Detection of Human Papillomavirus DNA in Esophageal Carcinomas by Polymerase Chain Reaction and in Situ Hybridization, and Its Relation to an Overexpression of p53 Antigen

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Abstract: Human papilloma viruses (HPVs) are associated with various epithelial lesions, especially squamous cell carcinomas. We studied 95 formalin-fixed, paraffin-embedded esophageal surgical sections to elucidate the relationship between HPV and esophageal carcinoma, using 6 cases of non-neoplastic benign lesions for comparison purposes. The presence of HPV-16, 18 and 33 was analyzed using DNA sequencing with type-specific primers containing E6 regions by polymerase chain reaction (PCR) and In situ hybridization (ISH). No HPV DNA was found in the benign lesions. HPV DNA was detected in 18 cases of esophageal carcinoma using the PCR method; HPV-16 in 9 cases (50%), HPV-18 in 16 cases (88.9%), and HPV-33 in 3 cases (16.7%). HPV-16 and 18 were detected together in 6 of 18 cases (33.3%), and all 3 types of the HPVs were detected together in 2 of 18 cases (11.1%) within the same tissue specimens. A total of 17 cases with amplified HPV genomes showed pan HPV DNA signals by ISH. The HPV was diffusely detected within the solid nests of the carcinoma and within the dysplastic lesions. When using ISH, however, utilizing type-specific probes, only a small number of positive cases (3 cases of type-16, 3 cases of type-18 and 2 cases of type-33) were found. The expression of p53 protein was detected in 56 out of 95 cases (58.9%). In addition, 31 out of 77 cases (40.5%) without any HPV DNA infection showed a strong p53 expression and all 21 cases of dysplastic lesions without HPV showed a strong p53 expression. However, only 2 out of 18 HPV DNA-positive cases showed a diffuse expression of p53 protein. The other 16 cases showed a weak p53 expression and 4 dysplastic lesions with the HPV genome showed a negative expression for p53 protein. We investigated the relationship between the HPVs and p53 expression in the esophageal carcinoma. Although in our series, no significant correlation was observed between HPV DNA and the mutant p53 expression, a strong p53 expression was observed in cases without HPV DNA infection. It was suggested that the relationship between HPV and p53 in the carcinogenesis.

Key words: esophageal carcinoma, Human papilloma virus, in situ hybridization, p53