Appendix S1

SUPPLEMENTARY MATERIALS AND METHODS

The study was reviewed and approved by the Clinical Research Ethics Committee of Nara Medical University, Nara, Japan.

The study included 10 patients with DIHS/DRESS (4 men and 6 women; median age: 63.3 years, age range 15–84 years), and 10 with maculo-papular eruption (MPE) (a milder type of drug reaction without systemic symptom) (5 men and 5 women; median age: 69.3 years, age range 25–90 years). A summary of the clinical and laboratory features of patients with DIHS/DRESS enrolled in the present study is shown in Table SI[1]. Clinical and laboratory data reported herein were obtained until 35 days after onset.

Blood samples in the acute stage were obtained from 10 patients with DIHS/DRESS at the time of their initial visits to our department. Patients with DIHS/DRESS were subjected to repeated blood sampling. Sera were separated from whole blood by centrifugation and stored at –80°C until use. Control serum samples were collected from 10 healthy volunteers.

Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood. DNA was isolated from PBMCs using the QIAamp DNA Blood Mini Kit (QIAGEN, Hilden, Germany) according to the manufacturer's protocol. In order to detect HHV-6B DNA copies, real-time PCR was performed with the Taqman Fast Advanced Master Mix (Applied Biosystems, Foster City, CA, USA), using HHV-6-specific primers and probe as described previously (10), and HHV-6B-specific primers and probe (STable I).

Isolation of miRNA from serum samples was performed with a miRNeasy Serum/Plasma Kit® according to the manufacturer's instructions with minor modifications. Complementary DNA (cDNA) was synthesized from total miRNA with a Taqman MicroRNA Reverse Transcription Kit with specific primers (miR-Ro6-1-5p, miR-Ro6-2-3p, miR-Ro6-3-3p, and miR-Ro6-4-3p) (Applied Biosystems). Quantitative real-time PCR was performed using Taqman MicroRNA Assays (miR-Ro6-1-5p, miR-Ro6-2-3p, miR-Ro6-3-3p, and miR-Ro6-4-3p) in a StepOnePlus Real Time PCR System (Applied Biosystems).

Statistical analyses were performed using a Kruskal–Wallis test. Values of $p < 0.05$ were considered significant.

STable I. Sequences of human herpesvirus 6B-specific primers and probe

Name	Sequences
Forward primer	5′-GGCTTACAGCCCCGATCAA-3′
Probe	5′-TCACAGACAAAAGAAAG-3′
Reverse primer	5′-TTCAGGAAAAAGGTTCTAACTCCAA-3′