

Letter to the Editor

Usefulness of rapid measurement of serum thymus and activation-regulated chemokine level in diagnosing drug-induced hypersensitivity syndrome



Dear Editor,

Drug-induced hypersensitivity syndrome (DIHS) is a unique adverse drug eruption, which causes reactivation of herpesviruses such as human herpesvirus type-6 (HHV-6) during its clinical course. DIHS has biphasic aspects of allergic reaction to drug and of immune response to viral reactivation. Diagnostic criteria of DIHS consists of 7 clinical features as previously described; maculopapular rash, prolonged clinical symptoms, high fever, leukocyte abnormalities, liver dysfunction, lymphadenopathy, HHV-6 reactivation.¹ However, it is not always easy to diagnose DIHS in an early stage because its clinical features mimic macropapular rash-type drug reaction or eruptions due to viral infection. It has recently been reported that high serum level of thymus and activation-regulated chemokine (TARC) is observed specifically in DIHS patients.² We report a case of carbamazepine-induced DIHS, showing extremely high serum level of TARC in an early stage, which helped early diagnose of the disease.

An 86-year-old Japanese woman was referred to our hospital because of widely spread erythema with itching. She had started to take carbamazepine because of trigeminal neuralgia refractory to non-steroidal anti-inflammatory drugs 1 month before she had generalized rash. On admission, she had generalized rash with facial edema (Fig. 1), pustules around her mouth, and a high fever (over 38 °C). Superficial lymph nodes were not palpable. Her hepatic failure was not remarkable, but renal failure was suggested (BUN 29.6 mg/dl, creatinine 1.29 mg/dl). Eosinophil count was 3501/mm³ and CRP was also high level (6.31 mg/dl). We suspected DIHS in this patient because of generalized rash developed after starting carbamazepine, high fever, and renal failure, but definite diagnosis of DIHS was not made.

Her serum TARC level was extremely high (88,179 pg/ml), when measured by utilizing HISCL[®] system (Sysmex, Hyogo, Japan) with TARC Assay kit (Shionogi, Osaka, Japan). We considered that the diagnosis was possibly DIHS and started prednisolone 30 mg/day on day 2. From then, her temperature declined to the normal level, and her rash and pustules were gradually disappeared. Since her condition improved, prednisolone intake was gradually tapered. After starting the prednisolone, her serum TARC level drastically decreased as shown in Figure 2. Reactivation of HHV-6 was suspected by increasing her serum HHV-6 IgG titers on day 25.

Drug-induced lymphocyte stimulation test indicated that carbamazepine was a culprit drug (stimulation index: 315%). We finally gave a diagnosis of DIHS since this case had 6 out of 7 diagnostic criteria of DIHS; maculopapular rash developing 1 month after

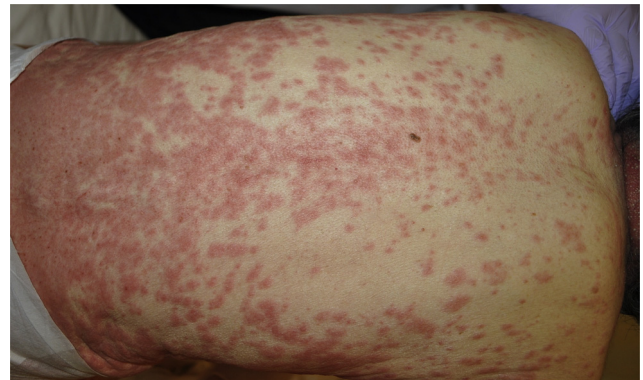


Fig. 1. Maculopapular rash on the back of the patient.

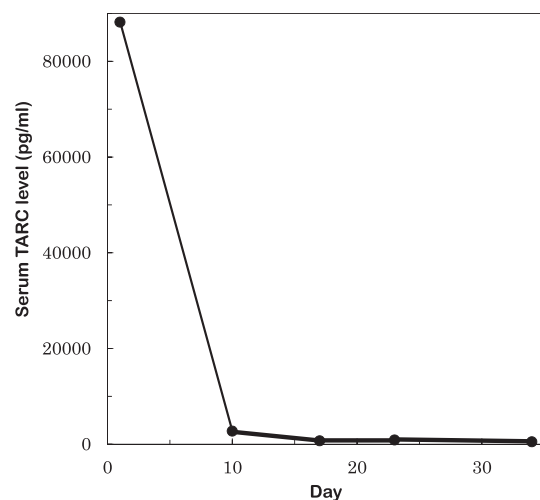


Fig. 2. Serum TARC level of the patient.

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starting carbamazepine, prolonged rash, high fever, renal failure and liver abnormalities (ALT 316U/l on day 11), leukocytosis with eosinophilia (WBC $13.1 \times 10^9/l$) and HHV-6 reactivation.

This case well supports the previous reports that serum TARC level is extremely high at an active stage of DIHS in contrast to other adverse drug reactions, such as Stevens–Johnson syndrome.^{2,3} There are also some other skin diseases causing high serum level of TARC, including atopic dermatitis, bullous pemphigoid, and mycosis fungoides.^{4,5} However, their serum TARC level do not exceed that of DIHS. In the present study we could not identify the cells producing TARC, although its serum level was well correlated with inflammatory condition of the patient. In the present case, HISCL[®] system was utilized to measure the serum TARC level, which enables us to show the result in a short time (17 min). This is also helpful in comparison with a widely used TARC test, which needs at least 2 or 3 days to figure out serum TARC level. In conclusion, HISCL[®] system is very useful in diagnosing DIHS by rapid measurement of serum TARC level in the patients with generalized acute rash.

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Conflict of interest

The authors have no conflict of interest to declare.

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