CASE REPORT

Radiation-induced pemphigus in a patient with an invasive ductal carcinoma of the breast: a case report

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Abstract

A 72-year-old woman with a known history of breast cancer was treated with adjuvant external beam radiation therapy. She initially developed radiation field localized blistering and erosions of the skin, before developing more widespread lesions. Immunofluorescence confirmed pemphigus vulgaris, which was responsive to corticosteroids. Pemphigus vulgaris is an autoimmune blistering disease of the skin that can rarely be associated with exposure to ionizing radiation.

INTRODUCTION

Breast cancer is the most common cancer in the UK population. Radiotherapy remains an important treatment modality in the treatment of breast cancer. Side effects from radiotherapy can be severe; however, in most cases, these are minor and short lived. Skin toxicity is a well-known side effect of radiotherapy. Exposure to ionizing radiation has been linked to the development of more severe skin eruptions, including the development of pemphigus vulgaris.

CASE REPORT

We present a case of a 72-year-old Caucasian female who underwent adjuvant chemoradiotherapy for a Grade 2 invasive ductal carcinoma of the left breast. She had no other significant past medical history, including dermatological history, and took no regular medications. She was a non-smoker and did not consume alcohol. Presenting from the national screening programme, she underwent a wide local excision with axillary lymph node clearance. Her tumor was estrogen receptor positive, HER2 negative and had 7/28 lymph nodes positive. Weekly paclitaxel treatments were stopped after four cycles due to anaphylactoid hypersensitivity. She underwent 40 Gy of radiotherapy in 15 fractions over 3 weeks to the left breast and left supraclavicular fossa. Before commencing radiotherapy, she had no noted skin changes.

Upon routine review 8 weeks post completion of radiotherapy, oedema and erythema with blistering and desquamation of the skin were noted over the left breast and chest wall. There was also an area of desquamation on the patient’s back consistent with a radiotherapy exit field. The patient had been using simple moisturizers as instructed and managing pain with simple analgesia. The skin changes were first apparent 4 weeks after completion of radiotherapy. Initially, the skin lesions were confined to the radiotherapy field. She was afebrile with otherwise normal observations. Differentials included radiation-induced skin changes with superimposed cellulitis, autoimmune bullous disorder or a paraneoplastic process. An admission for further treatment was organized where intravenous antibiotics and antivirals were commenced alongside a regular skin treatment regimen. This consisted of Viscopaste and Tubigrip, Hydromol and Dermovate ointment as required. An initial superficial skin swab showed mixed skin flora only.

Despite optimal medical management, her skin continued to deteriorate, with a new area of desquamation over the right hip. The patient also developed painful oral erosions. Serum samples for indirect immunofluorescence were requested and the patient was commenced on 40 mg of prednisolone once daily after a punch biopsy was performed. Biopsies revealed a...
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Figure 1: Desquamation of skin over radiotherapy exit field.

Figure 2: Moist desquamation of skin at presentation.

Figure 3: Radiation exit field after 6 weeks of high dose corticosteroids.

Figure 4: Improving lesions over the left breast 6 weeks after commencement of high dose steroids.

been no new skin blistering; however, oral ulceration remained problematic. Steroid mouth washes were added to her regime and the topical treatments were continued. Two months after initial diagnosis, a weaning regime of 5 mg per month of prednisolone was recommended after her oral lesions had completely resolved. Now 6 months after initial presentation, there has been no relapse of oral or skin lesions and corticosteroids continue to be weaned by 5 mg per week. All topical treatments have been discontinued.

DISCUSSION

We present a case of 72-year patient presenting with radiation-induced pemphigus 8 weeks after completion of a 3-week course of adjuvant radiotherapy. Radiation-induced pemphigus is a rare but potentially life-threatening treatment complication that can resemble many other skin conditions.

Acute radiation dermatitis is a well-recognized side effect of radiotherapy. Occurring within 90 days of treatment, symptoms can range from mild erythema to skin necrosis—all confined to radiotherapy fields [1]. When consenting for radiotherapy, patients are carefully assessed for conditions that can predispose to an increased risk of radiation dermatitis such as connective tissue disease, concurrent chemotherapy or past dermatological history. Following simple advice such as regular use of alcohol free, non-perfumed moisturizers can reduce the risk of developing radiation dermatitis [1]. Severe skin reactions can lead to early cessation of treatment and significant morbidity. Differential diagnoses for severe radiation dermatitis can include paraneoplastic pemphigus, pemphigus vulgaris, pemphigoid disease and other skin blistering dermatoses. Differentiation between these diagnoses can be determined using biopsy and blood samples [2].

Pemphigus vulgaris is a rare intra-epidermal autoimmune blistering disease caused by autoantibodies disrupting desmosomal attachments between keratinocytes. It is characterized by slow healing, irregular-shaped erosions. Over 80% of patients have circulating serum IgG autoantibodies detectable by indirect immunofluorescence. Direct immunofluorescence shows intercellular deposition of IgG in the suprabasal epidermis [3]. Untreated, pemphigus can be fatal with progressive blistering leading to secondary infections or considerable fluid and protein losses. In the UK, the incidence of pemphigus vulgaris is 0.7 per 100 000 with a mean age at presentation of 71 years [4].

Ionizing radiation therapy has been well documented to cause cutaneous reactions. Erythema, oedema and desquamation are common and are usually observed during radiation therapy and for several weeks after its completion.

Figure 5: Figure 5: Desquamation of skin over radiotherapy exit field.

Figure 6: Figure 6: Moist desquamation of skin at presentation.

negative direct immunofluorescence, with some increased mitotic activity indicating quick turnover of the epidermis. There was no superficial acantholysis suggestive of pemphigus foliaceus. Indirect immunofluorescence was positive for intercellular IgG antibodies and anti-desmoglein3 antibodies, consistent with a diagnosis of pemphigus (Figs 5 and 6).

Maintenance prednisolone was continued at 40 mg until review in dermatology outpatients 1 month later. There had
Longer term side effects usually consist of hyperpigmentation. Pemphigus appears to be a rare complication of radiation therapy, which has been highlighted in case reports [5]. Delaporte et al. [6] highlighted 13 cases of pemphigus following exposure to ionizing radiation, 12 of which had a pre-existing diagnosis of malignancy. Interestingly, a large number of case reports have involved patients with underlying breast carcinomas [6].

The mechanism by which ionizing radiation induces pemphigus vulgaris remains unknown. Hypotheses suggest it could relate to alterations to antigen distribution on keratinocyte membranes. Radiation could also interfere with immune surveillance by impairing T-suppressor cells [7]. An alternative theory developed following immunomapping of perilesional skin was suggestive of changes to the expression or distribution of desmoglein in the epidermis [8].

A literature review performed by Low et al. [9] suggests that ionizing radiation-induced pemphigus is not significantly different from endogenous pemphigus in terms of its response to standard medical management and outcomes remain similar.
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Interestingly, all cases identified by Low had a prodrome of apparent acute radiation dermatitis, which was present a number of weeks before skin eruptions developed. This would fit with the presentation of our case, with a latency period of ∼4 weeks before marked desquamation became apparent. Other cases of likely ionizing radiation-induced pemphigus have suggested a latency period of up to 14 months [10]. Furthermore, initial pemphigoid eruptions are often confined to areas of irradiation before becoming more generalized, as seen in our case with development of new eruptions over the hip. There has been no identified correlation between radiation doses and extent and severity of pemphigoid eruptions [10].

Management of pemphigus vulgaris can be considered in two main phases: induction of remission and maintenance of remission. Corticosteroids are the most rapidly acting and effective treatment for pemphigus, with disease control typically established in a median of 3 weeks [2]. Remission induction is defined as new lesions ceasing to form and existing lesions beginning to heal. Remission maintenance typically consists of tapering steroid doses and can be combined with immunosuppressive adjuncts such as azathioprine and mycophenolate. In broader pemphigus cases, initial relapse is high at ∼50% after 1 year [2]. The transferability of this relapse risk in patients whom have received radiotherapy is not known.

In summary, radiation-induced pemphigus is a rare but significant consequence of exposure to radiation therapy. The mechanism behind the pathophysiology remains unclear. The diagnosis should be considered all patients presenting with erosive or blistering skin disease with recent exposure to ionizing radiation. A thorough history and examination is imperative and early biopsy for histological analysis and direct immunofluorescence with serum samples for indirect immunofluorescence should confirm the diagnosis. Initiation and maintenance of high dose steroids lead to similar outcomes as those treated for endogenous pemphigus.

CONFLICT OF INTEREST STATEMENT
The author declares that they have no competing interests.

GUARANTOR
The author is the guarantor for this article.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE
The patient has consented for the use of personal health information including reports, test results, clinical images and radiology to be accessed and used for the purposes of publication as a medical case report.

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