3. Tomlinson SE, Bostock H, Grinton B, et al. In vivo loss of slow potassium channel activity in individuals with benign familial neonatal epilepsy in remission. Brain 2012;135:3144–3152.
4. Tomlinson S, Burke D, Hanna M, Koltzenburg M, Bostock H. In vivo assessment of HCN channel current (Ih) in human motor axons. Muscle Nerve 2010;41:247–256.
5. Howells J, Trevillion L, Bostock H, Burke D. The voltage dependence of Ih in human myelinated axons. J Physiol 2012;590:1625–1640.

ATYPICAL MANIFESTATIONS AND POOR OUTCOME OF HERPES SIMPLEX ENCEPHALITIS IN THE IMMUNOCOMPROMISED

Richard B. Tenser, Hershey, PA: In the article by Tan et al.,[1] atypical illness and poor outcome of HSV encephalitis in immunocompromised patients was likely due to their immune status, and possibly also to antiviral-resistant mutant HSV. Acyclovir and related antivirals are phosphorylated by the HSV-encoded thymidine kinase (TK) to the active antiviral state.

However, during HSV infections, mutants arise that are acyclovir resistant primarily because they lack viral TK activity (TK−) and do not phosphorylate acyclovir.[2] In non-immunosuppressed HSV-infected individuals treated with acyclovir, wild-type TK + HSV is inhibited by acyclovir, and the small amounts of TK− HSV that develop are likely controlled by the immune system. However, in immunocompromised individuals, while wild-type TK + HSV is inhibited by acyclovir, TK− mutants likely multiply.

We used an isotope plaque assay to estimate proportions of TK− and TK+ HSV in lesion swabs from an immunocompromised patient treated with acyclovir.[3] TK− HSV does not replicate well in non-dividing cells but does in replicating cells. In immunocompromised patients,[1] it is suggested that during the period of acyclovir treatment, TK− HSV probably replicated, more likely in glial cells than in neurons. Presumptive TK− HSV may have contributed to the atypical clinical course of these patients.

Author Response: Avindra Nath, Bethesda, MD: I thank Dr. Tenser for his comments and for agreeing that acyclovir-resistant HSV may have played a role in the pathophysiology of encephalitis in these patients.

1. Tan IL, McArthur JC, Venkatesan A, Nash A. Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised. Neurology 2012;79:2125–2132.
2. Sarisky RT, Quail MR, Clark PE, et al. Characterization of herpes simplex viruses selected in culture for resistance to penciclovir or acyclovir. J Virol 2001;75:1761–1769.
3. Westheim AI, Tenser RT, Marks JG. Acyclovir resistance in a patient with chronic mucocutaneous herpes simplex infection. J Am Acad Dermatol 1987;17:875–880.

Author disclosures are available upon request (journal@neurology.org).

Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised

Richard B. Tenser and Avindra Nath

Neurology 2013;81;514
DOI 10.1212/01.wnl.0000433164.29848.92