

Stevens-Johnson Syndrome Induced by Pembrolizumab in a Lung Cancer Patient



Naoki Haratake, MD, PhD,^a Tetsuzo Tagawa, MD, PhD,^{a,*} Fumihiko Hirai, MD, PhD,^a Gouji Toyokawa, MD, PhD,^a Reiko Miyazaki, MD, PhD,^b Yoshihiko Maehara, MD, PhD^c

^aDepartment of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

^bDepartment of Dermatology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

^cKyushu Central Hospital, Fukuoka, Japan

Received 4 May 2018; accepted 23 May 2018

Available online - 4 June 2018

Case Presentation

The case patient was 69-year-old male smoker who was receiving first-line treatment with pembrolizumab for postoperative recurrence of lung adenocarcinoma. Twelve days after the first administration of pembrolizumab, the patient experienced a fever and tiredness. Three days later, the patient was readmitted to our hospital because of a continuous high fever (39.0°C) and severe cough, with markedly increased indicators of an inflammatory response (C-reactive protein level 29.4 mg/dL). In addition, he had lost his appetite at the same time because of painful erosion of the oral mucosa (Fig. 1A). Whole body computed tomography showed no abnormal findings, and the results of all bacteriologic cultures of his blood, urine, and sputum were negative. A few localized skin lesions presenting with varicella were seen on both upper arms (Fig. 1B–D). Two days after the patient was hospitalized, his bulbar and palpebral conjunctivas showed painful intense congestion (Fig. 1E). In addition, an ophthalmic examination demonstrated significant pseudomembrane formation. Given these findings and the patient's history, Stevens-Johnson syndrome (SJS) induced by pembrolizumab was clinically diagnosed. A pathological examination of the small skin lesion showed prominent keratinocytic necrosis and acantholytic bullae (Fig. 2). The pathological diagnosis was also SJS. The patient was treated with oral prednisolone and dexamethasone/levofloxacin eye drops. After 30 days of internal and external corticoid treatment, his clinical symptoms and the eye lesions gradually improved.

Discussion

Immune checkpoint inhibitors such as pembrolizumab and nivolumab have been demonstrated to

prolong survival of patients with lung cancer. Cutaneous adverse reactions associated with immune checkpoint inhibitors are relatively common; however, most are not severe, and Common Terminology Criteria for Adverse Events grade 3 and 4 of the skin are rare, especially in lung cancer. Although the mechanism underlying anti-programmed death 1 treatment inducing SJS or toxic epidermal necrolysis remains unclear, the blockade of programmed death 1 and programmed death ligand 1 binding might result in loss of T-cell homeostasis within the skin or mucosa of the eyes or oral cavity, leading to the failure of immune tolerance and self-directed cytotoxic reactions.¹ Among patients with lung cancer, two cases of nivolumab-induced SJS have been reported in the literature.^{2,3} To our knowledge, ours is the first report of a patient with lung cancer in whom SJS developed during pembrolizumab treatment.

The diagnosis of SJS or toxic epidermal necrolysis is based on the clinical and histologic findings in a patient with a history of antecedent drug exposure. The histologic findings of a skin biopsy are supportive but not essential. The oral mucosa is typically involved, and ocular involvement has been reported in approximately 80% of patients with SJS. In the current case, there were a few skin lesions and the diagnosis of SJS

*Corresponding author.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Tetsuzo Tagawa, MD, PhD, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. E-mail: tetagawa@yahoo.co.jp

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ISSN: 1556-0864

<https://doi.org/10.1016/j.jtho.2018.05.031>



Figure 1. The oral mucosa had painful erosions (A). A few localized skin lesions presenting with itchy papules were seen on both the right (B and D) and left upper arms (C). The bulbar and palpebral conjunctivas showed painful intense congestion (E).

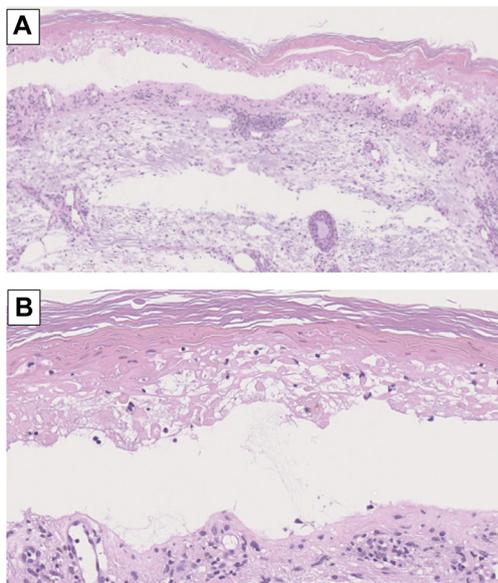


Figure 2. A biopsy of the skin lesion showed prominent keratinocytic necrosis, acantholytic bullae, and infiltration of lymphocytes and eosinophils (hematoxylin and eosin; original magnifications, $\times 40$ [A] and $\times 100$ [B]).

was difficult to achieve solely on the basis of the findings of the oral cavity and eyes. Given the risk of ablesia and the mortality of SJS (1%–3%), early diagnosis of SJS is very important. To this end, the oral mucosa and the bulbar and palpebral conjunctivas of patients with NSCLC should be observed carefully after administration of pembrolizumab.

Acknowledgments

We thank Brian Quinn for providing critical comments on the manuscript.

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