Journal of Clinical Infectious Diseases & Practice

Chen , Jin. J Clin Infect Dis Pract 2021,6:2

Commentary Open Access

Accomplice of Kaposin Sarcoma-Associated Herpesvirus Infection: Human Immunodeficiency Virus-Associated Exosomes: Commentary

Lechuang Chen and Ge Jin*

Department of Biological Sciences, Case Western Reserve University School of Dental Medicine, Cleveland, USA

Abstract

Kaposi sarcoma herpesvirus (KSHV; also known as Human Herpes Virus 8 (HHV8)) is a causal agent for Kaposiâ€™s Sarcoma (KS), a leading cause of mortality and morbidity in people living with HIV/AIDS. In most of sub-Saharan Africa, the seroprevalence of KSHV infection reaches over 50%. In the United States and Europe, the prevalence of KSHV is less than 10% in the general population. Although KSHV infection is a key factor for KS to develop, in most cases infection with KSHV alone does not lead to KS. Globally, KS incidence is around 1 in 100,000 in the general population compared to 1 in 20 in HIV-infected individuals. That means HIV infection is the most important cofactor of the KSHV infection. Despite advances in our understanding of virology and pathogenesis of KSHV in recent years, but how HIV infection strengthens does the infection and transmission of KSHV are still not well understood.

Keywords: KSHV; Exosomes; AIDS-KS

Description

Kaposi Sarcoma Herpes Virus (KSHV; also known as Human Herpes Virus 8 (HHV8)) is a causal agent for Kaposi's Sarcoma (KS), a leading cause of mortality and morbidity in people living with HIV/AIDS. In most of sub-Saharan Africa, the seroprevalence of KSHV infection reaches over 50% [1]. In the United States and Europe, the prevalence of KSHV is less than 10% in the general population [2,3]. Although KSHV infection is a key factor for KS to develop, in most cases infection with KSHV alone does not lead to KS. Globally, KS incidence is around 1 in 100,000 in the general population compared to 1 in 20 in HIV-infected individuals [4]. That means HIV infection is the most important cofactor of the KSHV infection. Despite advances in our understanding of virology and pathogenesis of KSHV in recent years, but how HIV infection strengthens does the infection and transmission of KSHV are still not well understood.

A recent article published in Journal of Virology (Feb 12, 2020), entitled "HIV-associated exosomes promote infection of Kaposi sarcoma-associated herpesvirus via epidermal growth factor receptor"; Chen et al. exhibited an effort to meet this challenge [5]. This research used a 3-dimensional culture model of immortalized and primary human oral epithelial cells to mimic the real oral mucosa due to the major transmission route for KSHV infection is the oral cavity through saliva [6]. The HIV-positive saliva samples were collected from eight HIV-positive donors. They isolated exosomes, a type of extracellular vesicles about 30–120 nm in diameter, that released in saliva by HIV-positive immune cells, which was demonstrated later that were the key factor to enhance KSHV infectivity in oral epithelial cells. Three key messages are present in this study based on the results: first, the saliva containing HIV-associated exosomes is a risk factor for the enhancement of KSHV infection in the oral cavity. Second, The TAR RNA in HIV-positive exosomes contributes to enhancing KSHV infectivity through the Epidermal Growth Factor Receptor (EGFR). An inhibitory aptamer to TAR RNA reduces KSHV infection facilitated by the synthetic TAR RNA in oral epithelial cells. Finally, Cetuximab, a monoclonal neutralizing antibody to EGFR, blocks HIV-positive exosome-enhanced KSHV infection. The inhibition of EGFR serves as a novel strategy for preventing KSHV infection and transmission in the oral cavity. This is the first report addressing whether HIV-positive saliva exosomes are involved in the infection and transmission of KSHV. The findings provide an insight into the mechanisms underlying HIV-specific components and co-infection of KSHV in people living with HIV/AIDS through the oral cavity. In addition, the results suggest that targeting the HIV TAR RNA and EGFR of oral epithelial cells may serve as novel approaches to control KSHV infection in the HIV-infected population.

Exosomes are a type of extracellular vesicle that contains various proteins, DNA, and RNA [7]. HIV-positive exosomes contain the HIV trans-activation response (TAR) element, Tat, and Nef RNAs [8]. Moreover, exosomes may incorporate viral proteins when formed in infected cells (Tat, Nef, Env, etc.) [9]. In this study, Chen et al. demonstrated HIV TAR RNA in exosomes contributes to enhancing KSHV infectivity. In another study, Zeng et al. revealed the Tat protein induces expression of KSHV ORF50 and KSHV lytic replication that is a potential factor in the pathogenesis of AIDS-KS [10]. Moreover, Zhu et al. investigated HIV Nef protein, which synergy with KSHV vIL-6, contributes to the pathogenesis underlying AIDS-KS [11].

Despite a dramatically decrease in the incidence of AIDS-KS globally after the introduction of Antiretroviral Therapy (ART), AIDS-KS remains the most frequent tumor in HIV-infected patients worldwide [12]. There are still no vaccines or curative drugs [3].

Conclusion

Considering the close interrelationship between KSHV and HIV-positive exosomes, inhibiting the HIV-positive exosome entry into the cells or dysfunction of the exosome embedding component may be a potentially effective therapeutic approach in AIDS-KS patients.

References

1. Rohner E (2016) HIV and human herpesvirus 8 co-infection across the globe: Systematic review and meta-analysis. Int J Cancer 138(1): 45-54.

2. Bhutani M (2015) Kaposi sarcoma-associated herpesvirus-associated malignancies: epidemiology, pathogenesis, and advances in treatment. Semin Oncol 42(2): 223-46.

***Corresponding author:** Ge Jin, Department of Biological Sciences, Case Western Reserve University School of Dental Medicine, Cleveland, USA, E-mail: lxc448@case.edu

Received March 03, 2021; **Accepted** March 16, 2021; **Published** March 23, 2021

Citation: Chen L, Jin G (2021) Accomplice of Kaposi's Sarcoma-Associated Herpesvirus Infection: Human Immunodeficiency Virus-Associated Exosomes: Commentary. J Clin Infect Dis Pract 4: 134.

3. Mesri EA, E. Cesarman, C. Boshoff (2010) Kaposi's sarcoma herpesvirus/ Human herpesvirus-8 (KSHV/HHV8), and the oncogenesis of Kaposi's sarcoma. Nature reviews. Cancer 10(10): 707.

4. Gallo R.C (1998) The enigmas of Kaposi's sarcoma. Science 282(5395): 1837-9.

5. Chen L (2020) Human Immunodeficiency Virus-Associated Exosomes Promote Kaposi's Sarcoma-Associated Herpesvirus Infection via the Epidermal Growth Factor Receptor. J Virol 94(9).

6. Li Y (2018) Evidence for Kaposi Sarcoma Originating from Mesenchymal Stem Cell through KSHV-induced Mesenchymal-to-Endothelial Transition. Cancer Res 78(1): 230-245.

7. Kalluri R, V.S. LeBleu (2020) The biology, function, and biomedical applications of exosomes. Science 367(6478).

8. Chen L (2018) Exosomes derived from HIV-1-infected cells promote growth and progression of cancer via HIV TAR RNA. Nat Commun 9(1): 4585.

9. Dias MVS, CS Costa, L.L.P daSilva (2018) The Ambiguous Roles of Extracellular Vesicles in HIV Replication and Pathogenesis. Front Microbiol 9: 2411.

10. Zeng Y (1989) Intracellular Tat of human immunodeficiency virus type 1 activates lytic cycle replication of Kaposi's sarcoma-associated herpesvirus: role of JAK/STAT signaling. J Virol 81(5): 2401-17.

11. Zhu X (2014) Synergy between Kaposi's sarcoma-associated herpesvirus (KSHV) vIL-6 and HIV-1 Nef protein in promotion of angiogenesis and oncogenesis: role of the AKT signaling pathway. Oncogene 33(15): 1986-1996.

12. Facciolà A (2017) Kaposi's sarcoma in HIV-infected patients in the era of new antiretrovirals. Eur Rev Med Pharmacol Sci 21(24): 5868-5869.