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"Post-mortem identification of Kaposi Sarcoma-Associated Herpesvirus reservoirs despite seronegative status"

Background

Kaposi Sarcoma-Associated Herpesvirus (KSHV) undergoes a biphasic lifecycle in which a latent infection is established, followed by periodic lytic reactivation. KSHV is endemic to areas such as sub-Saharan Africa, where KSHV is primarily transmitted during childhood via saliva. A major risk occurs in those co-infected with HIV, where Kaposi Sarcoma (KS), a vascular endothelial cancer, becomes a major cause of mortality in these individuals. The ability of KSHV to undergo latency allows the virus to establish reservoirs which can reactivate and mediate KS occurrence upon immune dysregulation. Although previous studies in Zambia have identified KSHV reservoirs within the central nervous system (CNS) of HIV positive adults and documented sero-reversion in children, it remains unclear whether adults with undetectable KSHV antibodies from endemic areas, in spite of being seronegative can also harbor the virus, and where are the potential reservoir sites.

Methods

An extensive list of post-mortem tissue samples was collected from autopsy cases and processed into Formalin Fixed and Paraffin Embedded (FFPE) blocks by our collaborator in Zambia. Sociodemographic information, such as the cause of death, age, and sex, were documented at enrollment. HIV-1 serostatus was determined using HIV-1 Rapid Test, and KSHV serostatus was determined by an in-house immunofluorescence assay. The presence of KSHV in the tissues was determined by PCR and southern blot. The positive tissues' viral loads were determined by digital PCR against KSHV LANA and ORF26 genes. Immunohistochemistry against LANA protein was used to localize infected cells in positive tissues that had highest viral copy numbers.

Results

Here we analyzed 62 tissue blocks from a 36-year-old, KSHV and HIV-1 seronegative female who died of Pontine Hemorrhage due to hypertension. We were only able to analyze one case due to the time limits that I was able to work on. We detected KSHV in multiple anatomic sites including the CNS, oral respiratory tract, lymph nodes, ovaries, adrenal glands and the pancreas. The CNS tissues; choroid and meninges, had relatively the highest copy numbers for both LANA and ORF 26.

Conclusion:

Detection of KSHV reservoirs in a KSHV seronegative individual, highlights that antibody testing may underestimate KSHV prevalence as well as presents a risk in transplant patients, where an infected seronegative donor could still transmit KSHV to a recipient, who is at an increased risk of developing KS upon transplant.