Presences of human papillomavirus DNA (HPV) and immunohistochemical p53 overexpression in papillomas of oral cavity

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Abstract

HPV belongs to a family of tumorigenic viruses and induces cutaneous and mucosal proliferation of epithelial cells (papillomas, condylomas, warts). The abnormality accumulation of p53 protein appears to be a common step in the development of many human cancers and has been frequently reports in human cancers including head and neck. The aim of this study was to examine HPV infection incidens and p53 alteration in oral papillomas. HPV was detected by PCR, p53 accumulation by immunohistochemical detection. The overexpression of p53 was revealed in 20 cases (55%) out of 36 papillomas. We found p53 overexpression in 8 out of 13 HPV positive papillomas (61.5%) and in 12 out of 23 HPV negative papillomas (52%). Our findings indicate that HPV infection and/or changes in p53 protein coexist in oral cavity papillomas.

Key words: HPV, overexpression p53, papillomas of oral cavity.

Introduction

Many pathological lesions associated with HPV infection affect the oral cavity. Some of them, including pointed condyloma, common warts and papillomas, correspond to the changes found in the genital tract. Heck's disease is a HPV-related oral cavity lesion. Benign oral mucosa lesions are associated with HPV types 2, 4, 6, 11, 13 and 32, while malignant lesions with types 16 and 18 [1]. Papillomas belong to benign lesions, which in some circumstances may turn malignant [2]. Perhaps, it is the coexistence of HPV infection and p53 gene mutation that promotes this transformation.

Papillomaviruses belong to the group of oncoviruses that differ in oncogenic potential and are therefore classified as "low risk" and "high risk" types of neoplastic transformation. The role of HPV in neoplastic transformation of the cell is associated with the expression of E6 and E7 viral oncoproteins which have the ability to form complexes with the products of the p53 and pRB cell-supressor genes. The p53 protein is a major factor involved in cell-cycle regulation. The loss of p53 ability to regulate cell proliferation may lead to neoplastic transformation. This condition can be caused by protein inactivation by mutation of the p53 gene affecting the protein structure. An alternative mechanism for p53 inactivation is the E6 protein potential to form complexes with p53 protein and its earlier degradation in the presence of ubiquitine. The cell cycle becomes deprived of a very important regulator. The condition observed in the cell after viral infection promotes carcinogenic agents and may lead to cell transformation into the neoplastic ones.

Material and methods

Thirty-six oral papillomas were used as the research material. DNA was isolated and HPV was detected in earlier studies [3]. Immunohistochemical investigations were performed using monoclonal antibodies against human p53 protein (DAKOCytomation/p53 No M7001) and the biotin-streptavidin-peroxidase complex. DAB (DAKOCytomation No S3000) was used as chromogen to visualize the antigen-antibody complex. Lung cancer with p53-positive immunohistochemical expression and p53 gene mutation detected earlier was used as positive control. The primary antibody was not applied in negative control.

Results and Discussion The overexpression of p53 was revealed in 20 cases (55%) out of 36 papillomas, figure 1a,1b.

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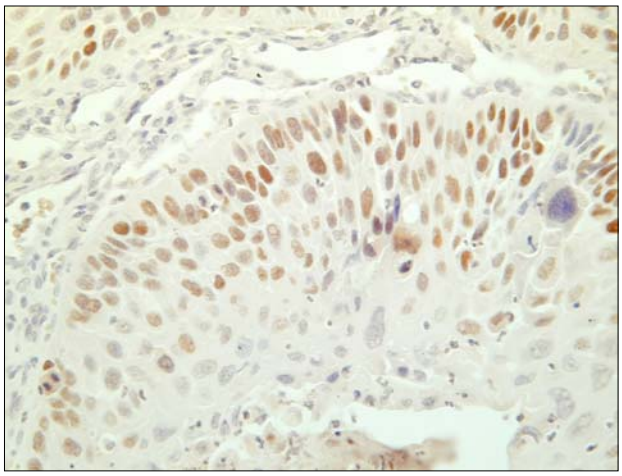
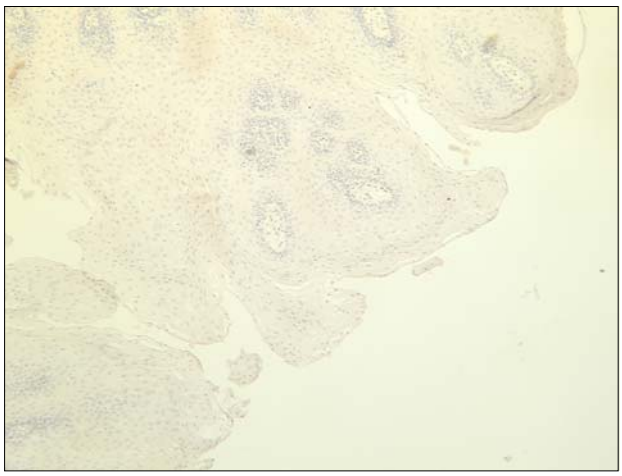
Figure 1. Detection of p53 protein expression in papillomas of the oral cavity.

1a. - case of p53 positive



1b. - case of p53 negative



We found p53 overexpression in 8 out of 13 HPV-positive papillomas (61.5%) and in 12 out of 23 HPV-negative papillomas (52%). HPV expression was detected in 13 papillomas (36%), including 11 cases of high risk HPV and 2 cases of low risk HPV.

Human papillomavirus in the oral cavity lesions occurs with varied frequency. Zeuss et al. examined 30 papillomas of the oral cavity, finding HPV in 13.3% of cases [4]. Syrjanen et al. when examining benign neoplastic growth in oral mucosa found HPV in 33.8% of papillomas [5]. Previously we detected HPV expression in 14 out of 38 oral papilloma cases (36.8%) [3]. Recent years have brough an interest in the relationship between HPV infection and p53 expression and p53 gene mutations. This relationship has been analysed for oral cavity carcinomas. Worthy of mention are the studies conducted by Barten et al. [6], who examined 37 cases of oral and pharyngeal squamous epithelial cell carcinoma for HPV expression and assessed p53 protein expression using the immunohistochemical method. The p53 gene mutations were determined by TGGE method. The investigators revealed coexistence of HPV infection with protein p53 overexpression in 15 out of 26 HPV-positive cases (57.7%). Also investigations performed by Mao et al. [7] demonstrated that p53 protein overexpression can be accompanied by HPV infection. Patients with both p53 gene mutation and HPV expression exhibited high degree of the disease advancement. Shindoh et al. [8] examined 77 oral squamous cell carcinomas, revealing HPV expression in 31% of cases. Using the immunohistochemical method, they detected p53 expression in 26 carcinomas. Protein overexpression was detected in 6 cases, of which 4 were HPV-negative and 2 HPV-positive. Moreover, these authors analysed PCNA expression and showed a close correlation between PCNA expression and HPV infection. Shindoh et al. [8] assume that high risk HPV, by maintaining the proliferative state of epithelial cells, may contribute to the formation of malignant phenotypes. Chiba et al. [9] analysed 38 cases of oral squamous cell carcinomas, revealing high risk HPV expression in 8 cases (21%). The analysis of SSCP showed the presence of p53 gene mutations in 9 cases (24%). Two cases were both HPV- and p53 mutation-positive. Contrary to Mao et al. [7], Chiba et al. [9] believe that patients with mutation of p53 gene or with HPV infection have better prognosis. Aggelopoulou et al. [10] evaluated p53 protein expression in HPV-positive lesions of the oral cavity, reporting its detection in 50% (5/10) of hyperplastic lesions and in 59% (22/39) of carcinomas. Sisk et al. [11] detected HPV expression in 15 out of 32 squamous cell carcinomas (13%), and p53 gene mutations in 2/15 HPV-positive and in 6/17 HPV-negative cases. The analysis of patients' survival rate made them assume that HPV-positive lesions and those with normally functioning p53 protein have better prognosis [11]. Sulkowska et al. [12] evaluated the expression of p53 protein and PCNA in oral cavity papillomas, finding p53 overexpression in 70.9% of papillomas, PCNA expression in 80% of cases. The authors suggest that p53 protein overexpression together with PCNA expression can be used as the index of oral cavity papilloma transformation into malignancy. In the present study, because of research material shortage, we assessed p53 protein expression in 36 out of 38 previously examined papillomas. Our findings indicate that HPV infection and/or changes in p53 protein expression coexist in oral cavity papillomas.

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