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

To the Editor: We thank Cho et al[1] for their comments on our study. Their input highlights the complexity of testing for viral reactivation in drug reaction with eosinophilia and systemic symptoms (DRESS). In our study, we showed that viral reactivation at the time of the initial DRESS presentation is an infrequent event in patients in the United States. Cho et al agree with our assertion that timing of viral studies is an important factor[1] and likely contributed to the low rate of viral reactivation observed in our study. Although viral reactivation may occur 2 to 4 weeks after the initial presentation,[2] the utility of these tests during the initial presentation is of limited clinical value.

We agree with Cho et al[1] in that testing methodology is another factor that should be considered. Our study used polymerase chain reaction (PCR) on serum samples. Cho et al. suggest that human herpesvirus 6 (HHV-6) PCR of whole blood is preferable. However, although PCR of whole blood more often shows positive test results, it risks a higher false positive rate than serum PCR.[3] We also note that several seminal publications on DRESS and herpesvirus reactivation used PCR on serum samples for reactivation of HHV-6, cytomegalovirus, and Epstein-Barr virus.[2,4,5]

They also point out the utility of serologies in assessing HHV-6 reactivation, which is defined as a 4-fold increase in the titers of anti-HHV6 IgG antibodies. We agree that this is an established method that can be used in conjunction with PCR studies but is of uncertain clinical value in most situations. This approach requires a baseline titer and serial monitoring of titers after the initial presentation to assess for a 4-fold increase. In 1 study, a subset of patients with DRESS had serial monitoring of both antibody titers and serum HHV-6 PCR.[2] Serum HHV-6 DNA was detected simultaneously or before the increase in antibody titers.[2] This suggests that serum PCR can be used for testing of viral reactivation. Although we do agree that the combination of both PCR and serology is complementary, given that a decision to discontinue a potentially critical medication, provide a presumptive diagnosis, and begin treatment cannot wait for 4 weeks or longer, we see little value in this methodology outside of a research setting.

Viral reactivation, particularly of HHV-6, does play a role in DRESS. Various factors such as timing of testing, prevalence of prior infections, study population, and methodology can affect the observed reactivation rates. Given the various testing methodologies and the delayed time course, we still affirm the results of our previous study that testing for viral reactivation at or near the time of DRESS diagnosis provides little, if any, clinical value.

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