

couraged because they will provide important tools for clinical medicine and public health.

Acknowledgments: The authors wish to thank Professor Souleymane Mboup and his team at the University Cheikh Anta Diop, Dakar, Senegal, for their help in the provision and characterization of the samples included in the study. This work was supported in part by grants from the U.S. Army Medical Research and Materiel Command 17-95-5005.

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Persistent Human Herpesvirus 8 Viremia Associated With Coinfection With Human T-Cell Lymphotropic Virus Type I and Myelofibrosis

To the Editor: Human herpesvirus 8 (HHV-8) infection appears necessary for the development of Kaposi's sarcoma. HHV-8 DNA is detected consistently in Kaposi's sarcoma tumors (1). Although HHV-8 infection remains asymptomatic in most individuals, Kaposi's sarcoma may develop with immunosuppression, especially when HIV-1 coinfection is present. Kaposi's sarcoma has occasionally been documented in people infected with HTLV-I, either during otherwise asymptomatic HTLV-I infection (2,3) or in association with adult T-cell leukemia/lymphoma (4).

The presence of detectable HHV-8 viremia in infected persons may indicate loss of control of latent HHV-8 infection and heightened risk for Kaposi's sarcoma. However, factors associated with HHV-8 viremia have not been well studied. Following primary HHV-8 infection, some individuals persistently harbor HHV-8 within circulating peripheral blood mononuclear cells (PBMCs), particularly within B lymphocytes and within spindle cells, which may be precursors of Kaposi's sarcoma. Viremia is detectable in 50% to 60% of HIV-infected persons with asymptomatic HHV-8 infection (5) and in a similar proportion of persons with Kaposi's sarcoma (6).

Here we describe a 66-year-old Jamaican woman coinfecting with HHV-8 and HTLV-I, whom we identified while examining HHV-8 seroprevalence in blood donors and recipients (7). She received multiple transfusions beginning in 1987 for myelofibrosis. In July 1987, she became infected with HTLV-I through a transfusion of red blood cells from an HTLV-I-infected donor. She remained without symptoms of HTLV-I infection until early 1990, when she developed increasing weakness and paresthesias in her lower extremities, diagnosed as HTLV-I-associated myelopathy/tropical spastic paraparesis. The patient died in October 1991 from sepsis.

HHV-8 test results for this individual are shown (Fig. 1). She was HHV-8-infected as early as August 1987, with HHV-8 DNA detected by polymerase chain reaction (amplifying 141 bp of orf26, a portion of the viral genome that encodes a capsid protein [1]) in multiple samples of PBMCs and plasma obtained over a 29-month period (Figs. 1 and 2). During this period, HHV-8 antibodies were detected inconsistently with three different serologic tests: an enzyme immunoassay using a lysate of whole virus (Advanced Biotechnologies, Columbia, MD, U.S.A.) and indirect immunofluorescence assays for antibodies against either latent-phase (6) or lytic-phase viral antigens (8). Even in positive samples, antibody levels were low (Fig. 1). Of interest, she received blood from an HHV-8-seropositive donor in February 1988, but she was already infected with HHV-8 before this date and HHV-8 antibody levels remained low following this transfusion.

Coinfection with HTLV-I might explain the prolonged HHV-8 viremia seen in this individual. HTLV-I infection is associated with deficits in cellular immune responses (9). Cell-mediated immunity is likely important in controlling HHV-8 viremia, given that among persons with HIV-associated Kaposi's sarcoma, viremia is most common among individuals with low CD4 counts (10). In prior reports, persistent HHV-8 vire-

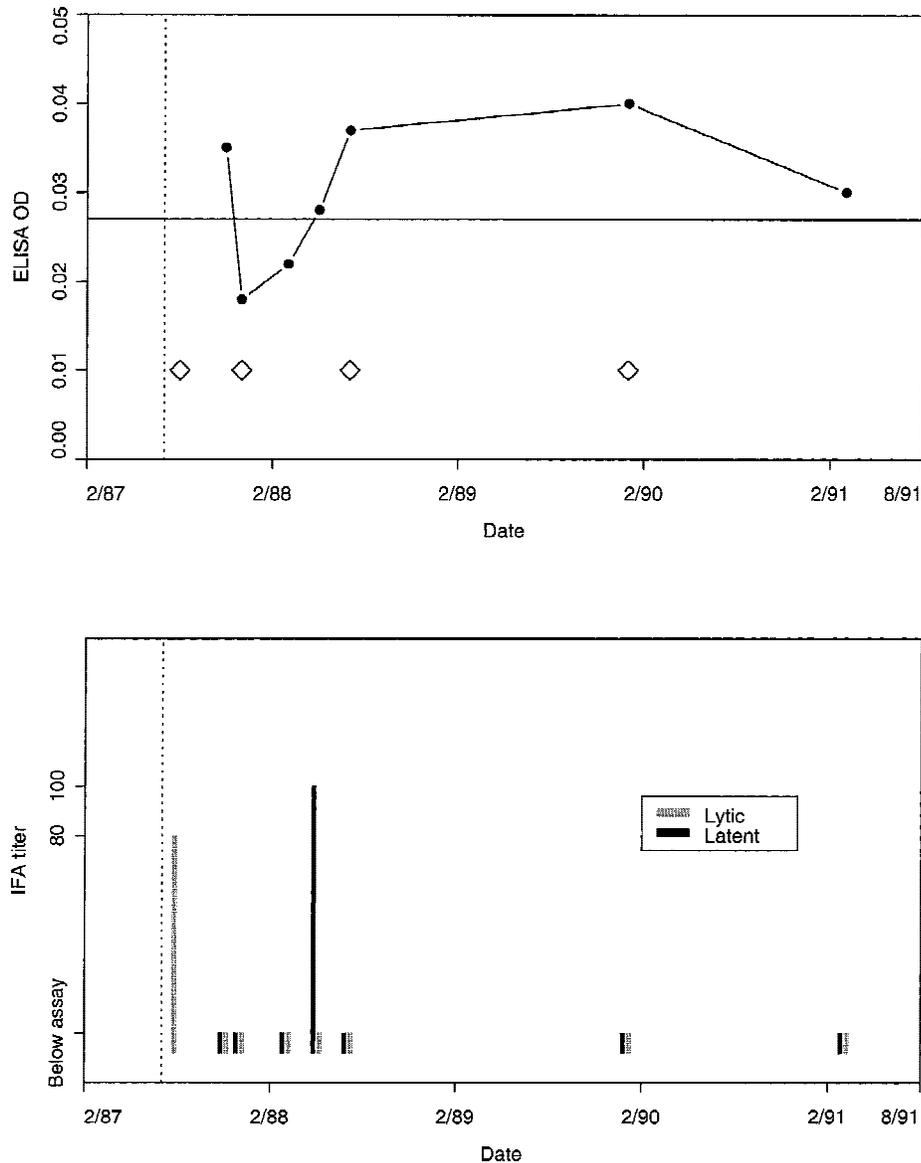


FIG. 1. Serial human herpesvirus 8 (HHV-8) assay results. Serial test results are displayed for an individual who was infected with HHV-8 and HTLV-I. In the top panel, diamond symbols (\diamond) show dates when peripheral blood mononuclear cell samples were positive for HHV-8 DNA using polymerase chain reaction. Also shown in the top panel are HHV-8 enzyme immunoassay optical density values, which were low and inconsistently positive (the cutoff value is shown as a *horizontal line*). The bottom panel shows test results for serum samples using indirect immunofluorescence antibody assays for lytic or latent viral proteins; only one serum sample was reactive for each assay. The vertical dashed line indicates a time point of July 1987, the date HTLV-I infection was acquired.

mia has been associated with either concurrent HIV infection (11) or, in those not infected with HIV-1, with a depressed CD4 count (12). The deleterious effects of HTLV-I infection on immune control of a second infection may be most pronounced if HTLV-I infection antedates the other infection. We cannot date the onset of our patient's HHV-8 infection, but it is likely that HHV-8 infection (first documented in August 1987) was present before the July 1987 HTLV-I-contaminated transfusion; in this respect, it is particularly striking that prolonged HHV-8 replication was seen in our patient.

Although persisting HHV-8 viremia in this patient supports an immunosuppressive effect of HTLV-I infection and the importance of cell-mediated immunity for control of HHV-8 replication, the limited extent of our observations and other existing data prevent strong conclusions. For example, in persons

infected with HIV, HTLV-I coinfection leads to a rapid clinical course (13), but surprisingly HIV replication is not increased in the presence of HTLV-I (14). Additionally, a prior study did not find HHV-8 viremia in 2 persons with Kaposi's sarcoma and HTLV-I (2). Importantly, our patient had myelofibrosis, which is itself associated with defective cell-mediated immunity (15) and might have facilitated prolonged viremia. Myelofibrosis is also associated with impaired humoral immunity and could have caused our patient's low HHV-8 antibody levels; to our knowledge HTLV-I-associated defects in humoral immunity have not been reported.

Finally, HHV-8 did not appear to affect the course of our patient's HTLV-I infection. As we report elsewhere in a larger study of HTLV-I natural history (16), our patient's levels of circulating HTLV-I proviral DNA were low early in her course,

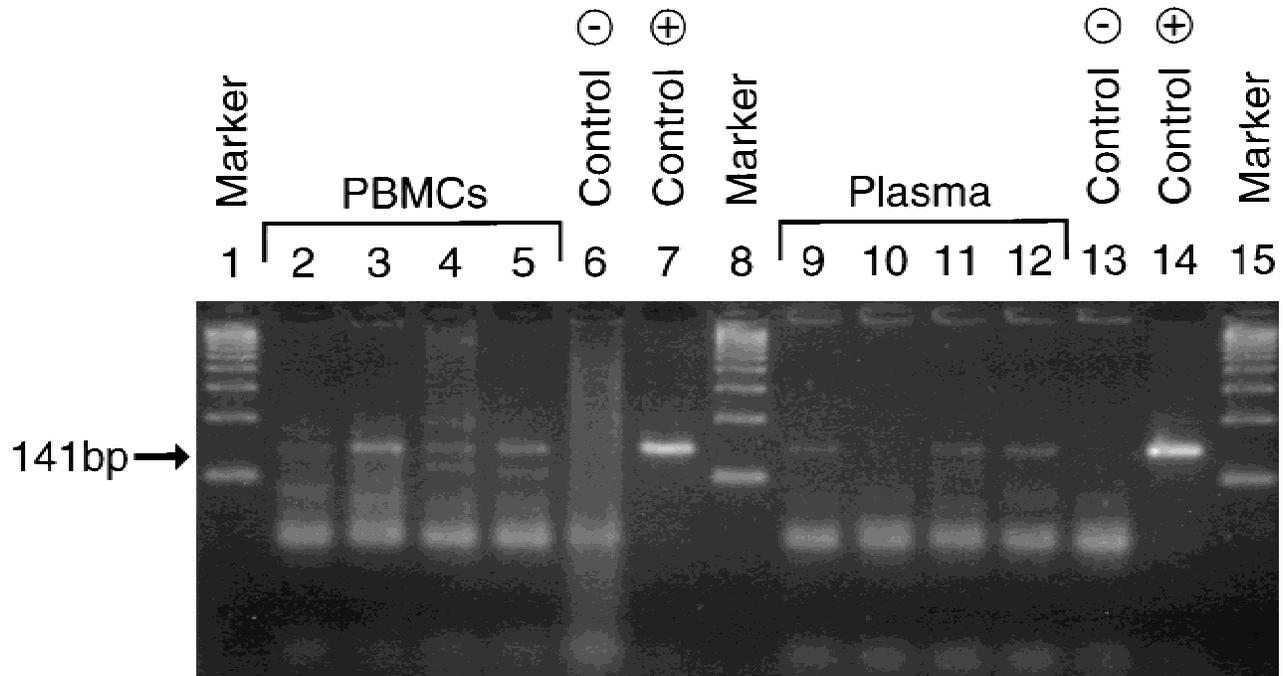


FIG. 2. Polymerase chain reaction. Results of human herpesvirus 8 (HHV-8)-specific polymerase chain reaction assays for peripheral blood mononuclear cells (PBMCs) and plasma samples are displayed. The expected product size was 141 bp (arrow). Lane 1, molecular weight markers (100–1000 bp); lanes 2–5, PBMCs from August 1987, December 1987, July 1988, and January 1990, respectively; lanes 6 and 7, PBMCs from HHV-8-seronegative and seropositive control subjects; lane 8, molecular weight markers; lanes 9–12, plasma samples from August 1987, December 1987, July 1988, and January 1990, respectively; lane 13, plasma from an HHV-8-seronegative control subject; lane 14, HHV-8 viral DNA; lane 15, molecular weight markers. The recipient had detectable DNA from PBMCs on all four dates and from plasma on all dates except December 1987.

consistent with those seen in other carriers, and higher when she developed HTLV-I-associated myelopathy/tropical spastic paraparesis, similar to other patients with this disorder.

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