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Radiation induced lichen planus - an uncommon side effect

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Abstract
Cutaneous lichen planus is classically 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. A diagnosis of 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 present with erythematous, edematous, desquamating, ulcerative, or fibrotic changes, whereas pseudorecidives present as 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 following radiation therapy for prostate 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 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 a 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 “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 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 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.

Figure 2. Physical examination revealed well demarcated, violaceous papules and plaques in a circumferential band-like distribution on the bilateral gluteal, lumbosacral, and pelvic region.
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 an 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 with 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 or 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].

**Conclusion**

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

**Potential conflicts of interest**

The authors declare no conflicts of interests.

**References**

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

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

<table>
<thead>
<tr>
<th>66/M</th>
<th>Prostate carcinoma</th>
<th>78</th>
<th>2 months</th>
<th>Bilateral gluteal, lumbosacral, pelvic regions</th>
<th>0.05% halobetasol ointment daily</th>
<th>Pos antibody; Neg RNA</th>
<th>Present case</th>
</tr>
</thead>
</table>

RT, radiotherapy; Gy, Gray; LP, lichen planus; Hep, hepatitis; Ref, reference; M, male; F, female; NS, not specified; IM, inframammary; Pos, positive; Neg, negative.