
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,3 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.

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Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised
Richard B. Tenser and Avindra Nath

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