

Association between human papillomavirus and urothelial carcinoma of the bladder

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Human papillomavirus (HPV) is the most common sexually transmitted viral pathogen in the world and poses a serious global socioeconomic burden due to its oncogenic nature. HPV is responsible for one of the most common virus-associated cancers worldwide, accounting for approximately 8% of all malignancies¹. HPV causes low-grade, benign lesions such as condyloma acuminata in the anogenital region and is also strongly associated with cervical, anal, vulvo-vaginal, and penile carcinomas². Although they are in close proximity anatomically, it has long been debated whether urothelial carcinoma of the bladder (UCB) is associated with HPV. The main hypothesis regarding the relationship between HPV and UCB is that HPV shows epithelial tropism and, during transmission, one of the first sites where HPV is encountered by the host is the urethral external meatus³. The lack of a clear consensus on this relationship until recently can be attributed to limitations related to the methodological differences in previous studies. These factors include small case series, not sampling fresh tissue, and the lack of adequate case-controlled studies⁴. In light of this information, a case-controlled study conducted with fresh tissue samples demonstrated a strong correlation between UCB and HPV infection (odds ratio: 4.24, 95% confidence interval 1.63–12.34)⁵. Once this relationship is established, the next question is about the prognostic value of HPV in UCB. HPV positivity has been shown to be a favorable prognostic

factor in cervical, anal, and head and neck cancers⁶. In UCB, in contrast, tumor grade is very important in terms of disease progression. However, it seems that there is also no consensus on the relationship between tumor grade and HPV in UCB. Tenti et al.⁷ reported that HPV was associated with low-grade tumors, Cai et al.⁸ determined that HPV was associated with high-grade tumors, and Sarier et al.⁵ observed no significant relationship between tumor grade and HPV.

This may explain the absence of studies investigating the prognostic value of HPV positivity in bladder carcinoma until recently. However, two recent studies sought answers to this question. In their study evaluating the 2-year follow-up results of HPV-positive UCB patients with pTa or PT1 disease, Sarier et al.⁹ observed no statistical difference in disease progression compared to HPV-negative patients. However, a noteworthy finding of the study was that HPV-positive patients had a higher tumor recurrence rate during the follow-up period. Moghadam et al.¹⁰, on the other hand, reported significant associations between HPV and both tumor recurrence and tumor stage. In summary, the increasing diagnostic use of nucleic acid amplification tests such as PCR in recent years has further elucidated the relationship between UCB and HPV. The significant relationship between HPV and tumor recurrence may guide future research to determine the prognostic value of HPV in UCB.

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