High-Risk Human Papillomavirus Infection in Different Histological Subtypes of Renal Cell Carcinoma

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Limited data exist regarding whether a high-risk human papillomavirus (HR-HPV) infection increases the risk of developing renal cell carcinoma. The aim of this study was to investigate whether HPV infection has a role in the pathogenesis or development of a certain histological subtype of renal cell carcinoma. Formalin-fixed paraffin-embedded (FFPE) specimens of 122 patients with histopathologically proven renal cell carcinoma and their respective peritumoral tissues were examined. The presence of HPV-DNA was determined by a combination of MY/GP+ consensus primers and HPV-16/18 type specific nested PCRs followed by direct sequencing. Catalyzed signal-amplified colorimetric in situ hybridization (CSAC-ISH) technique was applied to determine the physical status of viral genome. The expression of p16INK4a and HPV L1 capsid proteins was evaluated using immunohistochemistry. HPV genome was detected in 37 (30.3%) tumor specimens and their four (4.1%) corresponding peritumoral tissues. HPV-18 was the most common viral type identified followed by HPV-16 and 58. Immunexpression of p16INK4a was detected in 24 (20.3%) cases. Data analysis showed a significant correlation between p16INK4a expression and the presence of HR-HPV DNA (P<0.001). CSAC-ISH analysis confirmed HR-HPV infection in 45% of tumors, which were previously tested positive for HPV-DNA. Diffuse signal pattern was identified in 15 (83.3%) samples whereas a mixed pattern of diffuse and punctate signals was only detectable in three cases. The results indicate an association of HR-HPV types with renal cell carcinoma. It is proposed that HPV infection in high-grade tumors might precede disease progression in a number of tumors, particularly of the papillary subtype. J. Med. Virol. 86:1134–1144, 2014.
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INTRODUCTION

In recent decades, the occurrence of renal cell carcinoma has increased, accounting for about 3.8% of adult malignancies and approximately 90% of the entire renal neoplasms [Jemal et al., 2010]. Generally, it is believed that various subtypes of renal cell carcinoma arise from different specialized epithelial cells along the nephron [Shanks, 1999]. Renal cell carcinoma is regarded as a highly aggressive tumor. Metastasis can be found in a third of patients during diagnosis, which leads to over 40% mortality. However, for localized renal cell carcinoma, surgery is the treatment of choice [Janzan et al., 2003; Lam et al., 2005]. Recent advances in renal cell molecular biology

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