

Poster presentation

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## Evaluation of Epstein-Barr virus (EBV) and human herpes virus-8 (HHV-8) in HIV-associated persistent generalized lymphadenopathy (PGL)

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### Background

Human immunodeficiency virus (HIV) infection is associated with persistent generalized lymphadenopathy (PGL) resulting from polyclonal B cell activation with significant circulating Epstein-Barr virus (EBV). Does HHV-8 contribute to the hyperplasia when present? Unlike EBV, seroprevalence of HHV-8 in the HIV-negative U.S. population is low. Kaposi's sarcoma (KS) in HIV infected is thought to reflect "de novo" HHV-8 infection, not reactivation. Does primary HHV-8 infection present as a polyclonal B cell activation manifested as PGL such as other HHV-8 associated co-morbidities like primary effusion lymphoma and multicentric Castleman's disease? This study examines the association of HHV-8 (LANA-1) with B cells in HIV-associated PGLs.

### Methods

HIV-positive serum samples from four women and 18 men (nine African-American, one African (woman) and 12 Caucasian) with available matching lymph nodes (eight axillary, eight groin, two cervical, two mandible, one supraclavicular, and one lung) constituted the study set of 22 individuals. Serum samples were examined for HHV-8 antibodies. The lymph nodes were examined histologically for HHV-8 using LANA-1 immunohistochemistry (IHC) and EBV using EBER in situ hybridization (ISH).

### Results

Three sera had positive HHV-8 titers: 1). 1:1240 in a Caucasian man, age 28, with a 1.0 cm hyperplastic axillary lymph node with prominent vascular proliferation and an area in the capsule with HHV-8+ endothelial cells. No LANA-1+ cells were present within the germinal centers or paracortical areas. Clinical KS was present at the time of the biopsy. 2). 1:640 in African woman, age 47, with a 2.2 cm axillary lymph node with giant follicular hyperplasia showing many EBER+ cells in paracortical areas and focal LANA-1 positive germinal center cells and few positive paracortical plasma cells. Pleural lymphoma developed 6 months after this biopsy. 3). 1:320 in an African/American man, age 46, who had a 0.6 cm groin lymph node, both LANA-1 and EBV negative. Neither lymphoma nor KS developed during the following 7 years. Hyperplastic lymph nodes from HHV-8 seronegative patients were LANA-1 negative but EBER+ (13 of 19). EBV negative nodes were small (0.6–0.3 cm), groin lymph nodes.

### Conclusion

PGL is associated with EBV positive cells in the paracortical areas of hyperplastic lymph nodes. HIV-positive patients with HHV-8 positive serology had large, medium, and small lymph nodes. The HHV-8 seropositive African woman's hyperplastic lymph node showed EBV(EBER) positive cells in the paracortical regions and a few HHV-8 (LANA-1)+ B cells in the germinal centers and a few positive plasma cells in the paracortical areas demonstrating

that HHV-8 can be present in B cells. Reactivation of HHV-8 in the African woman with HIV is more likely than "de novo" infection. Significant HHV-8 associated lymph node hyperplasia in the absence of EBV appears uncommon. PGL biospecimens are available from the AIDS and Cancer Specimen Resource (ACSR) for further study.

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