

Photosensitivity in Hydroa Vacciniforme Is A Photo-Koebner Phenomenon Induced by Infiltration of Epstein-Barr Virus-Infected NK/T Cells

Keiji Iwatsuki ^{1*}, Zi-Gang Xu ², Mikio Ohtsuka ², Takenobu Yamamoto ¹,
Kazuyasu Fujii ¹ and Kazuhide Tsuji ¹

¹ Department of Dermatology, Okayama University Graduate School of Medicine and
Dentistry, Japan

² Department of Dermatology, Fukushima Medical University
School of Medicine, Fukushima, Japan.

Hydroa vacciniforme (HV) is a disease of Epstein-Barr virus (EBV)-associated NK/T cell lymphoproliferative disorder, and patients with severe HV-like eruptions have a high risk to progress to various EBV-related hematological complications. Photosensitivity in HV might be a 'photo-Koebner' phenomenon mediated by infiltration of EBV-infected NK/T cells.

Key words: hydroa vacciniforme, Epstein-Barr virus, latent infection, photosensitivity

INTRODUCTION

Hydroa vacciniforme (HV) is a childhood photosensitivity disorder of unknown etiology. No specific wavelengths to induce positive skin reactions have been determined yet, although HV lesions usually occur on the sun-exposed areas,

and similar lesions are inducible by artificial sun exposure or repetitive UVA irradiations. Recent studies have demonstrated that patients with severe HV-like eruptions have a risk to progress to EB virus (EBV)-associated malignant lymphoma [1,2]. We have studied a pathogenic link of latent EBV infection between HV and severe HV-like eruptions.

K. Iwatsuki, Department of Dermatology,
Okayama University Graduate School of
Medicine and Dentistry, 2-5-1 Shikata-cho,
Okayama 700-8558, Japan

E-mail: keijiwa@cc.okayama-u.ac.jp

MATERIALS AND METHODS

Biopsy specimens from 24 patients with HV or HV-like eruptions were examined for EBV-encoded small nuclear RNA (EBER) and immunophenotypes of the infiltrating cells, in comparison with control samples. A diagnosis of HV was confirmed by clinical and histologic features (Figure 1). Patients with 'definite' HV were positive for phototest reactions, and a diagnosis of 'probable' HV was made when phototests were negative or not performed. Patients with 'severe' HV were defined as cases with systemic symptoms such as fever and liver damage in addition to the HV-like eruptions. Phototests were performed by clinicians using various procedures and UV doses: single irradiation of UVB or UVA, repetitive UVA and sun exposure.

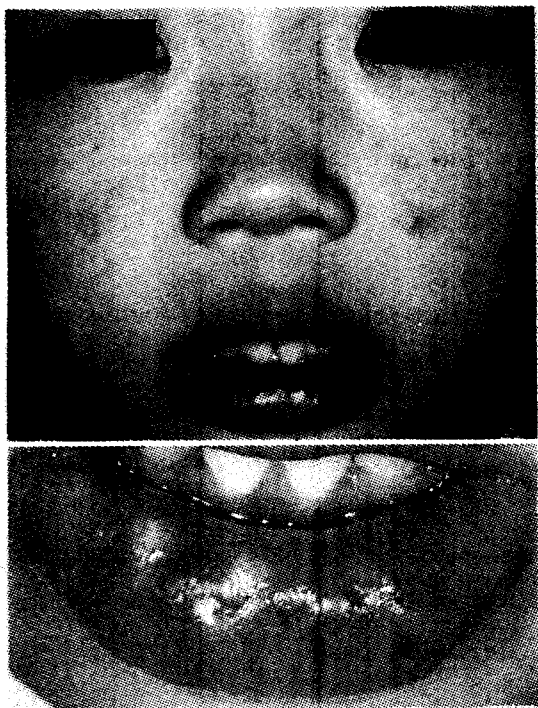


Figure 1. Typical clinical features of HV

RESULTS

The EBER+ NK/T cells were detected in 23 (96%) of 24 patients with HV or HV-like eruptions, including all 6 patients with 'definite' HV with a positive phototest reaction, 8 of 9 'probable' HV patients without evidence for photosensitivity, and all 9 patients with severe HV-like eruptions (Table 1, Figure 2). No EBER+ cells were observed in other inflammatory disorders.

Table 1. Detection of EBV+ cells in patients with HV-like eruptions

Diagnoses	EBER+	(positivity %)
'definite' HV(phototest+)	6 / 6	(100)
'probable' HV(phototest: - or not done)	8 / 9	(89)
'severe' HV	9 / 9	(100)
total	23/24	(96)
Pityriasis lichenoides	0 / 5	(0)
Chronic photosensitivity dermatitis	0 / 5	(0)
Panniculitis	0 / 5	(0)
Discoid lupus erythematosus	0 / 5	(0)

The UV-induced cutaneous reactions also showed histopathologic findings consistent with those of HV, containing many EBER+ cells. Infiltrating cells in the HV lesions were positive for cytotoxic T-cell markers without detectable CD56 antigens. Nine patients with severe HV-like eruptions had various types of EBV-associated hematologic complications (Table 2). Among this group, 5 patients died of

malignant lymphoma or hemophagocytic syndrome 2-14 years after the onset.

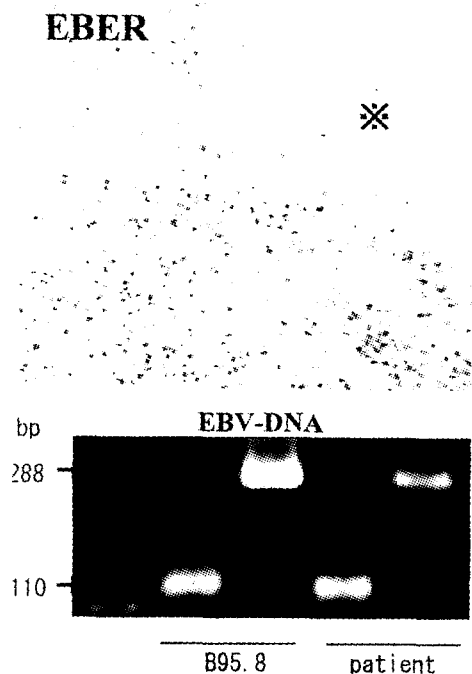


Figure 2. A considerable number of EBER+ cells were present in the dermal infiltrates of HV lesions, and EBV-DNA was detected by PCR.

Table 2. Complications and outcomes of patients with severe HV

Of 9 patients with severe HV	
Dead	5
Fatal HPS	4
EBV-associated disorders	8
Malignant lymphoma	4
Hypersensitivity to	
Mosquito bites	3

DISCUSSION

Our data indicate that HV is a disease of EBV-associated NK/T-cell lymphoproliferative disorder, and distinct from photoallergic or phototoxic reactions. The UV-induced local immunosuppression and IL-15 production by keratinocytes may provide a favorable milieu for EBV-infected NK/T cells to migrate and proliferate, evading the host immune responses. Therefore, photosensitivity in HV seems to be a sort of 'photo-Koebner' phenomenon. Furthermore, patients with severe HV-like eruptions had various EBV-related complications including malignant lymphomas, hypersensitivity to mosquito bites and fatal HPS. Therefore, those patients might progress from a smoldering stage to EBV-related malignant conditions.

This work was supported by Grant-in-Aid for Scientific Research (B) (No.14370261) and Grant-in-Aid for Exploratory Research (No.14657200) from the Ministry of Education, Culture, Sports, Science and Technology in Japan.

REFERENCES

1. Iwatsuki K et al (1999) The association of latent Epstein-Barr virus infection with hydroa vacciniforme. *Br. J. Dermatol.* 140, 715-721.
2. Iwatsuki K et al (2000) Cutaneous lymphoproliferative disorders associated with Epstein-Barr virus infection: a clinical overview. *J. Dermatol. Sci.* 22, 181-195.