HPV and p53 expression in dysplastic lesions and squamous carcinomas of the oral mucosa

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Abstract

We studied 18 premalignant and malignant lesions of the oral mucosa, 3 dysplasias, and 15 oral squamous carcinomas with varied localizations: lips, palate, and tongue. Immunoassays for HPV were positive in 42.8% of the squamous carcinomas, without correlation with the pattern or the degree of differentiation of the lesions. P53 immunoexpression was positive in 2 of the 3 studied cases of dysplasia (66.6%) and in 13 from the 15 cases of squamous carcinomas (86.6%). The p53 immunopositivity in both lesional categories, with a higher rate in carcinomas, indicates the fact that the p53 gene mutations can appear precocious in the oral carcinogenesis, but can not be used as malign potential prediction factor.

Keywords: oral dysplasias and squamous carcinomas, histopathology, immunohistochemistry.

Introduction

Because of them high incidence, especially in some regions of the word, the reduced rate of surviving and the functional and cosmetic defects that accompanied the disease and the treatment, oral carcinomas represent a major health problem.

The malignant tumors of the oral mucosa are in 90% of the cases carcinomas, majority being squamous carcinomas. U.S.A. studies concerning the annual incidence of the oral carcinomas indicated that 11 from 100 000 people develop this type of lesions [1, 2].

Annually, in Great Britain, are reported 3 400 of new case of oral carcinoma [3, 4].

A study made in Finland in interval 1953-1999 indicated 17 383 new cases, majority developed at males [5].

The medium age of diagnosis is 64 years, most of the patients being over 40 years. Males represent 75-80% of the diagnosed cases, but, in the last years was noted the increase of incidence at females and young peoples [2, 6, 7].

Because of the high rate of mortality, which was not ameliorate in the last two decenniums, and the invasive and mutilating surgical treatment, permanent efforts are made to eliminate the risk factors (nicotine, alcohol), to improve the diagnosis procedures and to understand the genetic mechanisms of the oral carcinogenesis.

Material and methods

This study concern 18 premalignant lesions and squamous carcinomas of the oral mucosa, surgical treated in the Oral and Maxillo-Facial Clinic of the Emergency County Hospital of Craiova.

Paraffin embedded, formalin fixed tissue sections were hematoxilin-eosine stained and immuno-histochemically investigated by LSAB2 technique for HPX and p53 in the Pathology Laboratory of the same hospital.

HPV was considered positive when the immunostainig was nuclear.

We mention the fact that, in some cases, because of using of polyclonal HPV, the cytoplasmatic immunostaining was present.

For the interpretation of the p53 immunostaining we used an appreciation system in 4 degrees:

- 25% positive cells (degree 1);
- 25-50% positive cells (degree 2),
- 50-75% positive cells (degree 3);
- 75-100% positive cells (degree 4).

Results

The 18 dysplasias and squamous carcinomas of the oral mucosa belong to 52-76 years old patients, 14 being males.

The topography of the lesions was varied: preinvasive lesions were located at the level of the lips, 9 of the squamous carcinomas were developed in the lips, 5 cases on the tongue, one having extension in the palate, and one with primitive developing at the level of palate.

Histopathologically, the preinvasive lesions were in two cases aggravated dysplasias and, in one case simple dysplasia with associated condyloma aspects.

The 15 squamous carcinomas had varied patterns and degrees of differentiation. 9 cases were low differentiated, 2 cases were mild differentiated, and 3 were well-differentiated tumors. The patterns of growing corresponded with keratinisated, unkeratinisated, adenoid-cystic and basaloid squamous.

HPV immunoexpression was negative in the two cases of aggravated dysplasias and positive in the case of simple dysplasia from the condyloma, confirming the koilocytic changes noted in usual staining (Figure 1).

In the squamous carcinomas, the HPV immunoexpression was positive in 6 cases from the 15 analyzed squamous carcinomas (40%).

The HPV positive tumors were in 2 cases mild differentiated squamous carcinomas and 4 low differentiated squamous carcinomas, without correlation with the growing pattern.

In all the positive HPV squamous carcinomas the immunostaining was focal (Figure 2).

P53 immunoexpression was positive in 15 of the 18 investigated cases (83.3%), both in the dysplasias and in squamous carcinomas.

The two cases of aggravated dysplasia were p53 positive (66.6%), immunostaining dysplasic lesions, both cases being degree 2, less of 50% of the cells being p53 positive (Figure 3).

In squamous carcinomas 13 of the cases were p53 positive (86.6%).

The p53 positive carcinomas corresponded to:

- in 7 cases degree 1 (Figure 4);
- in 3 cases degree 2 (Figure 5);
- in 2 cases degree 3 (Figure 6);
- in 2 cases degree 4 (Figure 7).

The pattern of the immunostaining did not correlate with the architectural pattern, or the degree of differentiation noted on usual staining.

P53 and HPV immuno-positivity were associated in 6 cases of oral squamous carcinomas, but we could not establish a correlation between these or the histopathologic aspects.

Discussions

Oral carcinogenesis represents one of the models used for the study of the multistage nature of the cancer. The subsequent presence at the same person of preinvasive and malign invasive lesions reflect the phenotypic and genotypic progression of the alterations associated with tumorigenesis.

The process could be considered a continuous lesional spectrum with precancerous lesions at one edge and the invasive, metastatic disease at the other one. During this process, at the molecular level, numerous mechanisms interfere in the neoplastic transformation of the squamous cells.

This study investigated the HPV and p53 immunoexpression, tacking in consideration that the HPV infection or/and the p53 tumoral suppressing gene alteration are associated with the majority of the oral squamous carcinomas.

Despite of all the progresses in this field, the causes of oral squamous carcinomas generally remain unknown, them etiology being in most cases obscure [8, 9].

The actual studies detect the presence of some HPV genotypes with high risk, both in association with squamous carcinomas and the oral dysplastic lesions.

The pathobiological and molecular mechanism remain un elucidated, but some authors consider that HPV DNA has the capacity of maintaining the proliferation of the malign squamous cells and can contributes to the apparition of the malign phenotype, being correlated with the unfavorable prognostic [10-12].

HPV immunostaining was positive in 42.8% of the analyzed cases.

The HPV positive squamous carcinomas were mild and low differentiated forms, without a correlation with the tumoral pattern or the topography of lesions.

Usually, the p53 protein detection is synonym with detection of p53 gene.

P53 tumoral suppressing gene expression is frequent in human cancers, including oral cancer, being detected in some of the premalignant lesions of the oral mucosa [9, 13, 14].

83.3% of the investigated lesions were p53 positive, both in dysplastic lesions and in squamous carcinomas. P53 positivity in both lesional categories and the increase of rate of the p53 positive cases from dysplasias (66.6%) to carcinomas (86.6%) suggest the fact that p53 gene mutations are implicated in neoplastic transformation and can act precocious in oral carcinogenesis.

Despite p53 positivity can be a tumoral progression indicator; it can not be used as prediction factor of the malign potential.

HPV and p53 immunopositivity coexisted frequent in investigated squamous carcinomas - 33.3% of the cases.

Squamous carcinomas were HPV positive in 40% of cases, and p53 in 86.6%. Almost all the HPV positive cases were p53 positive (5 from 6 cases), suggesting possible interactions in the oral carcinogenesis. Similar studies reported that the possible correlation between HPV infection and p53 alteration had a definite importance only in a limited number of oral carcinomas [10, 15, 16].

On the other hand, 53.3% from the squamous carcinomas investigated were p53 positive and HPV negative.

Such comportment suggests the intervention of other carcinogens from the environment, some without correlation with HPV action.

Conclusions

The present paper analyzed HPV and p53 immunoexpression in 18 oral mucosa lesions: 3 cases of dysplasia and 15 cases of squamous carcinomas.

33.3% of the dysplastic lesions and 40% of the squamous carcinomas were HPV positive, and 83.3% of dysplasias and carcinomas cases, were p53 positive. We did not note a correlation between HPV and p53 positivity and the degree of differentiation or the pattern of growing in the squamous carcinomas studied.

The HPV and p53 % concomitant positivity, present in 33.3% of cases, suggest them common intervention in a limited number of oral squamous carcinomas.

P53 positivity, both in dysplasias and carcinomas, indicates the fact that p53 gene mutations are involved in neoplastic progression and can interfere precocious in oral carcinogenesis.

Although p53 positivity can be used as tumoral progression indicator, its immune pattern can not be used like malign potential prediction factor.

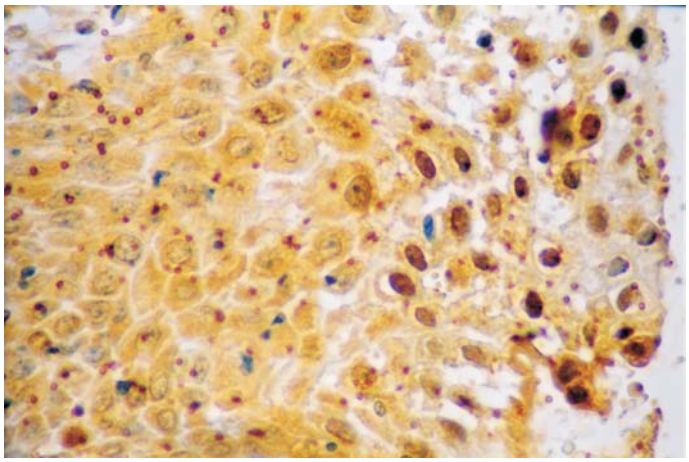

Figure 1 – ***Oral condyloma HPV, ob. ×10***

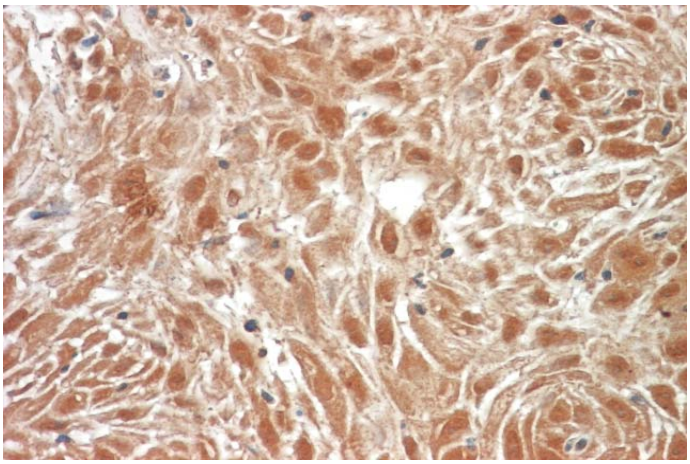

Figure 2 – ***Oral squamous cell carcinoma HPV, ob. ×10***

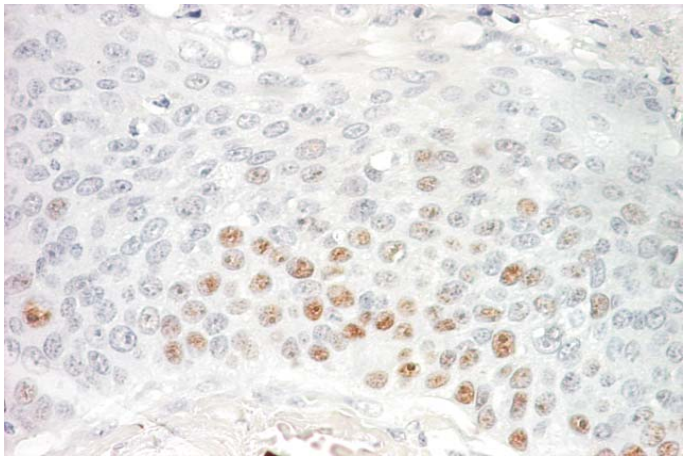

Figure 3 – ***Oral aggravate dysplasia p53 grade 2 (immunostaining between 25–50% of the neoplastic cells), ob. ×10***

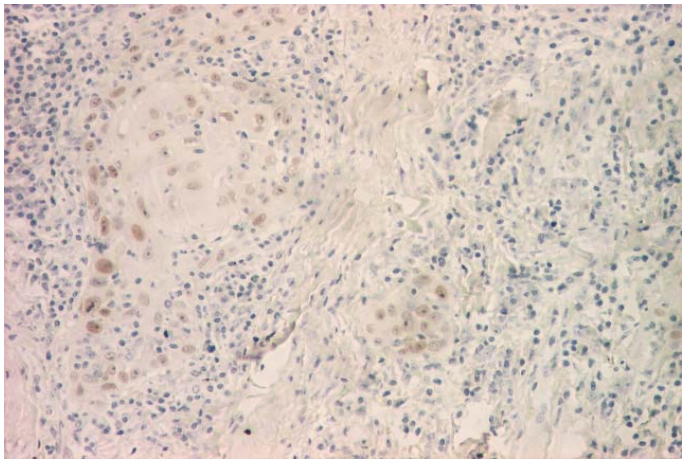

Figure 4 – ***Oral squamous cell carcinoma p53 grade 1 (immunostaining bellow 25% of the neoplastic cells), ob. ×10***

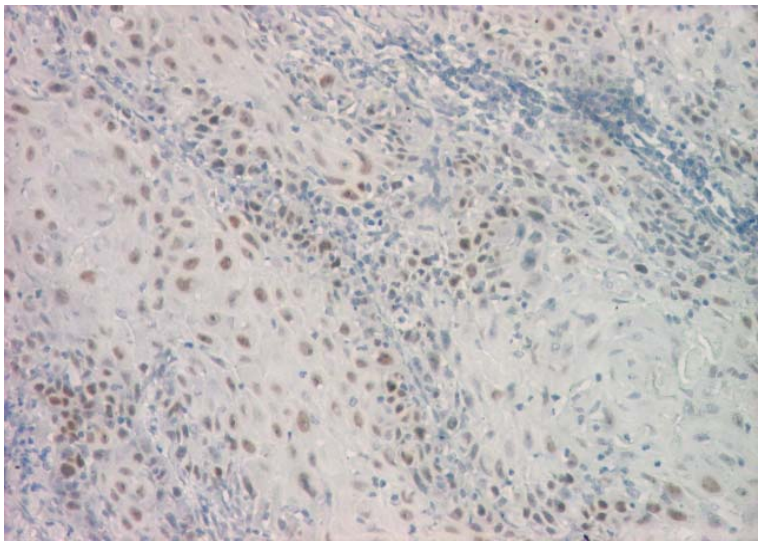

Figure 5 – ***Oral squamous cell carcinoma p53 grade 2 (immunostaining between 25–50% of the neoplastic cells), ob. ×10***

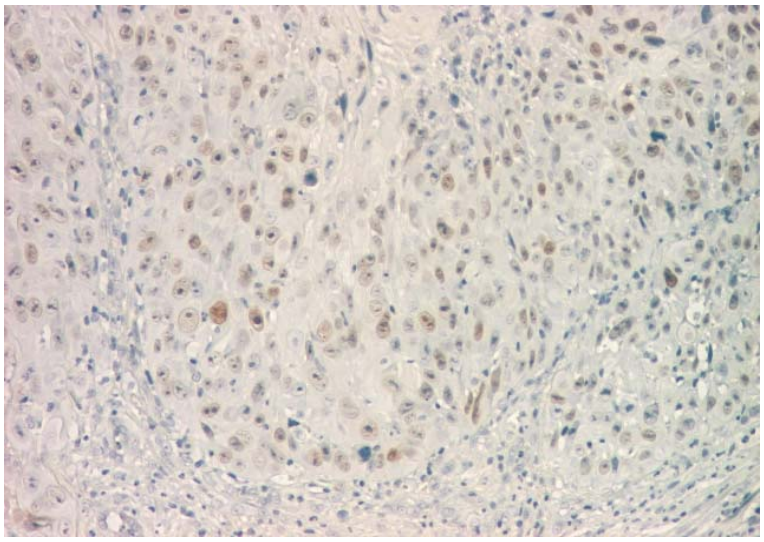

Figure 6 – ***Oral squamous cell carcinoma p53 grade 3 (immunostaining between 50–75% of the neoplastic cells), ob. ×10***

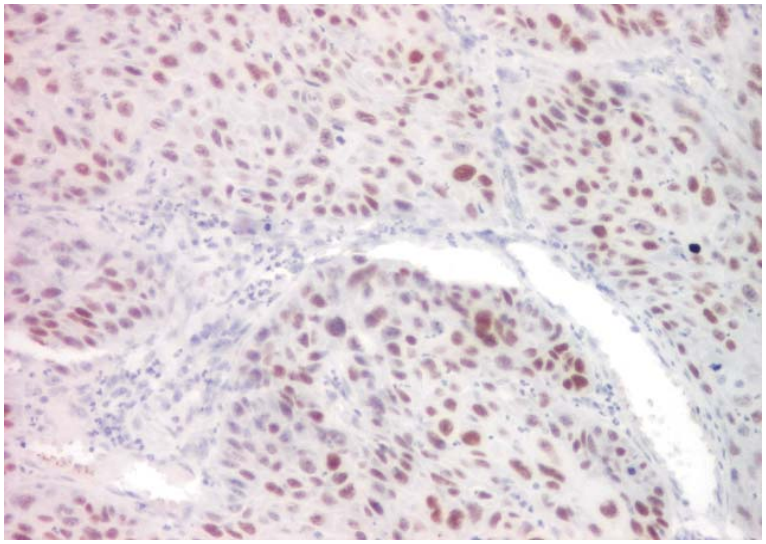

Figure 7 – ***Oral squamous cell carcinoma p53 grade 4 (immunostaining over 75% of the neoplastic cells), ob. ×10***

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