Characterization of cutaneous adverse events associated with PD-1 and PD-L1 inhibitors: A retrospective, single-institutional study

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Introduction

- PD-1 and PD-L1 inhibitors represent an increasingly important form of immunotherapy for various forms of metastatic and locally-aggressive cancers.
- Despite demonstrating promising results in various clinical and research settings, the prevalence, clinical presentation, and appropriate treatment regimen for the cutaneous adverse events related to their use are only partially characterized

Methods

- We conducted a retrospective analysis of the electronic medical records of a tertiary academic medical center with a dedicated supportive oncodermatology service.
- All 642 patients who received PD-1 or PD-L1 immunotherapy from 2016-2019 were included.
- Method of diagnosis, treatment, and outcomes of cutaneous adverse events were recorded, in addition to the specialty of diagnosing provider. Patient demographics, including gender, race, and ethnicity were summarized.

Results

- 26 cases demonstrated certain or probable adverse effects related to PD-1 or PD-L1 therapy.
- Eruptions consisted of lichenoid eruptions (4, 14.8%), psoriasis (4, 14.8%), vitiligo (3, 11.1%), eczema (3, 11.1%), morbilliform drug eruptions (3, 11.1%), pruritus (2, 7.4%), blistering disease (2, 7.4%), lichen sclerosus et atrophicus (1, 3.7%), cutaneous sarcoidosis (1, 3.7%), xerosis (1, 3.7%), and other (3, 11.1%).
- Cases classified as 'other' consisted of unusual morphologies without distinct classic nomenclature.
- While few patients with a known history of a prior dermatosis such as psoriasis flared with initiation of immunotherapy, the majority of patients presented with a new skin problem
- More significant manifestations such as blistering disorders required cessation of therapy, however multiple patients were able to have concurrent therapy

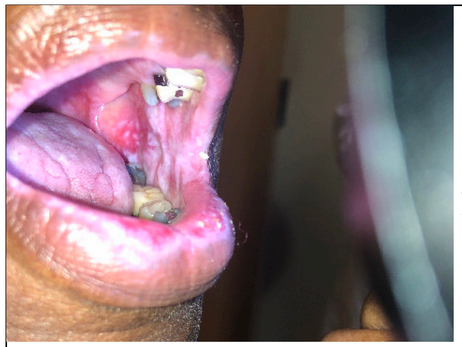

Figure A. Mucosal lichenoid dermatitis in setting of pembrolizumab

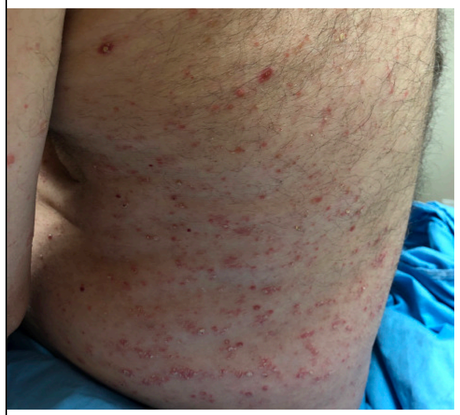

Figure B. Psoriasis in setting of pembrolizumab

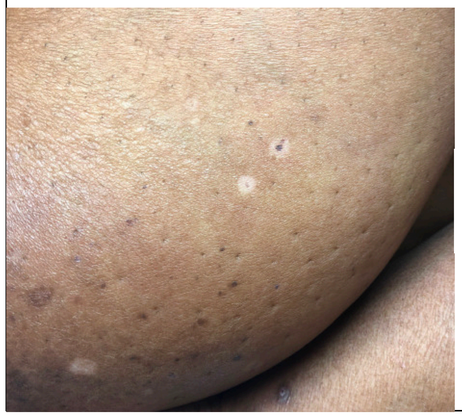

Figure C. Vitiligo in setting of nivolumab

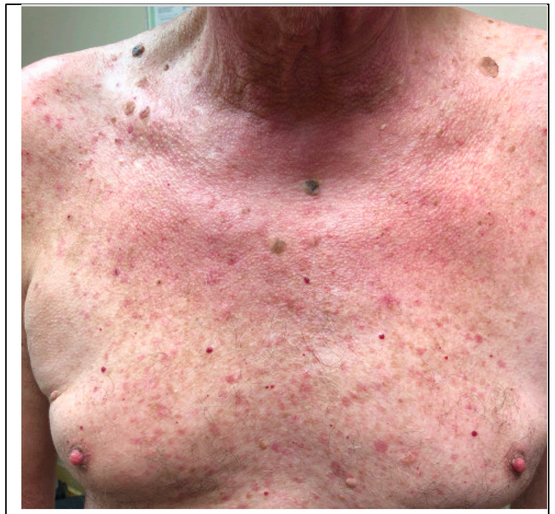

Figure D. Morbilliform eruption in setting of nivolumab/ ipilimumab

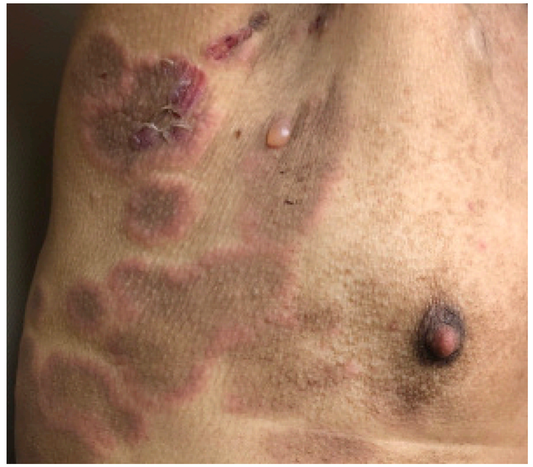

Figure E. Autoimmune blistering disease in setting of pembrolizumab

Discussion

- PD-1 and PD-L1 inhibitors are innovative new treatments in the treatment of multiple cancers however there is a growing body of literature describing their spectrum of cutaneous adverse events
- Previously published literature describes lichenoid, eczematous, psoriasiform, bullous, and morbilliform eruptions. Our data shows that the most common presentations consisted of lichenoid and psoriasiform eruptions, comprising 14.8% of cases each.
- The most severe presentations consisted of the bullous disorders. One patient presented with direct immunofluorescence confirmed bullous pemphigoid exacerbating a previous history of psoriasis. The second patient, show in Figure E, presented clinically with bullous pemphigoid however an indirect immunofluorescence was more consistent with a mixed pemphigus or paraneoplastic pemphigus spectrum.

Conclusions

- Clinicians, particularly in oncology and dermatology, should be aware of the wide spectrum of cutaneous adverse events associated with PD-1 and PD-L1 inhibitors as their growing use in oncologic management will likely increase their frequency of presentation.
- Diagnosis hinges on history, clinical assessment, and potentially histopathology as well.
- Close interdisciplinary care will be essential in ensuring a patient receives optimal oncologic management while also caring for their possible cutaneous adverse events.

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