Received: 27 January 2021 | Revised: 4 March 2021 | Accepted: 8 March 2021

DOI: 10.1002/cia2.12167

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

Drug-induced hypersensitivity syndrome/drug rash with eosinophilia and systemic symptoms due to diaminodiphenylsulfone during the treatment of pemphigus foliaceus

Dear Editor,

We report a case of 57-year-old Japanese male who developed drug-induced hypersensitivity syndrome (DIHS), also known as drug reaction with eosinophilia and systemic symptoms (DRESS) due to diaminodiphenylsulfone (DDS, also known as dapson). The patient started DDS for pemphigus foliaceus (PF) due to flare up of the disease while taking 1.0 mg/day of betamethasone. Thirty-three days after initiation of DDS, he visited our office with a high-grade fever (>38.0°C), generalized maculopapular rush and purpura over his whole body except around the eyelids. Pityriatic scales were found around the mouth, and lymph nodes swelling was also noted (Figure 1A,B). Laboratory examination identified leukocytosis (white blood cell 17,080/μl, neutrophils 88.0%, eosinophils 0.0%), atypical lymphocyte (1.0%), and liver dysfunction (aspartate aminotransferase 93 U/L, alanine aminotransferase 289 U/L). Elevation of thymus and activation-regulated chemokine was significant (12,200 pg/ml). A skin biopsy demonstrated exocytosis, liquefaction degeneration, spongiosis, and lymphocytic infiltration to the upper dermis (Figure 1C). He filled the six points of diagnostic criteria for DIHS and fulfilled that for DRESS and was diagnosed as DIHS/DRESS. The DDS was discontinued, and the oral prednisolone (0.6 mg/kg/day) was started. The erythematous lesion and liver dysfunction relapsed and were prolonged; thus, intravenous immunoglobulin therapy (400 mg/kg/day for 5 days) was added and he recovered. Reactivation of human herpes virus-6 (HHV-6) was confirmed by the elevation of serum IgG titers to HHV-6 (10 to 640) in 4 weeks after onset. Lastly, genetic examination revealed that our patient held human leukocyte antigen (HLA)-B*13:01.

DDS is an antibiotic against *Mycobacterium leprae*, a causative agent of leprosy. DDS is applied in a range of dermatological fields because of its anti-inflammatory and immunomodulatory effect. DIHS/DRESS is a rare yet serious adverse drug reaction involving multiple organs.[1] Recently, several HLA alleles have been associated with sever drug eruptions.[2] HLA-B*13:01 was first described as a marker of susceptibility to DDS-induced DIHS/DRESS among

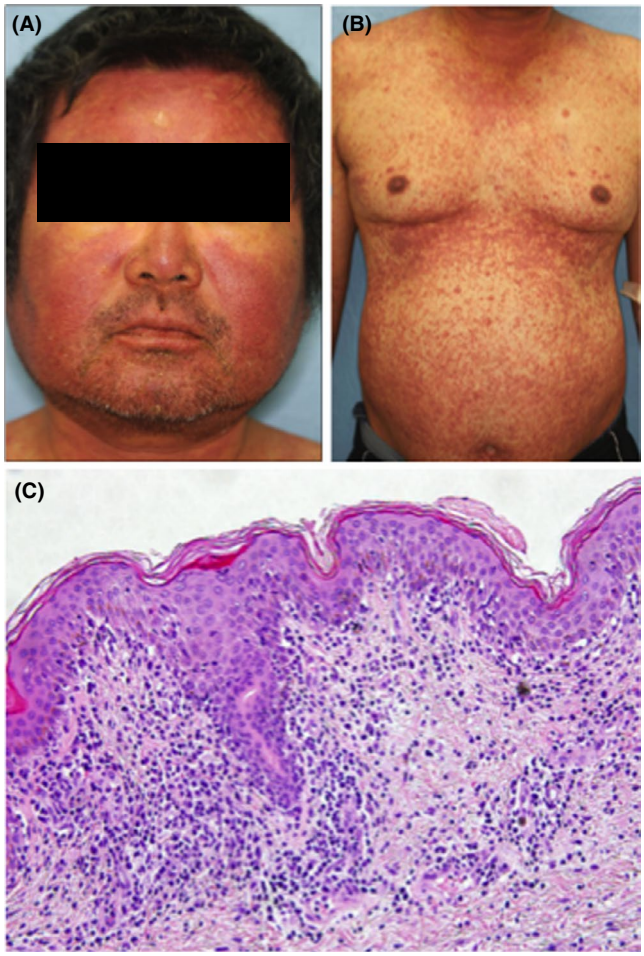

FIGURE 1 Clinical and pathological appearance of the current case. (A) The patient's face was covered by dark and indurated erythema except around the eyelids. (B) Generalized maculopapular rush and purpura were observed over his whole body. (C) Histopathological examination identified massive lymphocytic infiltration to the upper dermis with liquefaction degeneration, as well as exocytosis, and spongiosis within the epidermis (hematoxylin–eosin, original magnification: ×200)

patients with leprosy in Chinese populations.[3] Several investigators, then, reported the presence of HLA-B*13:01 among patients with DDS-induced DIHS/DRESS was not restricted to treat leprosy, but also other skin conditions.[4] To the best of our knowledge, this is the first Japanese case of the DIHS/DRESS due to DDS administered for PF patient with HLA-B*13:01. Exact mechanisms how DDS cause DIHS/DRESS in a patient with HLA-B*13:01 have not been clarified yet. Using computational analysis, Watanabe et al demonstrated that DDS would strongly fit within the antigen-binding site of HLA-B*13:01.[5] Functionally, Chen et al demonstrated that DDS was able to stimulate the drug-specific cytotoxic T cells to release glanulysin.[4] These results may in part explain the HLA-B*13:01 restricted immune mechanism underlying DDS-induced DIHS/DRESS. The presence of HLA-B*13:01 varies among the races. It is estimated to be positive for 2 to 20% of Chinese and 1.5% of Japanese population. In contrast, it is largely absent in European and African people.[6] Nonetheless, we propose that the prospective screening test and subsequent avoidance of the use of DDS for patients with HLA-B*13:01 might be beneficial to prevent this serious cutaneous adverse reaction.

KEYWORDS

diaminodiphenylsulfone, drug rash with eosinophilia and systemic symptoms, drug-induced hypersensitivity syndrome, HLA-B*13:01, pemphigus foliaceus

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DECLARATION SECTION

Approval of the Research Protocols: N/A.

Informed Consent: Informed consent was obtained from the patient.

Registry and the Registration No.: N/A.

Animal Studies: N/A.

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How to cite this article: Honobe A, Mitsui H, Kinoshita M, et al. Drug-induced hypersensitivity syndrome/drug rash with eosinophilia and systemic symptoms due to diaminodiphenylsulfone during the treatment of pemphigus foliaceus. *J Cutan Immunol Allerg.* 2021;4:135–136. https://doi.org/10.1002/cia2.12167