



Pembrolizumab-Induced Neutrophilic Dermatitis of the Dorsal Hands

Rabia Z Mayer^{1*}, George Ansstas² and Milan J Anadkat¹

¹Division of Dermatology, Washington University School of Medicine, USA

²Division of Oncology, Washington University School of Medicine, USA

Abstract

The prognosis for advanced and metastatic malignancies has been significantly altered due to the use of check point inhibitors. Due to the activation of CD4+/CD8+ cytotoxic T-cells, these drugs have a unique spectrum of adverse effects, of which cutaneous manifestations are the most common. This case report describes the first instance of pembrolizumab-induced neutrophilic dermatitis of the dorsal hands, a rare and localized variant of Sweet's syndrome in a patient being treated for metastatic melanoma.

Introduction

The use of immune checkpoint inhibitors has revolutionized the therapeutic approach for advanced malignancies. Pembrolizumab is a monoclonal antibody targeted against programmed cell death protein-1 (PD-1) which was initially approved in 2015 for unresectable or metastatic melanoma [1]. Due to its unique mechanism of action, immune related adverse effects may result, with cutaneous adverse effects being the most prevalent [2]. The morphology of cutaneous eruptions that have been reported vary. Most commonly, eczematous, psoriasiform, or lichenoid dermatoses occur, each with underlying pruritus. In addition, autoimmune reactions such as vitiligo, alopecia areata, dermatomyositis, and bullous pemphigoid have been reported [2]. Here we report a case of Neutrophilic Dermatitis of the Dorsal Hands (NDDH) as a novel cutaneous adverse effect of pembrolizumab.

Case Presentation

A 63 year old male with a history of recurrent and metastatic desmoplastic melanoma receiving treatment with pembrolizumab for six months presented with a two-week history of an exquisitely painful rash on the dorsal hands. The patient reported using topical silver sulfadiazine for the past two days without significant improvement. Physical exam revealed tender, erythematous, ulcerated and bullous plaques over the dorsum of both hands (Figure 1). A punch biopsy was performed, revealing a diffuse infiltrate of neutrophils throughout the upper part of the dermis with subepidermal edema (Figure 2). Staining for microorganisms and fungi was negative, and a diagnosis of neutrophilic dermatitis of the hands was confirmed. A complete blood count revealed neutrophilia and leukocytosis. Of note, the patient did not endorse any fever.

The patient was started on high dose oral steroids (prednisone 60 mg daily) and follow up in a week revealed significant improvement (Figure 3), at which point a rapid taper over the ensuing two weeks was instituted along with initiation of dapsone, with no evidence of relapse on subsequent clinic visits.

Discussion

Neutrophilic dermatitis of the dorsal hands is considered a localized and rare subtype of acute febrile neutrophilic dermatitis (Sweet's syndrome). It was first described in 1995 as a pustular vasculitis [3] and later renamed based on the dense neutrophilic infiltrate ubiquitously present in the dermis without vasculitis being a constitutive feature [4]. While several cases of Sweet's syndrome have been documented with the use of ipilimumab (CTLA-4 inhibitor) (Table 1), no documented evidence of localized acral variants occurring with pembrolizumab exist in the literature thus far.

Activated T-cells can be inactivated by the interaction of programmed cell death 1 (PD-1) with its ligand (PD-L1) that is expressed in peripheral tissues and tumors [5]. Immune checkpoint inhibitors like pembrolizumab serve to inhibit PD-1, thereby promoting anti-tumor activity *via*

OPEN ACCESS

*Correspondence:

Milan J. Anadkat, MD, Division of Dermatology, Washington University School of Medicine; 660 S Euclid Ave, Box 8123; St. Louis, MO 63110, Missouri, USA; Email: manadkat@wustl.edu

Received Date: 31 Jul 2020

Accepted Date: 21 Aug 2020

Published Date: 24 Aug 2020

Citation:

Mayer RZ, Ansstas G, Anadkat MJ. Pembrolizumab-Induced Neutrophilic Dermatitis of the Dorsal Hands. *Oncol Case Report J.* 2020; 3(2): 1024.

Copyright © 2020 Rabia Z Mayer. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 1: Erythematous, ulcerated and bullous plaques over the bilateral dorsal hands.

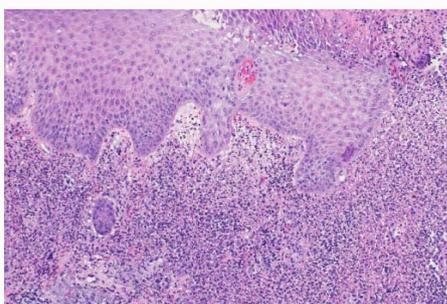


Figure 2: Punch biopsy showing subepidermal edema with diffuse neutrophilic infiltrate.



Figure 3: Significant improvement with minimal residual erosions and erythema over dorsal hands after seven days of 60 mg prednisone.

Table 1: Reported cases of sweet's syndrome occurring with checkpoint inhibitors.

Tumor type	Checkpoint inhibitor used	Area affected	Treatment
Melanoma	Ipilimumab	Diffuse	Prednisone [9]
Melanoma	Ipilimumab	Face and arms	Prednisone and dapsone [10]
Melanoma	Ipilimumab	Hands	Methylprednisolone [11]
Ovarian cancer	Ipilimumab	Diffuse	None [12]

activation of CD4+/CD8+ cytotoxic T-cells. Cutaneous side effects seem to be the most prevalent immune related adverse effect of this class of medication, affecting more than 30% of the patients being treated, irrespective of their underlying malignancy [6,7]. Existing

literature on neutrophilic dermatosis of the dorsal hands elucidates most common associations with hematologic malignancies, solid organ tumors, inflammatory bowel disease or antecedent infections [8]. This case is the first report of NDDH induced by pembrolizumab.

It is important for dermatologists and oncologists to be aware of this entity as this clinical presentation may commonly be misdiagnosed as an infectious process, which could result in undue cessation of therapy for advanced or metastatic disease. Most cases of neutrophilic dermatoses are highly sensitive to treatment with systemic steroids as was illustrated in our case as well as steroid-sparing agents like dapsone, colchicine and tetracyclines with good prognosis overall.

Acknowledgement

We thank Dr. Aaron Russell for his help in obtaining pathology images.

References

- Barone A, Hazarika M, Theoret MR, Mishra-Kalyani P, Chen H, He K, et al. FDA approval summary: Pembrolizumab for the treatment of patients with unresectable or metastatic melanoma. *Clin Cancer Res.* 2017;23(19):5661-5.
- Sibaud V. Dermatologic reactions to immune checkpoint inhibitors: Skin toxicities and immunotherapy. *Am J Clin Dermatol.* 2018;19(3):345-61.
- Strutton G, Weedon D, Robertson I. Pustular vasculitis of the hands. *J Am Acad Dermatol.* 1995;32(2 Pt 1):192-8.
- Galaria NA, Junkins-Hopkins JM, Kligman D, James WD. Neutrophilic dermatosis of the dorsal hands: Pustular vasculitis revisited. *J Am Acad Dermatol.* 2000;43(5 Pt 1):870-4.
- Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer.* 2012;12(4):252-64.
- Curry JL, Tetzlaff MT, Nagarajan P, Drucker C, Diab A, Hymes SR, et al. Diverse types of dermatologic toxicities from immune checkpoint blockade therapy. *J Cutan Pathol.* 2017;44(2):158-76.
- Naidoo J, Page DB, Li BT, Connell LC, Schindler K, Lacouture ME, et al. Toxicities of the anti-PD-1 and anti-PD-L1 immune checkpoint antibodies. *Ann Oncol.* 2015;26(12):2375-91.
- Micallef D, Bonnici M, Pisani D, Boffa MJ. Neutrophilic dermatosis of the dorsal hands: A review of 123 cases. *J Am Acad Dermatol.* 2019;S0190-9622(19)32678-7.
- Gormley R, Wanat K, Elenitsas R, Giles J, McGettigan S, Schuchter L, et al. Ipilimumab-associated sweet syndrome in a melanoma patient. *J Am Acad Dermatol.* 2014;71(5):e211-3.
- Kyllo RL, Parker MK, Rosman I, Musiek AC. Ipilimumab-associated sweet syndrome in a patient with high-risk melanoma. *J Am Acad Dermatol.* 2014;70(4):e85-6.
- Pintova S, Sidhu H, Friedlander PA, Holcombe RF. Sweet's syndrome in a patient with metastatic melanoma after ipilimumab therapy. *Melanoma Res.* 2013;23(6):498-501.
- Hodi FS, Butler M, Oble DA, Seiden MV, Haluska FG, Kruse A, et al. Immunologic and clinical effects of antibody blockade of cytotoxic T lymphocyte-associated antigen 4 in previously vaccinated cancer patients. *Proc Natl Acad Sci U S A.* 2008;105(8):3005-10.