論 文 要 旨

The etiologic role of human papillomavirus in penile cancers in Vietnam

ベトナム陰茎がんにおけるヒトパピローマウイルス感染とその役割に関する検討

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【序論および目的】（適宜、項目をたてて、必ず２頁で記載する）

Human papillomavirus (HPV) is a well-established risk factor of cervical cancer but its role in penile cancer is still un-established. To understand the etiologic role of HPV in the development of penile cancer, we examined the presence, genotype, viral load, and physical status of HPV and $p16^{INK4A}$ protein expression in penile squamous cell carcinomas (PSCCs) from Vietnam. We also examined PI3K p110α and VEGF 165 protein expressions and its correlation to the HPV infection.

【材料および方法】

The present study examined 120 formalin-fixed and paraffin-embedded penile squamous carcinomas (PSCCs) diagnosed at the National Cancer Hospital in Hanoi, Vietnam from January 2005 to May 2009. Seventeen cervical carcinomas (CCs) samples from the same Institute were used as a positive control. HPV DNA was detected by PCR using SPF10 primers and a primer set targeting HPV-16 E6. The INNO-LiPA HPV genotyping kit was used to determine genotype. HPV-16 viral load and physical status were determined by real-time PCR. $P16^{INK4A}$, PI3K p110α and VEGF 165 protein expressions were investigated by immunohistochemistry.

【結　果】

1. HPV detection rate

HPV DNA was detected in 27 of 120 (23%) PSCCs, including 2 of 3 (67%) basaloid PSCCs. In CCs, HPV was detected in 16 of 17 (94%) cases. The presence of HPV in PSCCs was not significantly related to any

clinicopathological features examined in this study.

2. Distribution of HPV genotypes

The most frequently detected HPV genotype was HPV-16 (24 of 27 cases, 89%). In addition, HPV-11, -18, -33, and -58 were detected in one case each. Multiple infections were found in 2 (7%) of HPV-positive PSCCs, which were HPV-16/-58 and HPV-16/-18. In CCs, HPV-16 was detected in 13 of 18 (81%) HPV-positive cases; other HPV genotypes detected were HPV-18, -11, and -52. HPV-18 was detected in 6 CCs (38%) and the rest was detected in one case each. Multiple infections were found in 4 (25%) of HPV-positive CCs, including 3 cases positive for HPV-16/-18 and one case positive for HPV-11/-16/-18.

3. Viral load and physical status

In 16 of 18 (89%) HPV-16-positive PSCCs, the HPV DNA was considered to be integrated into the host genome. The geometric mean of the HPV-16 viral load was 0.4 copies per cell. In HPV-16 positive CCs, the HPV DNA was integrated into the host genome in 7 of 13 cases (54%). The geometric mean of HPV-16 viral load in cervical cancers was 3 copies per cell. The HPV-16 viral load of 1 copy or more per cell was more frequently observed in basaloid and non-keratinizing PSCCs than in keratinizing PSCCs (P=0.032)

5. $P16^{INK4A}$, PI3K p110α and VEGF165 protein expressions

$P16^{INK4A}$, PI3K p110α and VEGF165 were expressed in 10 of 44 (23%), 48 of 53 (91%) and 37 of 52 (71%) of PSCCs, respectively. $P16^{INK4A}$ over-expression was significantly related to PSCCs infected with high-risk HPV (P = 0.018) and HPV-16 copy numbers (P < 0.001). The expressions of PI3K p110α and VEGF 165 protein were not related to high-risk HPV presence or HPV-16 viral load.

【結論及び考察】

The etiologic role of high-risk HPV in the development of PSCCs was suggested by its DNA integration into the PSCC genome and its association with $p16^{INK4A}$ overexpression. $P16^{INK4A}$ could be a biomarker for HPV-related PSCCs. The expression of PI3K and VEGF were observed over-expressed in the majority of PSCCs but not related to HPV infection.