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CORRESPONDENCE

Macular-type cutaneous adverse reaction due to atezolizumab and pembrolizumab

Dear Editor,

Anti-PD-1-/PD-L1-targeted therapy is widely used for the treatment of various intractable malignancies and develops the therapeutic option in the frontier fields of oncology treatment.[1,2] On the contrary, these immune checkpoint therapies sometimes develop an undesirable adverse reaction as a result of activation of immune reaction to various organs.[3,4] A cutaneous adverse reaction is a representative immune checkpoint treatment-mediated reaction.[3] Herein, we report a case of cutaneous adverse reactions during PD-1-/PD-L1-targeted treatment in both atezolizumab and pembrolizumab in a patient with lung cancer.

A 68-year-old man noticed erythematous plaques and papules on his trunk and extremities 4 days after first atezolizumab administration for the treatment of his right lung adenocarcinoma clinical stage IV, and his skin eruption gradually developed. On physical examination, erythematous plaques were localized in trunk and extremities without the involvement of the mucosal membrane (Figure 1A). A skin biopsy revealed liquefaction and spongiosis in the epidermis and lymphocyte infiltration in the dermis (Figure 1B). After the treatment with an antihistamine agent, topical application of betamethasone dipropionate, and the discontinuation of additional administration of atezolizumab, his skin eruption was gradually improved without recurrence of skin eruption. As an alternative treatment for his lung cancer, pembrolizumab was next administrated; however, he again recognized erythematous plaques on trunk and extremities after the first administration of pembrolizumab (Figure 1C). The second time cutaneous adverse reaction was more widely spread in his whole body. A skin biopsy again revealed that spongiosis and inflammatory infiltration in the interface of epidermis and dermis (Figure 1D). After the antihistamine agent, topical application of betamethasone dipropionate, and the discontinuation of additional pembrolizumab administration, his skin eruption was improved in several days.

One of the unique characteristics of this case was to cause similar cutaneous adverse reactions by the different action point targeted treatment, PD-1 and PD-L1. Although the detailed molecular mechanism remains unclear in our case, we thought 3 possible mechanisms to cause cutaneous adverse reaction by both atezolizumab and pembrolizumab. The first reason is that atezolizumab and pembrolizumab have same additives in the drug, such as L-histidine, white soft sugar, and polysorbate. In particular, polysorbate includes

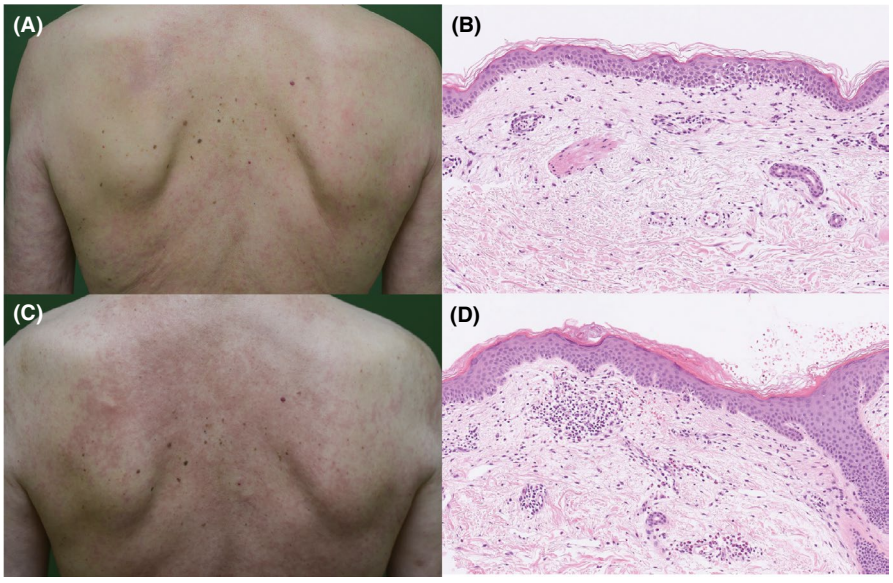

FIGURE 1 Clinical manifestations and histological examinations. (A) The clinical manifestation of cutaneous adverse reaction during atezolizumab treatment and (B) H&E histological examination (×10). (C) The clinical manifestation of cutaneous adverse reaction during pembrolizumab administration and (D) H&E histological examination (×10)

in various drugs and influenza vaccine and is known to cause allergic reaction in some cases.[5,6] Therefore, we speculated that cutaneous allergic reaction to polysorbate might be enhanced by atezolizumab and pembrolizumab. The second reason is another drug contribution to cause adverse reaction. However, he ordinally continued to intake acetaminophen without cutaneous adverse reaction. The third reason is atezolizumab and pembrolizumab might become a trigger to cause a cutaneous autoimmune-like reaction. Because skin eruption is relatively mild form and is improved by topical corticosteroid application and oral antihistamine agent, it seemed to be easy to recover his skin eruption even if his skin eruption is an autoimmunity-related skin eruption. Taken together, clinicians should keep in mind that adverse reaction might occur after switching into another anti-PD-1-/PD-L1-related inhibitor.

DECLARATION SECTION

Approval of the research protocol: No human participant was involved in this study.

Informed Consent: N/A.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

Hitomi Sugino MD
Yu Sawada MD, PhD
Motonobu Nakamura MD, PhD

Department of Dermatology, University of Occupational and Environmental Health, Fukuoka, Japan

Correspondence
Yu Sawada, Department of Dermatology, University of Occupational and Environmental Health, 1-1, Iseigaoka, Yahatanishi-Ku, Kitakyushu, Fukuoka, 807-8555, Japan.
Email: long-ago@med.uoeh-u.ac.jp

ORCID

Yu Sawada https://orcid.org/0000-0001-8793-708X

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