the patient presented a Radiation Therapy Oncology Group grade 1 acute radiodermatitis. B, At the final radiotherapy session, the patient presented a grade 2A skin reaction comprising erythema and dry desquamation in the treatment field.



basocellular epithelioma on his right auricle from the helix toward the external auditory canal on July 19, 2017.

Radiotherapy was applied from October 26, 2017, until December 12, 2017. The RT regimen consisted of 20 fractions of 2.5 Gy followed by a boost of 6 fractions of 2.5 Gy, resulting in a total of 26 fractions with a total dose of 65 Gy using photon beams. As bolus material, wet compresses were placed in the external auditory canal, in the concha, and on the helix to make up for missing tissue and to provide buildup of dose to the skin surface. He received standard institutional skincare from the start of RT. At fraction 21 of RT, the patient experienced a grade 2B skin reaction and received the skin barrier protectant (Figure 2A). The patient presented only one patchy moist wound (grade 2B) in the helix's fossa at the final RT session (Figure 2B). He scored his pain 1 out of 10. He mentioned that the skin barrier product was a bit sticky, but it did not bother him. Overall, the patient did not report adverse events related to the skin barrier protectant.

Case 3

A 61-year-old woman underwent a right parotidectomy in 2007 due to the presence of pleomorphic adenoma. On March 19, 2018, she was diagnosed with a recurrent pleomorphic adenoma in her right cheek, jaw, parapharyngeal tissue, and ear canal. She underwent a subtotal right parotidectomy. The patient received intensity-modulated RT using volumetric modulated arc therapy consisting of two arcs delivering 6-MV photons between May 8 and June 16, 2018. The RT regimen consisted of 25 fractions of 2 Gy to the tumor bed, resulting in a total dose of 50 Gy. She received standard institutional skincare from the start of RT. The skin barrier protectant was applied at fraction 12 when the patient presented a grade 1 ARD (Figure 3A). At fraction 24, she presented a grade 1 ARD with dull erythema (Figure 3B). She gave overall pain and pruritus scores of 3/10. No adverse events due to the skin barrier protectant were reported by the patient.

Case 4

A 72-year-old man was diagnosed on August 20, 2019, with a dedifferentiated liposarcoma in his right cubital fossa, which was a metastasis of a previous surgically resected fibrosarcoma. At the time of diagnosis, the patient was receiving chemotherapy for a glioblastoma diagnosed earlier that year.

From October 22, 2019, until December 4, 2019, the patient received external RT using photon beams on the tumor bed of the surgically removed liposarcoma including a safety margin; RT was applied with a bolus of 1 cm on the tumor bed. The RT regimen consisted of 25 fractions of 2 Gy followed by a boost of 5 fractions of 2 Gy resulting in a total dose of 60 Gy. From the start of RT, the patient received standard institutional skincare. At fraction 8, the patient presented a grade 1 ARD, and the skin barrier protectant was applied for the first time (Figure 4A). The patient developed a grade 2A skin reaction toward the end of RT, with moderate erythema (Figure 4B). The patient felt pain only inside his elbow (pain score 3/10). The patient's skin was not painful or itchy.

DISCUSSION

In this case series, the authors determined the effect of a novel skin barrier protectant on the skin toxicity of four patients with cancers of different etiologies undergoing RT. All patients received standard institutional skincare alongside the skin barrier product. In three cases, the

Figure 2. CLINICAL PHOTOGRAPHS OF A PATIENT WITH ACUTE RADIODERMATITIS ON HIS RIGHT AURICLE

A, At the first application of the skin barrier protectant, the patient presented a Radiation Therapy Oncology Group grade 2B acute radiodermatitis. B, At the final radiotherapy session, the patient presented a grade 2B skin reaction with only one patchy moist wound in the helix's fossa.

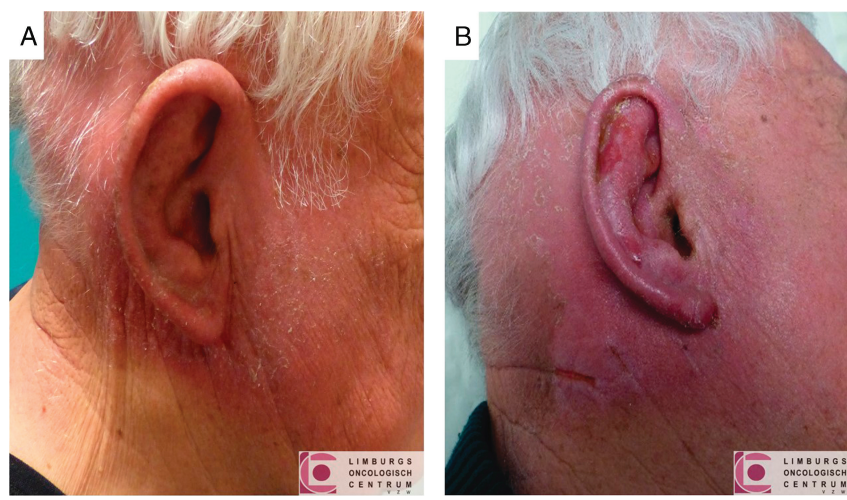
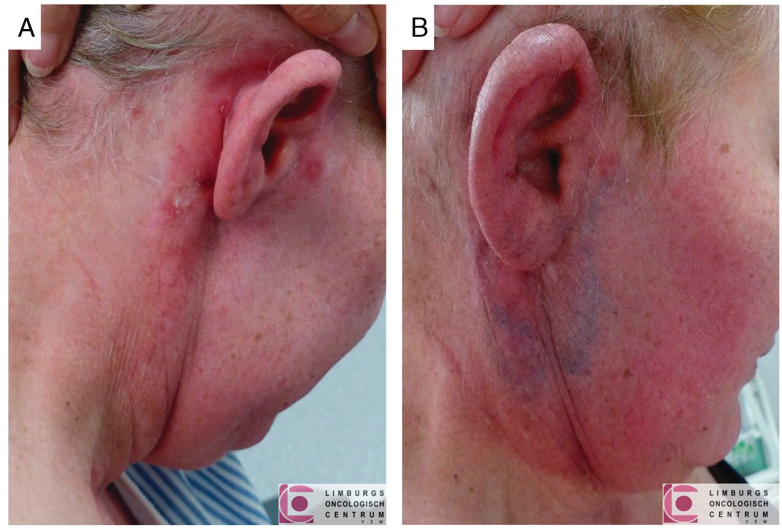


Figure 3. CLINICAL PHOTOGRAPHS OF A PATIENT WITH ACUTE RADIODERMATITIS ON HER RIGHT CHEEK

A, At the first application of the skin barrier protectant, the patient presented a Radiation Therapy Oncology Group grade 1 acute radiodermatitis. B, At the final radiotherapy session, the patient presented a grade 1 skin reaction with dull erythema.



product was applied from a grade 1 skin reaction, and in one case, the patient already presented a patchy moist wound in the treatment area (grade 2B). At the end of RT, one patient presented a grade 1, two patients a grade 2A, and one patient a grade 2B ARD. The patient with a grade 2B skin reaction presented only one minor patchy moist wound in the treatment area. No patient presented a confluent moist wound in the treatment area (grade 3).

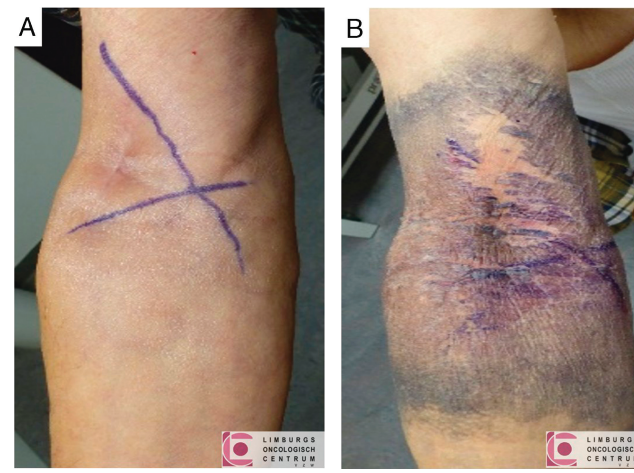
Regarding skin toxicity-related pain and pruritus, the patients reported average scores of 2 and 1, respectively. These low scores indicate that the skin barrier protectant had a clear benefit on the pain and pruritus scores. The patients did not report any adverse events related to the skin barrier protectant. However, most patients did find the product a bit sticky.

This study is the first to evaluate the novel skin barrier protectant in patients with ARD. In a previous publication by the research group,[21] the skin barrier protectant combined with standard skincare was evaluated in a patient with vulvar ARD and compared with a patient receiving only the standard skincare. The patient receiving the combination treatment presented a grade 2B skin reaction with patchy moist wounds at the final RT session. In contrast, the patient receiving only the standard skincare presented a grade 3 ARD characterized by confluent moist desquamation in the treatment area. These results indicate that the skin barrier product can reduce the intensity of the skin reactions. The patient treated with the skin barrier protectant also had an apparent reduction in pain (maximum score 6/10) compared with the control patient (maximum score 9/10).[21]

Only one open-label, nonrandomized, prospective study has evaluated the same skin barrier protectant's efficacy in patients with IAD (n = 16). The patients received the product twice weekly for up to 3 weeks (six sessions in total). The IAD score improved in 81% of the patients. The overall pain score significantly decreased from an average score of 8 at the enrollment to 1 at the end of the study. These results indicate that the skin barrier protectant could be a useful product in the management of IAD.[20] Nevertheless, the pathogenesis of IAD differs from ARD. These results align with the described case series, demonstrating a limited ARD severity and a low pain score due to the skin barrier protectant.

Figure 4. CLINICAL PHOTOGRAPHS OF A PATIENT WITH ACUTE RADIODERMATITIS ON HIS RIGHT CUBITAL FOSSA

A, At the first application of the skin barrier protectant, the patient presented a Radiation Therapy Oncology Group grade 1 acute radiodermatitis. B, At the final radiotherapy session, the patient presented a grade 2A skin reaction with moderate erythema.



This case series was not without limitations. The small sample size and the variety of cancer types and RT regimens make it challenging to generalize the results. In some cases, the skin barrier protectant was applied from a grade 1 ARD and sometimes from a grade 2B skin reaction, making it challenging to make precise suggestions. Because RT is applied daily, it might not be sufficient to apply the skin barrier protectant on a twice-weekly basis to prevent the development of patchy moist wounds (grade 2B).

Therefore, it is essential to perform future studies with a specific cohort of patients with cancer undergoing a more comparable RT regimen in a randomized controlled setting to increase the evidence level. Moreover, these studies should also investigate if an earlier starting point (eg, Radiation Therapy Oncology Group grade 1) and a higher frequency of weekly applications could improve the skin barrier protectant's efficacy.

CONCLUSIONS

This case series is the first to demonstrate the applicability of the skin barrier protectant in managing ARD in patients with cancer of different etiologies. The skin-barrier product seems to reduce the risk of confluent moist desquamation, improve patients' comfort, and reduce pain. Moreover, the product is safe to use on oncologic patients undergoing RT, without any adverse events. This case series serves as a basis for future studies in evaluating the efficacy of the skin barrier protectant for patients with ARD. ●

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