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Radiation induced lichen planus - an uncommon side effect

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Abstract

Cutaneous lichen planus classically is characterized by violaceous, pruritic, planar papules and plaques, most commonly affecting the extremities. Lichen planus following radiation therapy is extremely rare and lichen planus following radiation therapy for prostate carcinoma has not been previously reported in the literature. We report a 66-year-old man who presented to the dermatology clinic with a symmetric pruritic eruption affecting the pelvic and gluteal region within two months of radiation therapy targeting the prostate and pelvic lymph nodes for prostate adenocarcinoma. The patient did not have a prior history of lichen planus. Physical examination demonstrated well demarcated, violaceous papules and plaques in a circumferential band-like distribution on the bilateral gluteal, lumbosacral, and pelvic region. In addition, he had a few discrete lesions on the calves and dorsal feet. Punch biopsy revealed an acanthotic epidermis with "saw-tooth" rete ridges and a lichenoid inflammatory infiltrate. Α diagnosis hypertrophic lichen planus was made, reinforcing the importance for clinicians to recognize radiation therapy as a risk factor for developing lichen planus despite no prior history of lichen planus.

Keywords: lichen planus; radiation; prostate carcinoma

Introduction

Cutaneous reactions to radiation therapy include acute dermatitis, chronic dermatitis, keratosis-like nodules (called pseudorecidives), and lichen planus [1, 3]. Radiation-associated dermatitis may with erythematous, present edematous, desquamating, ulcerative, or fibrotic changes, pseudorecidives whereas present spontaneously resolving keratoses, which tend to appear immediately after irradiation [1, 2]. Cutaneous lichen planus is classically characterized by violaceous, pruritic, polygonal, planar papules and plaques, most commonly affecting the extremities [2]. In addition to the skin, lichen planus may affect the mucous membranes, hair, and nails [2]. The surface of the lesion often presents with a reticular pattern of fine, white streaks or punctations referred to as Wickham striae [2]. Lichen planus following radiation therapy is uncommon, and lichen planus radiation therapy for carcinoma has not been previously reported. We report a patient who developed hypertrophic lichen planus following radiation therapy for prostate adenocarcinoma.

Case Synopsis

A 66-year-old man presented to the dermatology clinic with a symmetric pruritic eruption of the

pelvic and gluteal region. He had been treated with radiotherapy for prostate adenocarcinoma and noted the skin lesions after about two months of the radiation therapy. Treatment consisted of primary radiotherapy with an initial 4400cGy to the prostate and pelvic lymph nodes (Figure 1), followed by a boost such that the prostate received a total of 7800cGy over 39 treatment sessions. Total skin dose was approximately 400cGy delivered over the 39 treatments for about 10cGy per treatment. The radiation treatment technique used for the high dose "boost" to the prostate gland was "Volumetric Modulated Arc Treatment" (VMAT), in which the treatment machine delivered a beam of radiation as it rotated around the patient. Volumetric Modulated Arc Treatment concentrated the prescription high dose on the internal target, the prostate, and delivered a small "entry" dose to the skin and internal tissue between the skin and the target (prostate). Historically, radiation treatment was delivered through static "ports" such that the dose was not spread out as much and one would expect more skin reaction at the skin site of the

Figure 1. Radiation targeted the prostate and pelvic lymph nodes with Volumetric Modulated Arc Treatment, in which the treatment machine delivered a beam of radiation as it rotated around the patient. Dosage ranged from approximately 400cGy (blue) to approximately 7700cGy (red) in the radiation field.

port. In this case, the VMAT technique kept the radiation entry dose acceptably low, below the usual threshold to trigger a skin reaction such as erythema. However, on analysis, the skin exposed to low dose radiation as the treatment machine rotated around the patient corresponded to the main areas of skin involvement. The patient's past medical history was significant for treated hepatitis C and he did not have any prior history of lichen planus.

Physical examination revealed well demarcated, violaceous papules and plaques in circumferential band-like distribution on the bilateral gluteal, lumbosacral, and pelvic region (Figure 2), with isolated lesions on the bilateral calves and dorsal feet. Punch biopsy demonstrated an acanthotic epidermis with "sawtooth" rete ridges, necrotic keratinocytes along the basal layer and scattered within the spinous layer, and a dense infiltrate of lymphocytes and melanophages that filled the papillary dermis and focally obscured the dermal-epidermal junction (Figure 3), consistent with a diagnosis of hypertrophic lichen planus. Hepatitis C RNA was negative.



Figure 2. Physical examination revealed well demarcated, violaceous papules and plaques in a circumferential bandlike distribution on the bilateral gluteal, lumbosacral, and pelvic region.

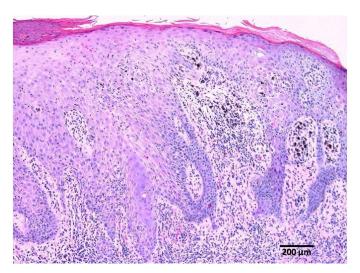


Figure 3. Histology demonstrated an acanthotic epidermis with "saw-tooth" rete ridges, necrotic keratinocytes along the basal layer and scattered within the spinous layer, and a dense infiltrate of lymphocytes and melanophages that fill the papillary dermis and focally obscure the dermal-epidermal junction (hematoxylin & eosin, original magnification x100).

Case Discussion

Risk factors for lichen planus include trauma, hepatitis, certain medications, autoimmune diseases, and malignancies [2]. Lichen planus following radiotherapy is extremely rare, and to the best of our knowledge, lichen planus following radiotherapy for prostate cancer has not been previously reported in the literature [3]. The cases of oncological radiotherapy-associated lichen planus reported in the English literature are summarized in **Table 1**. Upon review of the literature, including our case, the average age of onset was 58 years, and 54% (7/13) of patients were female [3-15], (Table 1). The average onset of lichenoid reaction was within three months of a mean total radiation dose of 50 Gy [3-15], (Table 1). Most cases reported a generalized distribution extending beyond the localized radiation field [3-5], (**Table 1**).

Although the pathophysiology of lichen planus has yet to be fully elucidated, an aberrant lymphocyte-mediated inflammatory reaction has been implicated in its pathogenesis [2, 3]. It has

been proposed that radiotherapy may induce a lichenoid reaction owing to cellular injury and release of keratinocyte self-antigens, thereby instigating a local inflammatory response [3, 10, 15]. This phenomenon is also referred to as radiation-induced koebnerization with isoradiotopic response [10, 15]. The locations of our patient's lesions correspond to the radiation port with minimal extension into the surrounding region; thus, radiation-induced koebnerization isoradiotopic response is the likely mechanism for our patient's condition.

Another mechanism that has been described in the literature is Wolf isotopic response, which is the new onset of a dermatosis in the same anatomic site as a previously resolved, different dermatosis [12]. For example, cases of lichen planus arising in a location that has previously been affected by herpes zoster dermatofibrosarcoma protuberans have been reported [12]. However, our patient had not experienced any notable skin lesions in the affected areas beforehand and his past medical history was negative for herpes zoster or varicella. Furthermore, although our patient's clinical presentation may resemble zosteriform lichen planus, the presenting distribution did not precisely follow sacral dermatomal distribution and zosteriform lichen planus usually presents unilaterally [16], unlike our patient.

As hepatitis C is also a risk factor, it is possible that our patient's history of hepatitis C may have played a contributory role to developing lichen planus in response to the precipitating event of radiation-associated trauma. Therefore, it is important for clinicians to gather a thorough patient history and recognize recent radiotherapy as an additional risk factor. Furthermore, owing to the risk of non-melanoma skin cancer associated with radiotherapy [1] and lichen planus [17], longitudinal follow-up for patients with radiation-associated lichen planus may be prudent.

Treatment of radiotherapy-associated lichen planus is consistent with any type of lichen planus [2, 3]. Topical corticosteroid, low-dose oral corticosteroid, or phototherapy are the recommended therapeutic options [2, 3].

recognize a recent history of radiation therapy as a risk factor for developing lichen planus. Correlating the sites of radiation with the distribution of skin lesions may help in diagnosing this uncommon entity.

Conclusion

Although lichen planus following radiation therapy is rare, it is important for clinicians to

Potential conflicts of interest

The authors declare no conflicts of interests.

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Table 1. Previously reported cases of lichen planus subsequent to oncological radiation therapy.

Age/		RT Dose	Post-RT				
Sex	Malignancy	(Gy)	LP Onset	LP Site	Treatment	Нер С	Ref
66/F	Lung carcinoma	30	1-2 weeks	Upper left back, bilateral lower limbs, hands, oral cavity	Betamethasone valerate ointment; 0.1%×6 weeks-3 months; triamcinolone acetonide mouthwash×3 months**	NS	[3]
64/F	Breast carcinoma, right breast	61	3 months; 13 months for right shoulder	Right axilla, lateral breast, IM fold, right shoulder	0.1% triamcinolone ointment 1-2x daily, 3x/week	NS	[4]
56/F	Breast carcinoma, right breast	50.4	Concurrent	Right breast, trunk, bilateral forearms, oral cavity	Initially topical ichthyol, followed by betamethasone propionate; topical tretinoin for oral lesions	Neg	[5]
44/F	Breast carcinoma, left breast	60	1 month	Left IM fold	0.05% clobetasol propionate×1 month	NS	[6]
59/F	Breast carcinoma, left breast	NS	NS	Left breast, arm, and thigh	0.1% triamcinolone acetonide ointment	Neg	[7]
67/F	Breast carcinoma metastasized to hepatic lymph node and cervical vertebrae (hepatic lymph node & cervical irradiated)	30 to hepatic; 30 to cervical vertebrae	5 weeks for mid- back; 4 weeks for extremities	Mid-back, lower extremities, hands	0.05% difluprednate ointment×8 weeks to midback; 0.05% clobetasol ointment to extremities → unresponsive → systemic corticosteroid; cessation of nivolumab	NS	[8, 9]
58/M	Thyroid carcinoma involving superior mediastinum	59.4	1 month	Neck, anterior chest	0.05% fluocinonide, 0.05% clobetasol propionate at unspecified times over 5 months	Neg	[10]
46/M	Nasopharyngeal carcinoma	66.8	2 months	Upper and lower lip, esophagus	Topical mometasone furoate; oral prednisone 30mg/day	Neg	[11]
48/F	Dermatofibrosarc oma protuberans, right lower back	50	5 months	Right lower back	0.05% clobetasol propionate ointment×8 weeks	NS	[12]
40/M	Diffuse large B- cell lymphoma of right knee	45	NS	Right knee, left foot	NS	NS	[13]
67/M	Extramedullary plasmacytoma (cranial vault irradiated)	45	3 months	Scalp, lip, trunk, glans penis	0.05% clobetasol propionate ointment, oral prednisolone 30 mg tapered×6 weeks	NS	[14]
68/M	Penile carcinoma	NS	2 months	Pubic and suprapubic regions, bilateral inguinal, right anteromedial thigh	Topical steroids	Neg	[15]

66/M	Prostate carcinoma	78	2 months	Bilateral gluteal, lumbosacral, pelvic regions	0.05% halobetasol ointment daily	Pos antibody; Neg RNA	Present case
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RT, radiotherapy; Gy, Gray; LP, lichen planus; Hep, hepatitis; Ref, reference; M, male; F, female; NS, not specified; IM, inframammary; Pos, positive; Neg, negative.

^{**}Patient had also received oral prednisolone followed by dexamethasone for unspecified duration to treat radiation pneumonitis and brain metastasis.