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CORRESPONDENCE

A possible case of maculopapular eruption associated with glecaprevir/pibrentasvir treatment for chronic hepatitis C virus infection

Dear Editor.

Glecaprevir/pibrentasvir (G/P) is one of direct-acting antiviral (DAA) reagents targeting multiple steps in hepatitis C virus (HCV) lifecycle; glecaprevir works by blocking nonstructural protein (NS) 3/4A protease, while pibrentasvir works by blocking NS5A.[1]

A 59-year-old Japanese woman was referred to our department with pruritic skin rash on her trunk, which occurred 5 days after starting G/P treatment for chronic HCV infection. Physical examination revealed 3 to 5 mm erythematous papules scattered on her trunk and limbs (Fig. 1a and b). There were no blisters or target lesions. The laboratory findings showed slight elevation of serum hepatic enzyme levels. HCV-DNA was not detected in the blood. Skin biopsy taken from the abdomen exhibited vacuolar degeneration of the epidermal basal layer, superficial perivascular lymphocytic infiltration, individual cell keratinization, and mild exocytosis with lymphocytes (Fig. 1c). Immunohistochemical staining showed mixed infiltration of $CD4^+$ and $CD8^+$ T cells (Fig. 1d–f). The patient was treated with topical corticosteroid (0.05% betamethasone butyrate propionate) and oral antihistamine, which controlled pruritic papules that occurred upon treatment with G/P. The skin manifestation was completely resolved 2 weeks after the completion of 12 week G/P treatment. During the course of G/P treatment, the patient did not show clinical symptoms of bacterial infection, nor take any other medications including over-the-counter drugs. Based upon the clinical and histological findings, the patient was diagnosed as a possible case of maculopapular drug eruption associated with G/P treatment, with a score of 5 (probable adverse drug reaction (ADR)) by the ADR Probability Scale.[2]

Some DAAs such as telaprevir and sofosbuvir are reported to induce serious cutaneous adverse events (AEs).[1] Several clinical studies of G/P treatment reported no serious cutaneous AEs,[3,4] though one case of discontinuation as a result of rash was reported in another clinical study.[5] In addition, there is another case of cutaneous AE possibly related to G/P treatment, which showed pruritic skin rash with mucocutaneous involvement together with neutrophil infiltration into the skin.[6] Because of the early onset (only two days after initiating the drug) and neutrophil dominant inflammatory cell infiltration, the adverse reaction was considered to be mediated by nonallergic mechanism.[6]

In the present case, on the other hand, the skin rash appeared 5 days after G/P treatment. T cell-mediated allergic drug eruption typically appear 4 to 21 days after exposure of causative drug[7]; therefore, we considered our case mediated by allergic responses rather than nonallergic responses. Consistently, immunological staining revealed the mixed infiltration of $CD4^+$ and $CD8^+$ T cells into the skin, whereas neutrophil infiltration was not apparent.[7] To our knowledge, this is the first reported case of allergic drug eruption possibly associated with G/P treatment, though a lack of drug provocation test or patch test could be a limitation of this case. Because of its high efficacy and safety, DAAs including G/P are currently the mainstream of chronic HCV treatment. Therefore, clinicians should be aware that G/P may cause cutaneous drug eruption mediated by allergic responses.

Dr. Kenji Kabashima is a member of the Journal of Cutaneous Immunology and Allergy Editorial Board. Management of the peer review process, and all editorial decision-making, for this article was undertaken by Editor in Chief.

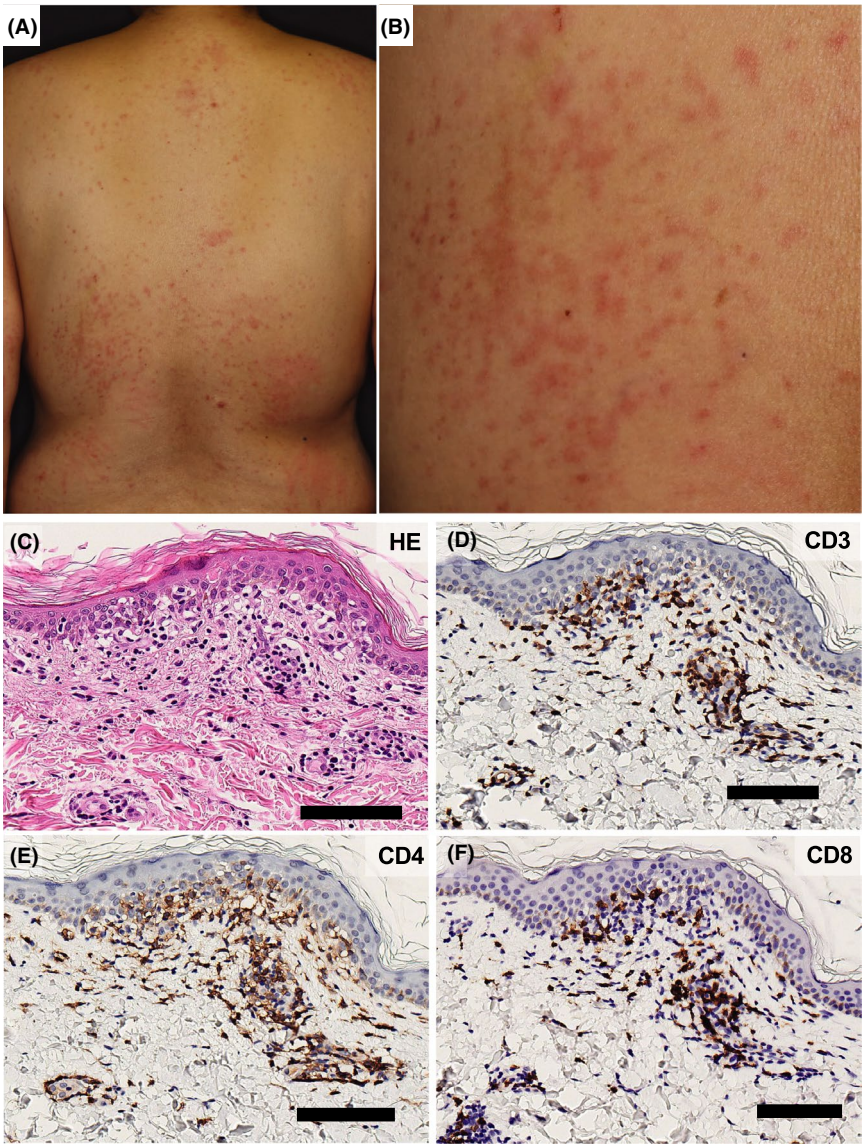

FIGURE 1 Clinical manifestations and histopathological findings. (A) Palpable erythema on the back (B) enlarged image of the papules on the back. (C) Vacuolar degeneration of epidermal basal layer and superficial perivascular lymphocytic infiltration. Hematoxylin–eosin stain; Original magnification × 100. (D–F) Immunohistochemistry for CD3 (D), CD4 (E), and CD8 (F). Scale bars, 250 μm

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed consent: Informed consent was obtained from the patient.

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

Animal studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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