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Comparison of Ganciclovir Sensitivity of Cytomegalovirus (CMV) Isolated from Marrow Transplant Recipients at Diagnosis and During Treatment of CMV Pneumonia. MA Slavin, CA Gleaves, RA Bowden. Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

Recently, the combination of ganciclovir and intravenous immunoglobulin has dramatically improved survival from CMV pneumonia after marrow transplantation. However, 20 of 25 patients still had CMV detected in bronchoalveolar lavage (BAL) after 9 days of treatment. When the titer of CMV in the BAL was compared by quantitative shell vial cultures for 5 patients who had both initial and day 9 follow-up BAL, it fell by 1 log or less in 4/5 patients. These findings raised the question of whether CMV resistance to ganciclovir developed during treatment. CMV isolated from conventional tube cell culture at diagnostic and day 9 follow-up BAL was tested for ganciclovir sensitivity by the Hybriwix probe DNA hybridization assay (Diagnostic Hybrids, Inc., Athens, OH). Positive cultures obtained from 6 patients at day 9 BAL were tested and found to be sensitive to ganciclovir with ID_{50} values of <5 μL. Five of the 6 patients survived. Three of the survivors had initial and day 9 viral titers. Titer fell by 1 log in 2/3 and was unchanged in 1/3. CMV resistance to ganciclovir was not the explanation for the persistent high titers of virus during treatment of CMV pneumonia. Sensitivity testing of CMV isolated from patients who died while on treatment for CMV pneumonia and had virus detected at autopsy is in progress.

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Spontaneous Reactivation of Thymidine Kinase Deficient (TK^-) Herpes Simplex Virus (HSV) Infection Without Acyclovir (ACV) Pressure in a Patient with the Acquired Immunodeficiency Syndrome (AIDS). J.J. Sasadeusz, B.A. Rennie, S.L. Sacks. University of British Columbia, Vancouver, BC Canada.

To further characterize ACV resistance in immunocompromised patients, HSV isolates from patients treated with foscarnet (PFA) have been tested for TK activity and ACV susceptibilities. A 45 year old woman with AIDS since 1987 was treated since 1984 with intermittent courses of ACV. In September of 1989, while being treated with oral ACV, the patient developed a clinically resistant, progressive perineal ulcer. HSV-2 isolates from this ulcer were resistant by 50% plaque reduction (ID_{50}) assays (3.8 to 7.4 μg per mL). Clinical isolates were TK^-, with 0 to 1.5% of TK activities compared with reference strains based on relative uptakes of 1-ß-D-arabinofuranosyl-*E*-5-(2-[^{125}I]-iodovinyl)uracil (^{125}IVaraU) in infected fibroblasts. The patient suffered multiple severe and progressive HSV recurrences, each successfully treated with intravenous PFA (40 to 60 mg per kg q8h), and each followed by high dose oral ACV suppression (400 mg four times daily). During the fourth hospital admission for IV PFA, she became HSV-culture-negative 2 days following PFA commencement, and then refused further ACV suppression. Following cessation of ACV, the patient suffered multiple PFA-responsive HSV episodes and expired in December, 91 of unrelated complications of AIDS. The initial (16 weeks) post-ACV cessation isolate was ACV-resistant with an ID_{50} of 6.6 μg per mL and TK activity of 1.2% [^{125}IVaraU uptake] compared with wild type (TK^+). Reactivation of ACV-induced resistance in this patient occurred in the absence of continuing ACV pressure. Subsequent HSV-2 relapses in this patient were again, TK^+. Heterogeneity and virulence factors associated with the spontaneously reactivated ACV resistant HSV-2 mutant are now under investigation.