

Viral infections in drug-induced hypersensitivity

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A relationship between viral infections and the simultaneous or subsequent development of drug rashes has been observed in a number of clinical situations; but the full cascade of events to the development of drug rashes remains poorly understood. In this regard, we have provided evidence to indicate an intimate relationship between reactivation of human herpesvirus 6 (HHV-6) and the development of a severe systemic hypersensitivity reaction, termed drug-induced hypersensitivity syndrome (DIHS), which is characterized by rash, fever, lymphadenopathy, hepatitis, and leukocytosis with eosinophilia. Importantly, we found that not only HHV-6 but also other herpesviruses such as EBV and CMV can be sequentially reactivated during the course of this syndrome in the same order as demonstrated in graft-versus-host disease (GVHD): sequential reactivations of these herpesviruses could be reflected in exacerbations and remissions of clinical symptoms resembling GVHD after withdrawal of the causative drugs. In this syndrome, these herpesviruses might be functionally linked in vivo, the reactivation of one leading to the reactivation of the other. In some patients with DIHS as well as those with GVHD, autoimmune diseases such as type 1 diabetes mellitus often develop long after clinical resolution of DIHS. These findings indicate the importance of recognizing DIHS and other drug rashes associated with viral infections at risk of eventually developing autoimmune diseases.