

Human Herpesvirus 8 Overview

ABOUT THE VIRUS

Human herpesvirus 8 (HHV-8), also known as Kaposi's Sarcoma (KS) associated herpesvirus, is a member of the Herpesviridae family. It has a linear, double-stranded DNA genome with an icosahedral capsid. HHV-8 is a member of the Gammaherpesvirinae subfamily, along with EBV. HHV-8 is found only in humans. AIDS-related KS was first discovered in 1981; the association with HHV-8 was identified through DNA sequencing by Chang and colleagues in 1994. HHV-8 has subsequently been identified in all types of KS: classic, endemic, post-transplant and AIDS-related KS; all of which have identical histological features. Research has shown a possible role for HHV-8 in the development of two rare lymphoproliferative disorders, multicentric Castlemann's disease (MCD) and primary effusion lymphoma (PEL).

In Europe and North America, the epidemiology of HHV-8 is very close to that of KS. HHV-8 antibodies are typically seen in people who have KS or are at high risk of developing it, such as homosexual men; but are usually not found in low-risk individuals, such as general blood donors. HHV-8 infections in the general population are high in Africa, intermediate in Eastern Europe and the Mediterranean, and low in Europe and the United States.

Similar to other herpesviruses, HHV-8 establishes latency in the human host after a primary infection. The preponderance of evidence suggests that sexual contact, predominantly among homosexual men, is the principal route of transmission in Europe and North America, where it is rare to nonexistent among children. Recent prevalence data from Central Africa and the Mediterranean suggest a horizontal, nonsexual method of transmission among children in those regions.

CLINICAL MANIFESTATIONS

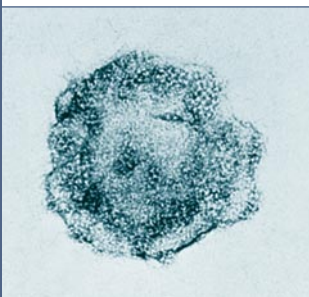
Primary HHV-8 infection presents as a fever and rash. The fever typically lasts from 2-14 days, with the maculopapular rash persisting for 3-8 days.

HHV-8 reactivates in the form of KS, which was first identified in 1872 by Moriz Kaposi. It has since been characterized into 4 well-documented clinical variants:

1. **Classic KS** primarily affects older males of Eastern European and Mediterranean lineage, and typically presents as cutaneous lesions on the lower extremities.
2. **Endemic KS** occurs in Africa, and may involve the lymph nodes in addition to typical skin lesions. This variant is often seen in children and HIV-negative individuals.
3. **Latrogenic KS** occurs in recipients of solid organ transplants who are treated with immunosuppressive medications. This form of KS occurs more commonly in individuals of Mediterranean descent.

4. **AIDS KS** is a very aggressive form first identified in the early 1980s in homosexual men who were otherwise healthy. In addition to cutaneous and lymphatic involvement, this variant often spreads to the lungs, GI tract, liver and spleen. When AIDS KS was originally identified, the lifetime incidence was approximately 50% in gay men. As a result of antiviral therapy advances in the late 1990s, the incidence has declined markedly.

Transplant patients have a high risk of KS due to their level of immunosuppression. In renal transplant patients, the overall risk is in the range of 1-3%, with a median diagnosis interval of 29-31 months following transplant. One study of patients who were HHV-8 positive prior to renal transplant found that 23% of them developed KS, while only 0.7% of the seronegative controls developed KS. KS development post-transplantation has also been seen in heart and lung patients.



Transmission electron micrograph of a virus member from the Herpesviridae family. Image courtesy of CDC.

HHV-8 infection has been noted as a cause of hematopoietic stem cell transplant (HSCT) failure. In these patients, the reactivated infection presents as fever with plasmacytosis, resulting in disseminated KS.

LABORATORY DIAGNOSIS

Serology and molecular testing methods, such as PCR, are recommended. HHV-8 is not cultured in the clinical virology laboratory. Quantitative real-time PCR allows for rapid, sensitive and specific monitoring of the viral burden (viral load) in the patient, which allows the clinician to track the patient's response to therapy.

TREATMENT

While low dose cidofovir and high dose foscarnet or ganciclovir have been shown to suppress reactivation of HHV-8, they do not inhibit episomal virus DNA polymerase. This is suggestive of replication by host DNA polymerase with the latent form of the virus. Acyclovir has not been shown to be effective against HHV-8. Highly active retroviral therapy (HAART) has been shown to effectively reduce the incidence of AIDS KS.

Selected References

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