Chapter 2

Relation between Human Papilloma Virus (HPV) and Cancer Bladder

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Keywords

Human papilloma virus; Carcinoma; Cancer; Urinary bladder

Introduction

More than 12 million new cases of cancer occur every year worldwide [1]. Urinary bladder cancer UBC ranks ninth in worldwide cancer incidence. It is the seventh most common malignancy in men and seventeenth in women [2]. Worldwide approximately 145,000 patients die from UBC annually [3].

There are thirteen different HPV genotypes, among others HPV 16 and 18, are associated with malignancy and are referred to as high-risk HPVs. In contrast HPV 6 and 11 are associated with nonmalignant genital disease and are called low-risk anogenital-specific HPVs [4].

HPV-16 and -18, have been shown to be the necessary cause of cervical cancer [4]. There has also been investigation of the possibility that HPV may cause cancers of other sites, such as head and neck, anus, vulva This because the virus is epithelium-tropic [5]. However, the association between HPV infection and some other cancers, for example, breast cancer [6] and bladder cancer [5], is still inconclusive.

The question whether bladder cancer is related to HPV infection has been raised. Since 1990, a series of descriptive studies have investigated the HPV prevalence in various histological types of bladder cancers, this was
mainly in transitional cell carcinoma (TCC). Meanwhile, a growing number of case control studies have detected HPV DNA in both malignant and benign or normal bladder tissues [5].

Thus, our present objective was to collect published information on HPV prevalence in bladder tissues to explore the prevalence of HPV in bladder cancer cases and to test the association between HPV infection and risk of bladder cancer.

**Literature Review**

It is certainly true that the epithelia of the bladder can also be infected by HPV, especially the condyloma acuminate, which is characteristic of HPV infection and has been reported in the bladder [7].

There is an association between HPV infection and presence of malignancy of the urinary tract. HPV DNA has been detected in both transitional cell and squamous cell carcinoma of the bladder, and an increased high-risk HPV prevalence has been found in bladder tumours compared with normal urinary bladder specimens [8,9]. This may be attributed to the fact that, HPV encodes two oncoproteins: E6 and E7. The E6 protein interacts with p53, stimulating the degradation of p53-associated proteins via the ubiquitin-dependent pathway [10]. And as the HPV is a sexually transmitted disease, a man with transitional cell carcinoma can transmit the virus to his partner and causes cervical cell carcinoma [11].

According to a meta-analysis that showed the distribution of HPV and its prevalence geographically, HPV may be caused due to smoking, sexual behavior and other cultural causes. Also geographically HPV prevalence is distributed across many countries, but cancer bladder resulted from HPV infection is more common in Asia and Europe. Most cancer bladder occurs in men, and cancer affecting the bladder due to HPV infection, is more prevalent than HPV caused cancer in larynx and oral cavity and even prostate, but less than the prevalence of tonsil cancer caused by HPV and is equal to breast cancer [6].

Another study showed that HPV is not only present in the neoplastic cells, but also may be present in the non-neoplastic cells, but with smaller percentage. By using PCR, that was more sensitive and accurate than the immunochemical methods. The study resulted in that, there is a high risk of HPV infection in cases of urinary bladder carcinoma compared to normal urinary bladder specimens. Also there is increase in the multiple HPV infections in the urinary bladder carcinoma that may be due to the synergistic effect of the different kinds of HPV [8].

In a study that investigated HPV 16, 18 and 33 in cases with transitional cell carcinoma. There is an over expression of p53 protein in 35.6% of these cases. The study suggested that HPV infection and overexpression of p53 are linked together to TTC. Based on the fact that p53 protein has short life span so its presence in the specimen and its
over expression indicates over production or decrease in the destruction of this protein. So, this indicates its mutation. The study also found a strong association between the superficial bladder cancer and early grades of tumor as N1, and HPV infection, on the other hand this association is very weak in case of advanced stages of the tumor [12].

In the same context another study found that, there is increase in the HPV 6\11 and 16 \18 expressions in schistosomiasiis cystitis with dysplasia more than in case of TCC with schistosomaisis patient. and also their expression is more common in invasive TCC groups than superficial TCC [13] groups.

In the contrary, another study suggested that we can’t use HPV testing as a diagnostic adjust for inverted papilloma cases as based on 27 patients with inverrted papilloma. Their ages range from 35 to 78 and male: female ratio is 11:1 and by using immunochemical methods there is no evidence of presence of HPV marker but there is immunoactivity to p16 in 41% of cases so p16 isn’t a surrogate marker for HPV infection in urothelial inverted papilloma [14].

In 2012 there was a case report of 35 male patient presented with bladder carcinoma developed in 2 months, after urethral condyloma acuminatum, and a history of persistent of HPV58 infection in the urinary tract 8 years ago. The study suggested that the patient had HPV infection after its transmission from distal urethra after sexual contact that explains the presence of the same high risk HPV in the condyloma and bladder carcinoma. By ISH analysis they could detect HPV DNA in the tumor tissues and also they could find diffuse and punctuate patterns of high risk HPV-DNA signals in condyloma and bladder cancer specimen respectively. According to the study p16-INK4a and mcm-7 protein have high expression in HPV- positive bladder cancer and rarely found in HPV-negative bladder cancer. Finally the study resulted in HPV58 plays important role in developing bladder cell carcinoma [15].

Conclusion

The association between bladder cancer and HPV isn’t clear enough and more investigation and clinical studies should be done to understand the main link and pathogenesis.

References


