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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.

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