**Transient acantholytic dermatosis in a patient with prostate cancer**

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**Abstract**

Transient acantholytic dermatosis (TAD) is a relatively common entity that has been also noted to occur in patients with cancer. Herein, we describe a case of transient acantholytic dermatosis occurring in a patient with a history of prostate cancer status post radiation, now being treated with combination therapy with pembrolizumab and carboplatin-pemetrexed for advanced lung adenocarcinoma. Our case emphasizes the importance of being cognizant of TAD and its associations, particularly in cancer patients.

Keywords: Transient-acantholytic dermatosis, TAD, immune-related adverse events, irAEs

**Introduction**

Transient-acantholytic dermatosis also known as transient acantholytic dermatosis occurs generally among Caucasian males (male-to-female ratio 2.4:1 with a mean age at diagnosis of 61 years) with an incidence of 0.8%. It presents clinically as a papulovesicular eruption on the trunk and proximal extremities [1]. Histologically, the disease manifests as small well-circumscribed foci of supra-basal acantholysis with dyskeratosis, a spongiotic epidermis, lymphohistiocytic interface dermatitis, and peri-vascular infiltrates [2]. The rash can be exacerbated by exercise, heat, sweat, ultra-violet light, friction, and malignancy.

Particularly in cancer patients, TAD has been reported to occur in four different settings: (1) idiopathic, (2) after antineoplastic therapy, (3) after radiation therapy, and (4) paraneoplastic. Peculiarly, as part of a paraneoplastic syndrome, the appearance of TAD has led to the detection of a co-existing malignancy or the resolution of TAD has coincided with a favorable response to therapy for that malignancy [3]. Predominantly hematological malignancies have been associated with TAD, occurring in 8% of cases [4]; reports of somatic malignancies associated with TAD are fewer in number (see Box 1).

On the other hand, in this era of an ever-expanding list of drugs used to treat advanced cancer, it is no...
suprise that the list of drugs associated with TAD also keeps growing. Drug-induced triggers known to precipitate TAD include interleukin-4 [5], D-penicillamine [5, 6], ribavirin [6], anastrozole [7], and anti-neoplastic drugs, including immunotherapy [2, 8-11], among many others (see Box 2). TAD has also been associated with 2-chlorodeoxyadenosine in patients being treated for hairy cell leukemia [3]. Given the multifactorial etiology of TAD, it is then important to be cognizant and familiar with this entity and its associations, particularly in managing cancer patients.

Box 2. Drugs associated with transient-acantholytic dermatosis.

<table>
<thead>
<tr>
<th>Anastrozole [7]</th>
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<tr>
<td>Penicillamine [5,6]</td>
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<tr>
<td>CTLA-4 inhibitors (ipilimumab) [2, 10-11]</td>
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<tr>
<td>PD-1/PDL-1 inhibitors (pembrolizumab) [8-9]</td>
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<tr>
<td>Ribavirin [6]</td>
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<tr>
<td>2-chlorodeoxyadenosine [4,36]</td>
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<tr>
<td>BRAF inhibitors (vemurafenib and dabrafenib) [37]</td>
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Shortly after initiation of the second cycle of combination therapy, the patient developed a generalized rash. Physical examination revealed a widespread painless polymorphic papulo-vesicular dermatosis on photo-distributed areas to include the upper back, chest, and upper extremities with intense pruritus and mild exfoliation; there was no notable improvement with oral benadryl and topical hydrocortisone (Figure 1). The patient reported no history of prolonged sun exposure, fever, infection, abundant sweating, autoimmune disease or a previous episode of TAD-like eruption. Skin biopsy of the lesions on the mid chest revealed focal vacuolar alteration of the dermal/epidermal junction with necrotic keratinocytes, lymphocytes, and rare eosinophils in the dermis (Figure 2). The epidermis also demonstrated multiple foci of superficial acantholytic dyskeratosis accompanied by keratinocyte dysmaturation and parakeratosis.

In this clinical context, the differential diagnosis was TAD versus drug eruption, including drug-induced TAD. The lesions were relatively asymptomatic and stable and treatment with combination therapy was continued owing to the mild severity of the rash. The patient was prescribed 0.1% topical triamcinolone cream to relieve pruritus and advised to avoid sun exposure. A close follow-up assessment eight days after initial presentation revealed that the rash was responsive to topical corticosteroids with complete resolution. No other therapy related adverse events were noted in the patient at that time.

Long term follow-up revealed that the patient had completed four cycles of combination therapy

Case Synopsis
We report a case of a 78-year-old man with a history of prostate cancer, status post radiation therapy and currently being treated with pembrolizumab and carboplatin-pemotrexed combination therapy for stage IV lung adenocarcinoma of the left lower lobe. The tumor cells were positive for PDL-1 with 40% expression analyzed via immunohistochemistry. Pertinent laboratory values were unremarkable with peripheral eosinophil counts being normal.
followed by maintenance pembrolizumab with an initial partial response followed by recent disease progression demonstrated by CT scans. No recurrence of a rash or a dermatologic immune-related adverse event (irAE) have been reported since the initial skin biopsy in 2017. Given that the patient was not a good candidate for aggressive cytotoxic therapy and recent disease progression, hospice care was recommended owing to failure to thrive.

**Case Discussion**

Given that our patient had multiple cancers and was currently receiving anti-neoplastic therapy, the possibility of drug-induced TAD was clinically raised because a wide range of irAEs have been associated with both anti-CTLA-4 and anti-PD-1/PDL-1 inhibitors [8, 12-24]. In particular, TAD-like irAEs have been previously reported in patients treated with both ipilimumab [2, 10-11] and PD-1/PDL-1 inhibitors [8, 9], but are rare events. In our case however, the fact that the patient’s rash resolved despite continuation of combination therapy and the patient did not develop a TAD-like rash despite subsequent cycles of combination therapy followed by maintenance pembrolizumab favors that the eruption was not drug induced. Given that TAD is a known association in multiple different settings in cancer patients, this finding is not surprising, but invariably helpful for patient management.

**Conclusion**

Our case demonstrates that it is important to be aware of TAD and its association within a variety of cancer settings, particularly with the ever-expanding list of therapies being used to treat advanced cancers. More importantly, the need for active dermatological surveillance and close follow-up has become ever more important in such patients, often requiring clinicopathological correlation to ultimately dictate clinical management.

**Potential conflicts of interest**

The authors declare no conflicts of interests.

**References**


