Human papillomavirus DNA in plasma of patients with cervical cancer

ABSTRACT

The plasma HPV DNA originated from the CC, was associated with metastasis and could be used as a marker representing the circulating free CC DNA.

INTRODUCTION

Background Cervical cancer (CC) is one of the most common malignancies in women worldwide, especially in developing countries. Several studies have suggested that human papillomavirus (HPV) initiates and causes endogenous genetic alterations in the progression of CC. First, epidemiological studies have shown that most human CCs harbor the "high risk" HPV types 16, 18, 31 and 33. Second, some HPV proteins such as E6 and E7 interact with human tumor suppresser gene products and change cellular phenotypes. Finally, the integration linearizes HPV DNA between E1 and L1 genes and disrupts the viral E2 gene, which consequently induces expression of E6 and E7 genes. This genomic rearrangement is thought to be critical for the transformation and proliferation of the early precursors to these cancers. From a diagnostic viewpoint, the consistent presence of HPV in CC allows the viral DNA to be used as a genetic marker. For example, cervical pre-malignant lesions can be screened for highly sensitive HPV DNA detection technology in cell scrapings. Accumulating lines of evidence have elucidated that there is tumor DNA in patients' circulation. Such DNA can be detected in plasma or serum via specific genetic and epigenetic alterations of the primary tumor. Though the mechanism of this phenomenon is not clear, the presence of tumor DNA in blood may have diagnostic and prognostic value. Interestingly, viral DNA has been documented to occur as tumor DNA in the circulation of patients with primary tumors caused by viral infection. For example, there is a high frequency of hepatitis viral genomes and Epstein-Barr viral (EBV) DNA in the circulation of patients with hepatoma and nasopharyngeal cancer (NPC), respectively. In addition, the circulating EBV DNA may be an invaluable tool for patient monitoring. Since HPV DNA serves as a genetic marker for CC, we tested whether HPV DNA could be detected in the plasma of CC patients and whether it originated directly from tumor cells. Moreover, we determined whether the circulating HPV DNA has any diagnostic and prognostic clinical potential for patients with CC.

CONCLUSION

Conclusions The results of the present investigation indicated that it was possible to identify HPV DNA in DNA extracted from the plasma of some patients with CC. More importantly, The HPV genomes from both tumor and plasma were revealed the same type and physical status by integrating into the host genome. Thus the viral DNA most likely originated from the tumor itself and the plasma HPV DNA represented the circulating free cell CC DNA. Finally, plasma HPV DNA was a specific, but not a sensitive, genetic marker in which strongly associated with CC metastasis.