

Acyclovir Resistance In HSV-2 Isolates From A Patient With AIDS

F. BEVILACQUA, A. MARCELLO, G. GERNA¹, M. TONI & G. PALU'

Institutes of Microbiology and Infectious Diseases¹, Universities of Padova and Pavia, Italy.

A number of sequential isolates has been recovered from a patient with AIDS undergoing acyclovir (ACV) treatment for an extended genital lesion. The isolates have been characterized as far as the chemosensitivity, the *in vitro* and *in vivo* growth, the genotypic profile, the structure and function of the thymidine kinase (TK) locus were concerned. ACV resistance (ACV^R) was related to a TK⁻ phenotype in all isolates, as revealed by the production of a truncated TK polypeptide and the absence of enzymatic activity. The cloning and sequencing of the TK gene documented that the mutation responsible for the ACV^R trait was caused by the occurrence of a stop codon within the TK open reading frame. A partial gene duplication might also be involved in one case. Sequencing data and restriction profile analysis would suggest that the different isolates represent a single strain which has undergone multiple reactivations from latency. Selection of the mutant clone would have arisen during the retrograde way from the ganglion to the skin. This view was confirmed by the observation that soon after ACV was discontinued and a treatment with foscarnet was undertaken, a new isolate was recovered characterized by an ACV^S phenotype, the presence of a functional TK and a genotypic profile virtually identical to that of the ACV^R isolates.

Our data stress the need for monitoring the chemosensitivity and the biological properties of HSV-2 isolates in patients with AIDS. Such an investigation could favor a better understanding of the HSV infection behavior in these subjects. It could also encourage the development of new therapeutic regimens based on antiviral drugs with different molecular targets.

Rapid Screening of Clinical Herpes Simplex Virus Isolates for Resistance to Acyclovir. DG Ketchum *, RS Gohd #, ED Starszak *, and RB Van Dyke *.

Department of Pediatrics, Tulane Medical School * and Department of Pathology, Louisiana State University Medical School #, New Orleans, LA, USA.

Resistance of herpes simplex virus (HSV) to the antiviral agent acyclovir is of growing concern. Such resistance is increasing as acyclovir is used more frequently, especially in immunosuppressed patients with HSV infections. We sought to determine the frequency of acyclovir resistance among clinical HSV isolates from the greater New Orleans area. Clinical resistance to acyclovir is commonly due to a loss of viral thymidine kinase (TK) activity; TK being necessary for the conversion of acyclovir to the monophosphate form. We have used a rapid screening assay previously developed by us to determine presence of TK activity in HSV-infected Vero cells by measuring uptake of [¹²⁵] iododeoxycytidine, a sensitive and specific indicator of such activity. Of 34 HSV specimens isolated from July through early December, 1990, 31 (91%) demonstrated TK activity (TK+) and were thus presumably sensitive to acyclovir. Three isolates (9%) lacked TK activity (TK-) and were classified as resistant. Two of these resistant isolates were from HIV infected patients. We will confirm all isolates suspected to be resistant by plaque reduction assay. Acyclovir resistance may be more common among clinical isolates of HSV than previously suspected.