Drug-induced Liver Injury with Human Herpesvirus (HHV)-6 Reactivation but without Exanthema or Fever

Key words: drug-induced liver injury, drug hypersensitivity syndrome, herpesvirus 6, reactivation

To the Editor We read the article by Fujita et al. in a recent issue of Internal Medicine with great interest (1). The authors reported that human herpesvirus (HHV)-6 reactivation should be considered in patients with drug-induced liver injury, even in the absence of exanthema. We recently encountered another case of drug-induced liver injury with HHV-6 reactivation in which exanthema and fever were absent.

A 33-year-old woman with a history of mood disorder, who had been receiving lamotrigine and valproic acid for 17 and 14 months, respectively, came to our hospital with complaints of nausea and epigastralgia. The laboratory findings revealed liver dysfunction. Three days after the cessation of medications, the liver dysfunction was exacerbated [alanine aminotransferase (ALT): 729 to 843 IU/L, alkaline phosphatase (ALP): 360 to 694 IU/L, total bilirubin (T-Bil): 1.6 to 8.0 mg/dL]. Mild eosinophilia (950/μL) was also noted, and the patient was positive for HHV-6 DNA. However, there was a sudden, spontaneous remission of the patient’s symptoms and liver dysfunction.

Exanthema frequently develops due to HHV-6 infection, but it is not always present. In a reported case series of patients with exanthem subitum-associated encephalitis, 12.5% of the patients did not exhibit exanthema (2). We suggest that drug-induced liver injury with HHV-6 reactivation should be considered in the following situations, even if exanthema and fever are absent: 1) when culprit drugs, which are the major causative drugs of drug-induced hypersensitivity syndrome (such as anticonvulsants, allopurinol, dapsone, salazosulfapyridine, mexiletine, and acetaminophen), are administered; 2) when liver dysfunction develops several weeks or longer after the initiation of drug administration; 3) When eosinophilia and/or atypical lymphocytes is present; and 4) when liver dysfunction does not show satisfactory improvement after the discontinuation of medications.

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References