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A Case of Pityriasis Lichenoides et Varioliformis Acuta-Like Eruption Developed after Pembrolizumab Treatment for Invasive Thymoma

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Dear Editor:

Immune checkpoint inhibitors are considered promising agents for various malignancies[1]. However, a significant percentage of patients treated with immune checkpoint inhibitors have experienced diverse cutaneous adverse events (AEs)[1-3].

A 51-year-old male patient with invasive thymoma was referred to our department for a 2-week history of non-pruritic erythematous to purpuric macules and papules (Fig. 1A). The eruption began on the trunk 1 week after the first infusion of pembrolizumab, along with cough and fever (39.1°C). In spite of empirical antibiotics combined with prednisolone (20 mg daily) for nine days, the skin lesions continuously spread to the entire trunk and extremities, and some lesions progressed to purpuric papulovesicles with persisted fever (Fig. 1B). Punch biopsy from a purpuric lesion on the leg showed confluent parakeratosis, numerous necrotic keratinocytes, and a perivascular and lichenoid, predominantly lymphocytic infiltrate roughly in a wedge-shaped pattern. Pronounced basal vacuolization, erythrocytes extravasation, and endothelial swelling were also observed (Fig. 1C, D). Laboratory findings revealed elevated levels of C-reactive protein (7.99 mg/dl [reference, 0～0.5 mg/dl]), aspartate amino-transferase (156 IU/L [reference, 4～37 IU/L]), and alanine amino-transferase (97 IU/L [reference, 4～41 IU/L]). Microbiological examination including blood and sputum cultures, serology for *Mycoplasma pneumoniae*, Epstein-Barr virus, and cytomegalovirus, and polymerase chain reaction for herpes simplex virus, respiratory virus, and parvovirus B19 revealed negative results. Chest X-ray showed no active lesion in both the lungs and negative findings were observed in computed tomography of the liver. A diagnosis of pityriasis lichenoides et varioliformis acuta (PLEVA)-like eruption induced by pembrolizumab was suspected. The dose of prednisolone was increased to 80 mg daily (1 mg/kg/day) and the patient showed significant clinical improvement with normalization of laboratory findings (Fig. 2). Considering highly suspected causal relationship and the severity of adverse reactions, pembrolizumab was permanently discontinued by oncologist.

Sanlorenzo et al.[4] have reported that 24 of 83 (28.9%) patients treated with pembrolizumab develop morbilliform eruptions, which mostly occur after the first dose of pembrolizumab. Although they were usually resolved by topical corticosteroids without discontinuation of pembrolizumab, two (2.4%) patients needed systemic corticosteroid (prednisone, 10～60 mg/day) and had to discontinue pembrolizumab[4]. Coleman et al.[3] analyzed inflammatory eruptions associated with immune checkpoint inhibitors. In total, 9 of 103 (8.7%) patients resulted in permanent discontinuation of immunotherapy because of severe cutaneous eruptions, mostly immunobullous eruptions.

It is suspected that the immune checkpoint inhibitors interfere with suppression of autoimmunity and induce cytotoxic T-cell response against native cellular systems[2,5]. In this respect, it may not be surprising that lichenoid dermatitis have occurred during immunotherapy and a pityriasis lichenoides chronica-like eruption during pembrolizumab

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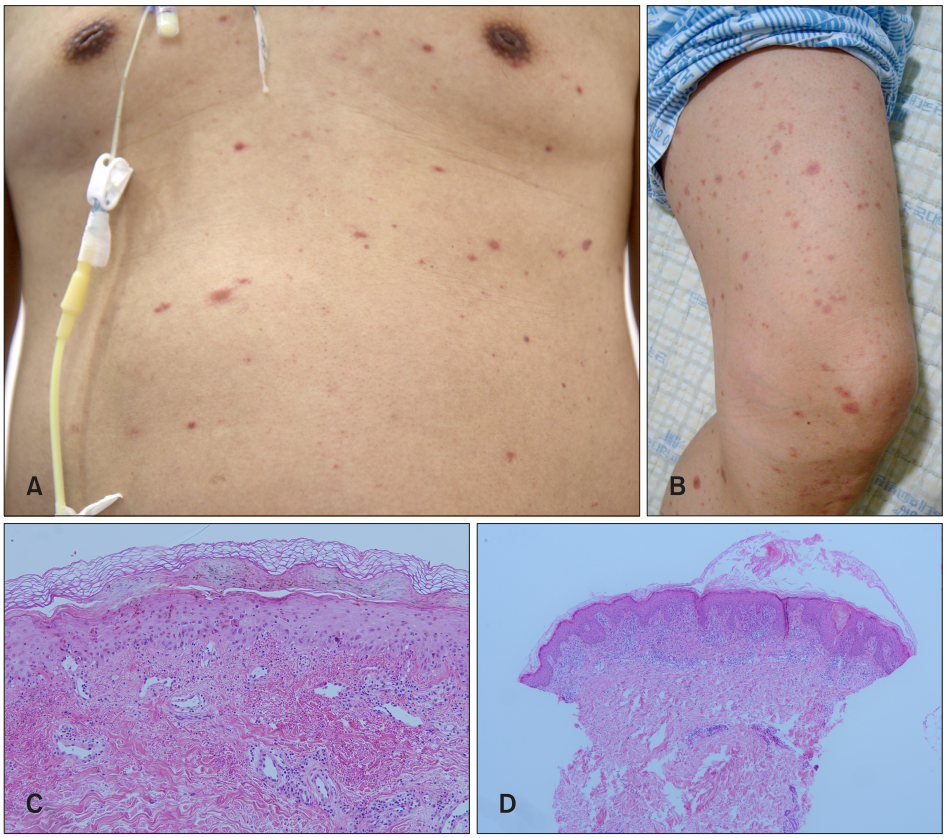

Fig. 1. Multiple scattered erythematous to purpuric papules and a few purpuric papulovesicles on the trunk (A), and both extremities (B). There are confluent parakeratosis, numerous necrotic keratinocytes, basal layer vacuolization, erythrocytes extravasation, endothelial swelling (H&E, ×100) (C), and lichenoid and roughly wedge-shaped dermal lymphocytic infiltrate (H&E, ×40) (D).

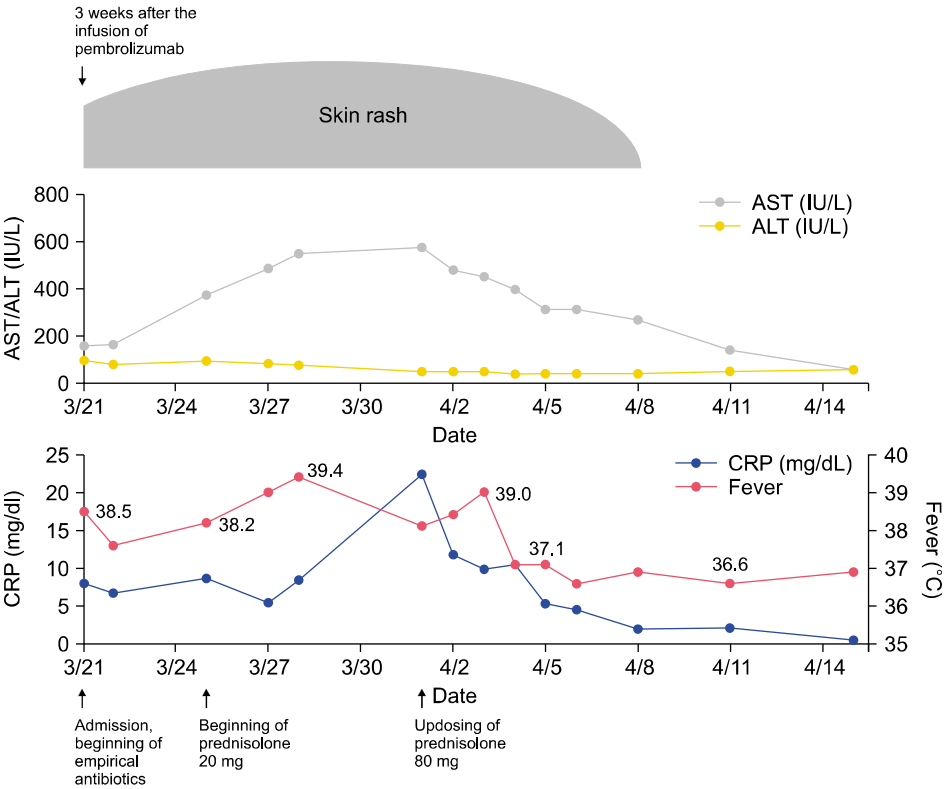

Fig. 2. Clinical course of the patient. AST: aspartate amino-transferase, ALT: alanine amino-transferase, CRP: C-reactive protein.

treatment was recently reported[5]. However, our case was favoring a diagnosis of PLEVA-like eruption in that clinically, purpuric papules and histologically, numerous necrotic keratinocytes, marked basal vacuolization, erythrocytes extravasation, and endothelial swelling were observed. To our knowledge, this is the first report of a PLEVA-like reaction in a patient treated with pembrolizumab. Although the clinical and histological findings of PLEVA-like drug reaction are not so different from authentic PLEVA, early recognition and discontinuation of causative agent are important for the treatment and prevention of recurrence.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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