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Epstein-Barr virus and Uterine Cervical Carcinoma Risk

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Abstract

Uterine Cervical Carcinoma (UCC) is the most common gynecological malignancy internationally, with a rising incidence in recent years. Accumulating data indicates that specific viral infections, especially that are caused by oncogenic viruses including Epstein-Barr virus (EBV) that may contribute to UCC development in addition to progression. Understanding the complex interplay between EBV infections and UCC risk is crucial for developing novel preventative and therapeutic interventions. Consequently, this review study intends to explain the relationship between the occurrence of UCC and Epstein-Barr virus infection.

Keywords: Epstein-Barr virus and UCC, Risk factors, Women.

Introduction

Uterine Cervical Carcinoma (UCC) at a standstill a leader global health concern, secretarial for significant morbidity as well as mortality in women at universal. Despite considerable study efforts and advances in screening and protecting strategies, UCC continues to sham a substantial public health challenge, particularly in low- and middle-income countries (1). A comprehensive understanding of the etiological factors underlying the development of UCC is essential for devise enhanced prevention, premature detection, as well as treatment strategies. Although extensive research has been conducted on the etiology or pathogenesis of UCC, the specific mechanisms underlying its development are not yet completely understood. An assortment of factors, include obesity, age, hormonal imbalance in addition to genetic predisposition and environmental exposures have been implicated in UCC development. newly, a growing body of data has painted viral infections, EBV, as one of the key factors of UCC pathogenesis (2).

Viruses are obligate intracellular parasites, they are well-recognized for their capability to influence host cellular processes, potentially leading to malignant transformation. Quite a lot of viruses like HPV, Epstein-Barr virus (EBV), hepatitis B and C viruses (HBV and HCV) have been notorious as oncogenic viruses that playing vital roles in the pathogenesis of various human cancers. Yet, the association between viral infections especially HPV infection and UCC remains an active area of investigation, with inconsistent findings reported in the literature (3). This study aim to provide a comprehensive overview of the current state of facts regarding the relationship between EBV infections and UCC risk. We will discuss the evidence supporting the involvement of this virus in the development of UCC, focusing on their potential roles in oncogenesis, molecular mechanisms, and clinical implications. Eventually, elucidating the role of viral infections in UCC may lead to novel preventive and therapeutic strategies for this prevalent and life-threatening disease.

Relation between EBV and UCC

Epstein-Barr virus, also known as human herpesvirus 4 (HHV4), is a virus that has been connected with different types of cancers, including Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma, as well as some types of stomach cancer like gastric carcinoma. Though, the relationship between EBV and UCC is not well-established (4). Some studies have detected EBV DNA or viral proteins in UCC tissues (4), while others have not found any important association between EBV infection and UCC Several mechanisms have been proposed to clarify the role of EBV in the development of UCC (5). Two crucial viral proteins, Epstein-Barr nuclear antigen 1 (EBNA-1) as well as latent membrane protein 1 (LMP-1), (Figure. 1) have been concerned in the oncogenic process during EBV infection (5).

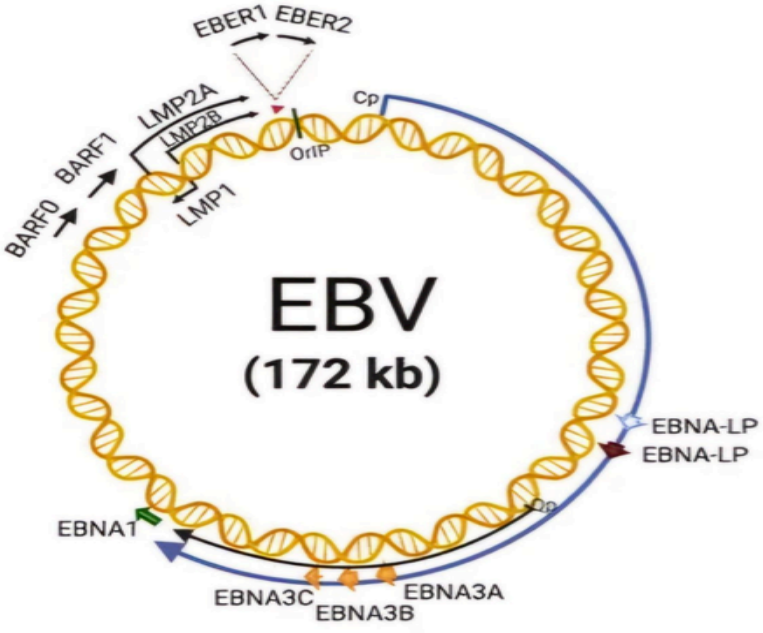

Figure. 1: EBV genomic structure (6)

EBNA-1 is a multifunctional protein involved in the replication, maintenance, and segregation of the EBV episome in latently infected cells. It is expressed in all EBV-associated malignancies and plays a pivotal role in the persistence of viral episomes within host cells.

Additionally, EBNA1 contributes to the immortalization of infected cells by altering cellular gene expression and promoting genomic instability. During clinical diagnosis, the detection of EBNA-1 expression may serve as a marker of latent EBV infection as well as its associated cervical malignancies (5). L LMP-1, on the other hand, is a trans-membrane protein that functions as a constitutively active copy of the tumour necrosis factor receptor (TNFR) family, stimulating numerous signalling pathways that promote cell survival, proliferation, as well as differentiation. LMP-1 exerts its oncogenic effects by activating the nuclear factor-kappa B (NF-κB), mitogen-activated protein kinase (MAPK), as well as Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathways. Detection of LMP-1 expression during clinical diagnosis can indicate the presence of an active EBV infection and suggest a additional aggressive disease course, as LMP-1 is implicated in immune evasion, angiogenesis, and metastasis (7).

EBV has developed a variety of strategies to avoid the host immune response, allowing the virus to persist in infected cells. This immune evasion can cause chronic inflammation as well as contribute to the development of a favourable microenvironment for UCC initiation and progression (8). There have been some studies suggesting that coinfection with EBV and HPV may increase the risk of UCC development. The hypothesis is that the two viruses could act synergistically, with EBV potentially promoting HPV-induced cervical carcinogenesis. Co-infection with EBV, HPV, and human immunodeficiency virus (HIV) could potentially increase the risk of UCC development. Infection with these high-risk types can lead to the formation of abnormal cervical cells, which may progress to UCC if not detected and treated early. HIV infection impairs the immune system, making it more difficult for the body to fight off infections, including HPV (9). Women with HIV are more likely to have persistent HPV infections, which can increase the risk of developing UCC. Additionally, HIV-infected women are more likely to have faster progression from pre-cancerous lesions to invasive UCC compared to women without HIV. Although EBV is not directly linked to UCC, co-infection with HIV could further increase the risk due to the impaired immune response. Co-infections can complicate the clinical picture, and it is essential for healthcare providers (8).

HPV, EBV, and KSHV coinfections can stimulate angiogenesis, the formation of new blood vessels, by upregulating pro-angiogenic factors (e.g., VEGF and IL-8), which may promote tumor growth and metastasis. Upon coinfection, EBV and HPV oncoproteins have been shown to cooperatively activate several critical signalling pathways, including PI3K/AKT, MAPK/ERK, JAK/STAT, β-catenin, and p53. These pathways are known to regulate various cellular processes, such as cell survival, proliferation, differentiation, and migration, which are often dysregulated in cancer (9).

Consequently, the simultaneous activation of these pathways by EBV and HPV oncoproteins can contribute to enhanced UCC development and progression. Given the current state of research, the direct relationship between EBV and UCC risk remains unclear. Further studies are needed to investigate the potential association between EBV and uterine cancer, as well as the underlying mechanisms involved if such a link exists (10)

Conclusion

Recognizing the implications of EBV infection in UCC aetiology and pathogenesis is vital for addressing the escalating burden of UCC. Developing innovative preventative and therapeutic

interventions requires a thorough understanding of the intricate relation between viral infections and UCC risk.

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No competing of interest raises from any third party upon publication this manuscript.

Ethics statement

The author approved that this research follows the journal's ethical guidelines as appeared on the journal's author guidelines page.

Author contributions

AMZ; Conceptualization, and writing the original draft & editing; QAJ; final revising. Both authors have read and agreed to publish this manuscript.

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