Comment on "Viral reactivation in hospitalized DRESS patients: A retrospective study from a tertiary medical center in the United States"

To the Editor: We read with interest the article by Milani-Nejad et al.[1] They found that their patients with drug reaction and eosinophilia and systemic symptoms (DRESS) showed an extremely low rate of viral reactivation, especially that of human herpesvirus 6 (HHV-6). Among the 24 patients being examined for HHV-6 reactivation, only 1 patient had a positive result on polymerase chain reaction (PCR) testing of serum samples 5 months after the initial diagnosis. The authors discussed and suggested that the discrepancy of rates of viral reactivation between their study and previous reports might result from the differences in patient population, prevalence of prior infections, and, possibly most important, timing for detecting viral reactivation.

We agree with the authors' opinion that timing is indeed an important factor that can influence rates of viral reactivation. Our previous reports[2,3] and the studies of Japanese experts[4] all showed that reactivation of HHV-6 usually could be detected 2 to 4 weeks after the initial diagnosis. However, in addition to timing, the methods used to detect HHV-6 reactivation may also affect the results. The presence of HHV-6 DNA in the blood is usually transient during active infection. Quantitative PCR for detecting the presence of HHV-6 DNA in serum or plasma is a good indicator of active infection but, unfortunately, may lead to false negative results for the abovementioned reason. In our previous study[2] of 19 patients with DRESS, 10 patients were defined as having HHV-6 reactivation (52.6%). Among these patients, only 1 (5.3%) could be identified by quantitative PCR using serum samples, whereas the other 9 patients (47.4%) were identified by serology changes (ie, at least 4-fold elevations of anti−HHV-6 antibodies). This result suggests that using quantitative PCR to detect viral HHV-6 DNA on serum or plasma samples may largely underestimate the rates of HHV-6 reactivation. A combination of other detection methods, such as serology changes, is needed to obtain more accurate results.

On the other hand, using quantitative PCR to detect HHV-6 DNA in whole blood samples is a useful method suggested by the HHV-6 Foundation (https://hhv-6foundation.org/patients/hhv-6-testing-for-patients) and another recent publication from Japan.[5] A positive result was defined by presence of a viral load of more than 200 copies/mL or 20 copies/μg of DNA. We have used this method in another recent study.[3] In that study, 33 patients with DRESS received whole-blood quantitative PCR to detect the presence of HHV-6 DNA. Among them, 11 patients showed positive results (33.3%).

All the results of our work show that detecting methods indeed largely influence the detection rates of HHV-6 reactivation. In addition to timing of detection, carefully choosing a suitable method or a combination of tests is also critical to obtain a more accurate result.

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