

Localised Bullous Pemphigoid Following Radiotherapy

Sir,

Localised bullous pemphigoid (BP) is a rare complication of radiotherapy. There have been three documented cases (1–3) of BP developing in the irradiated area and several others in which the BP was initially localised before becoming disseminated (4–6). BP is known to be triggered by a number of factors including PUVA (7) and UVB (8). Pre-existing BP can also be exacerbated by radiotherapy (9). We report two patients who were treated with radiotherapy for known carcinoma of the breast and subsequently developed BP at the site of radiotherapy. Additionally, we describe the first case of BP occurring on a lymphoedematous arm following radiotherapy for carcinoma of the breast.

CASE REPORTS

Case 1

A 55-year-old Maltese woman presented with carcinoma of her left breast in 1983. This was treated with excision and subsequent radiotherapy. In 1985 radical axillary node clearance was carried out for recurrent disease, and she was commenced on tamoxifen therapy. Her treatment was complicated by the development of a lymphoedematous arm on the side of irradiation. The following year she presented with a number of itchy erythematous plaques with blistering, which were confined to the lymphoedematous left arm (Fig. 1) with no mucosal involvement.

Skin biopsy of an intact bulla revealed a subepidermal split with re-epithelialisation of its base. Eosinophils were present within the blister. Direct immunofluorescence showed linear IgG and C3 deposition along the basement membrane, consistent with a diagnosis of BP. There was remission with oral prednisolone (40 mg/day), but she subsequently defaulted from follow-up.

Case 2

A 56-year-old woman had received radiotherapy (4,600cGy) to the right breast and axilla in 1978 following a partial mastectomy. In



Fig. 1. Case 1 presented with erythematous plaques with blistering localised to the lymphoedematous arm.

1980 a total mastectomy for recurrent disease was performed, which was followed 3 years later by the development of lymphoedema and radionecrosis of the axilla. Ten years later blisters appeared, along with painful erosions around the radionecrotic area.

Histological examination of an intact blister showed subepidermal separation with the accumulation of eosinophils. Direct immunofluorescence showed a linear pattern of IgG and C3 deposition along the basement membrane. Saline split skin examination identified IgG and C3 localised to the epidermal side of the blister. Indirect immunofluorescence was negative. The localised BP was treated effectively with clobetasol propionate cream for a period of 3 months.

Case 3

A 78-year-old woman with breast cancer developed itchy, scaly, haemorrhagic and eroded areas over her breast (Fig. 2) 4 years after radiotherapy (5,000cGy). A biopsy revealed suprabasal eosinophilic spongiosis. Telangiectasia and bizarre fibroblasts were also present in the dermis, in keeping with previous radiotherapy. Again direct immunofluorescence findings were in keeping with BP. Indirect immunofluorescence confirmed the presence of circulating skin basement membrane antibodies. The BP responded well to 3 months of a reducing course of oral prednisolone.

DISCUSSION

Several reports have implicated cancer radiotherapy in the pathogenesis of BP (4–8). The time interval between radiotherapy and the development of BP is unpredictable. The median interval appears to be about 3 weeks, but the longest delay has been 3 years (11). A summary of the previous cases is outlined in Table I.

We have reported here three patients who developed BP confirmed both histologically and with direct immunofluorescence which was localised to the area of radiotherapy, (cases 2 and 3) or to the post-irradiated lymphoedematous arm (case 1). In the second case blisters developed 12 years after treatment, which is unusual when compared to previous cases.

To our knowledge, patient 1 is the first reported case of BP localised to a post-irradiated lymphoedematous arm. Callens et al. (12) reported a patient who developed localised cicatricial pemphigoid confined to the lymphoedematous arm 9 years after radiotherapy and 3 years after the onset of lymphoedema.

It is unclear how cutaneous radiation damage can precipitate



Fig. 2. Case 3 presented with haemorrhagic eroded areas over the breast following radiotherapy for carcinoma of the breast.

Table I. Case reports of bullous pemphigoid and radiotherapy

DXT = radiotherapy

Reference	Year	Age	Sex	Radiotherapy details	Onset of BP after DXT (days)	IgG	C ₃	BMZ Ab
Abadir ¹⁵	1967	53	M	DXT Ca Bronchus	Generalised (12)	-	-	-
Ive ¹¹	1963	39	F	Radium implant Ca cervix	Generalised 3 years	-	-	-
Emery ⁴	1967	53	M	DXT Ca Bronchus	Generalised itchy bullous eruption (13)	-	-	-
Furukawa ⁵	1981	77	M	DXT Ca Oesophagus	Immediate localised Generalised (120)	+	+	+
Ernst ¹	1982	79	F	DXT Ca Breast	Localised (120)	+	+	+
Duschet ⁶	1988	-	M	Electron beam SCC metastatic nodes	Localised immediate Generalised (7)	-	+	-
Bernhardt ²	1989	-	F	DXT Ca breast	Localised	?	?	?

BP. Several hypotheses have been put forward. Firstly, radiation may alter the basement membrane proteins, causing an unmasking locally of a new BP antigen that results in the production of antibodies producing localised lesions. This hypothesis could explain why it takes many years for the cutaneous radiation damage to progress and why there is a long delay between radiotherapy and the development of lesions.

Secondly, patients may already have circulating antibasement membrane antibodies at a low titre. The tissue changes caused by radiotherapy could enhance deposition of antibody at the basement membrane. In vitro studies have also shown that radiation results in an increase in basement membrane antibody binding in normal skin (9). This may explain why the indirect immunofluorescence was negative, whilst the more sensitive saline split skin technique was positive in case 2. Thirdly, radiation may cause immune dysregulation, resulting in inhibition of T-cell suppressor activity, thereby leaving T-cell helper function unopposed. This could result in the over-production of basement membrane antibodies locally.

The pathophysiology of PB affecting the lymphoedematous arm remains unknown. Disturbances in lymphatic drainage may influence local immunosurveillance. This mechanism is proposed to explain the increased number of primary tumours reported in association with lymphoedema (13). Whatever the cause, these three cases further support the evidence that radiotherapy either directly or indirectly may precipitate BP.

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Accepted January 15, 1996.

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