

Psoriasiform eruption on the face and extremities associated with nivolumab therapy



Amit Om, MD,^a Brandon Cardon, BS,^b and George Cohen, MD^a
Tallahassee, Florida

Key words: drug eruption; nivolumab; psoriasis.

INTRODUCTION

Nivolumab is an IgG4 anti-programmed cell death protein 1 monoclonal antibody, part of a newer class of drugs known as *immune checkpoint inhibitors*.¹ Nivolumab has been approved for use in previously treated patients with non-small cell lung cancer, renal cell carcinoma, and metastatic melanoma and is in the advanced stages of development for the treatment of squamous cell carcinoma of the head and neck, urothelial cancer, gastric cancer, glioblastoma, and other lung cancers.¹⁻³

The blockage of the programmed cell death protein 1 pathway has been linked to promotion of autoimmune reactivity such as colitis and autoimmune thyroiditis,⁴ and several types of cutaneous reactions occurred with the use of nivolumab—most commonly lichenoid reactions, eczema, vitiligo, and pruritus.⁵ These reactions are usually mild and self-limiting.⁶ Less commonly, actinic keratoses, seborrheic keratoses, and squamous cell carcinomas have been reported as adverse cutaneous events.⁵ To our knowledge, only a few cases of psoriasis induction or exacerbation have been reported with the use of nivolumab.⁶

CASE REPORT

A man in his 60s with stage IV lung cancer diagnosed in February 2016 presented to the dermatology clinic in August 2017 with an eruption on his face, arms, and legs. The eruption was nonpruritic, nonpainful, and otherwise unbothersome to the patient, except for the appearance. The patient underwent lobectomy of his right lung in February 2016 with adjunctive nivolumab treatment beginning

in March 2016. He was scheduled to receive an infusion every 2 weeks by his oncologist. The patient presented to the clinic 1 week after his most recent treatment, with the eruption beginning few days before presentation. Physical examination found a well-defined, erythematous plaque involving the medial cheeks and spanning across the nasal bridge with appreciated scale and on his right lateral arm, a well-defined, scaly, pink plaque with overlying crust. No nail changes were noted.

Medications included atorvastatin, 40 mg daily, and metformin, 500 mg twice daily, in addition to nivolumab infusions every 2 weeks. The patient was unaware of any drug allergies and denied any previous personal or family history of psoriasis.

Two punch biopsies were performed. On the right upper arm, histology found irregular acanthosis with mild spongiosis, diminution of the granular cell layer, and abundant neutrophils in the cornified layer. In the dermis, a perivascular lymphocytic inflammatory infiltrate with numerous eosinophils was appreciated. Periodic acid-Schiff test was negative for fungal elements and Gram stain was negative for bacteria. The left cheek biopsy displayed similar findings, with additional subcorneal pustules. Antinuclear antibody test result was negative (Figs 1 and 2).

The patient was prescribed triamcinolone ointment 0.1% for his arm, hydrocortisone cream 2.5% for the face, and a methylprednisolone dose pack and told to follow up in approximately a week for suture removal. The eruption was controlled with the aforementioned combination of topical and oral steroids.

From Florida State University Division of Dermatology^a and Florida State University College of Medicine.^b

Funding sources: None.

Conflicts of interests: None declared.

Correspondence to: Amit Om, MD, 1632 Riggins Road, Building E, Tallahassee, FL 32308. E-mail: Amitom4@gmail.com.

JAAD Case Reports 2018;4:373-5.

2352-5126

© 2017 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2017.11.014>

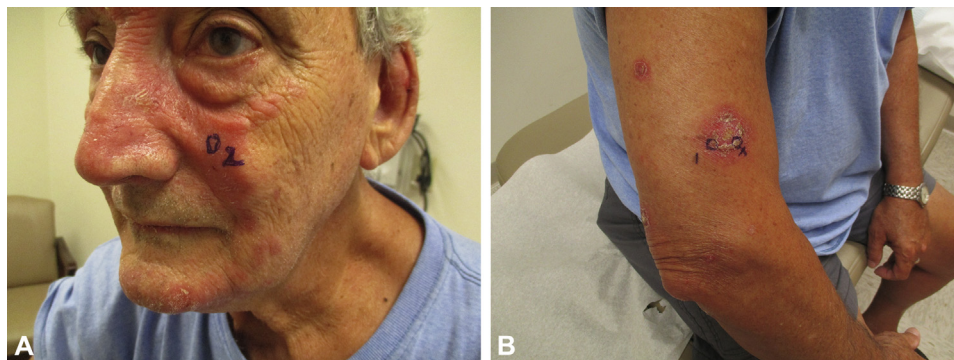


Fig 1. **A**, A well-defined, erythematous plaque involving the medial cheeks and spanning across the nasal bridge. **B**, A well-defined, scaly, pink plaque with overlying crust on the right lateral arm.

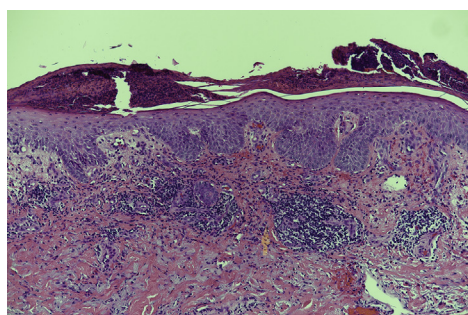


Fig 2. Punch biopsy from right lateral arm shows irregular acanthosis with mild spongiosis, diminution of the granular cell layer, and abundant neutrophils in the cornified layer with eosinophils in the dermis.

DISCUSSION

Psoriasis occurrence or exacerbation as a result of nivolumab is a rare but reported dermatologic complication in the current literature. Sibaud et al⁶ reviewed the use of nivolumab and its cutaneous adverse effects and concluded that immunotherapy could be continued in most cases, and the psoriasis outbreak can be treated with topical steroids, vitamin D₃ analogues, and retinoids. Patients most frequently reported asymptomatic plaques on the trunks and limbs. Less commonly, there have been reports of palmar involvement and plaques in skin fold regions consistent with inverse psoriasis.⁶ No reports of psoriatic plaques on the face have been reported.

A review of the literature found one reported case in which a patient treated for oral mucosal melanoma with metastases to the lungs with a history of psoriasis vulgaris developed an exacerbation of his psoriatic condition.² Another case of de novo psoriasis was observed in an 80-year-old man treated for primary mucosal melanoma. He had no personal or family history of psoriasis. The eruption developed

on his trunk and extremities.⁷ Lastly, in another patient with no prior or family history of psoriasis treated with nivolumab for metastatic squamous non-small cell lung cancer, psoriatic skin lesions developed on the legs and arms.⁸ He was also found to have psoriatic arthritis based on his clinical presentation. In all of these cases, the distributions of the rashes were consistent with the clinical presentation of plaque psoriasis and, notably, spared the face.

Our case adds to the growing body of knowledge of possible cutaneous adverse effects associated with nivolumab. Specifically, no facial plaques consistent with a psoriasiform eruption associated with nivolumab have been described to the authors' knowledge. The differential diagnosis for our patient included lupus vulgaris, drug-induced lupus, psoriasis, and of course, drug reaction. Given the well-defined plaques with scale plus the pathology findings of eosinophils in combination with the subcorneal pustules, we feel this is a drug-related psoriasiform eruption related to the patient's use of nivolumab. Antinuclear antibody test result was negative, and biopsy found no granulomas, thus reducing the likelihood of drug-induced lupus and lupus vulgaris, respectively. With the increasing use of immune checkpoint inhibitors in dermatology, it is important to recognize side effects, especially dermatologic ones.

REFERENCES

1. Vivar KL, Deschaine M, Messina J, et al. Epidermal programmed cell death-ligand 1 expression in TEN associated with nivolumab therapy. *J Cutan Pathol*. 2017;44(4):381-384.
2. Kato Y, Otsuka A, Miyachi Y, Kabashima K. Exacerbation of psoriasis vulgaris during nivolumab for oral mucosal melanoma. *J Eur Acad Dermatol Venereol*. 2016;30(10):e89-e91.
3. Medina PJ, Adams VR. PD-1 pathway inhibitors: immuno-oncology agents for restoring antitumor immune responses. *Pharmacotherapy*. 2016;36(3):317-334.
4. Nonomura Y, Otsuka A, Ohtsuka M, Yamamoto T, Dummer R, Kabashima K. ADAMTSL5 is upregulated in melanoma tissues in

- patients with idiopathic psoriasis vulgaris induced by nivolumab. *J Eur Acad Dermatol Venereol*. 2017;31(2):e100-e101.
- Collins LK, Chapman MS, Carter JB, Samie FH. Cutaneous adverse effects of the immune checkpoint inhibitors. *Curr Probl Cancer*. 2017;41(2):125-128.
 - Sibaud V, Meyer N, Lamant L, Vigaros E, Mazieres J, Delord JP. Dermatologic complications of anti-PD-1/PD-L1 immune checkpoint antibodies. *Curr Opin Oncol*. 2016;28(4):254-263.
 - Ohtsuka M, Miura T, Mori T, Ishikawa M, Yamamoto T. Occurrence of psoriasiform eruption during nivolumab therapy for primary oral mucosal melanoma. *JAMA Dermatol*. 2015; 151(7):797.
 - Law-Ping-Man S, Martin A, Briens E, Tisseau L, Safa G. Psoriasis and psoriatic arthritis induced by nivolumab in a patient with advanced lung cancer. *Rheumatology*. 2016; 55(11):2087-2089.