P53 Expression in Oropharyngeal Squamous Cell Carcinoma is Increased in HPV Positive Smokers

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BACKGROUND & OBJECTIVES

High risk HPV is associated with oropharyngeal SCC (OSCC) and is responsible for the increasing incidence of this cancer type among younger patients.

Patients with HPV positive oropharyngeal SCC have a better prognosis when compared with HPV negative, tobacco induced SCC.

HPV E6 inactivates p53 leading to low expression of p53; tobacco induced oropharyngeal SCC is characterized by p53 overexpression, resistance to treatment and poor prognosis. However, in many cases of HPV OSCC, there is a history of current or remote smoking, making this disease a multifactorial process. We expect that smoking will influence the level of p53 expression in HPV positive smokers.

The objective of our study is to evaluate the differences in p53 expression in HPV positive and HPV negative patients, smokers and nonsmokers.

DESIGN

Retrospective study that included 101 cases of OSCC, 65 p16 positive and 36 p16 negative patients. In each group patients have been divided in nonsmokers, smokers and patients with remote smoking history (quit smoking at least 3 years prior to diagnosis).

IHC stain for p53 was performed in all cases. Low expression was defined as staining in less than 20% of tumor cell nuclei. High expression was defined as staining in more than 20% of tumor cell nuclei.

RESULTS

P16 positive and p16 negative patients demonstrated significantly different p53 profile.

Low p53 expression was noted in the vast majority of p16 positive patients. P16 negative patients, especially current and remote smokers, demonstrated the highest percentage of high p53 expression.

	Smoking status	Nr. cases	P53 staining	Nr. Cases (%)
P16 positive	smokers	14	low	12 (85%)
			high	2 (15%)
	nonsmokers	22	low	20 (90%)
			high	2 (10%)
	Remote smoking history	29	low	28 (96%)
			high	1 (4%)
P16 negative	smokers	24	low	15 (62%)
			high	9 (38%)
	nonsmokers	7	low	7 (100%)
			high	0 (0%)
	Remote smoking history	5	low	3 (60%)
			high	2 (40%)

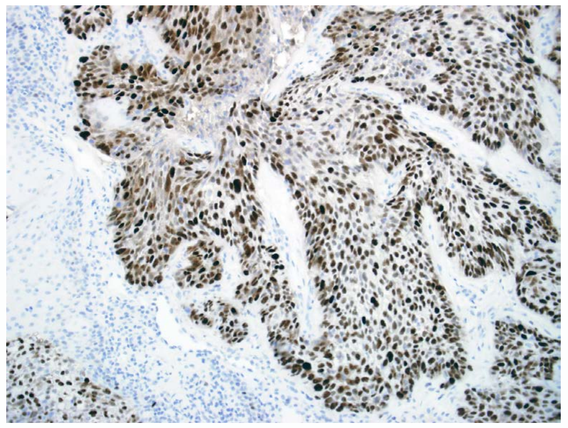

Figure 1: Immunohistochemistry stain for p53 in OSCC (high expression), 200x

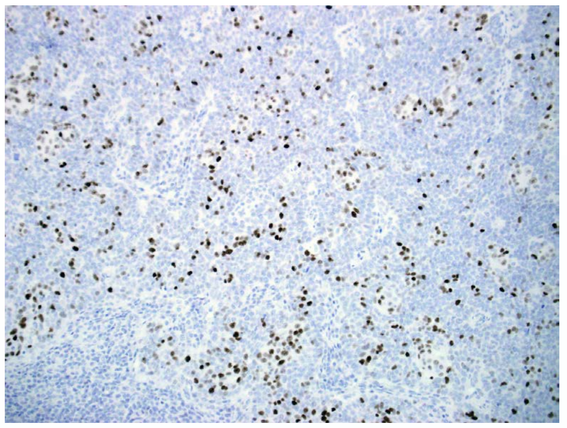

Figure 2: Immunohistochemistry stain for p53 in OSCC (low expression), 200x

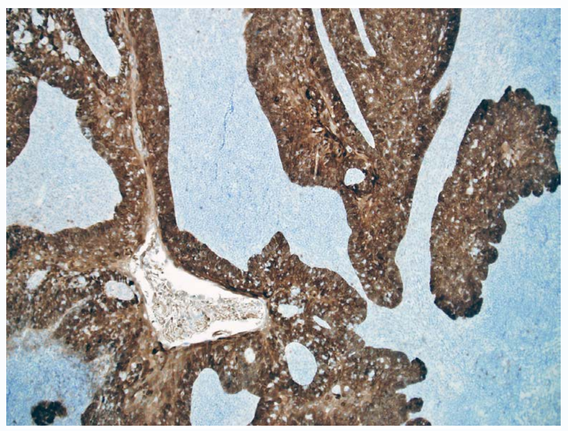

Figure 3: Positive immunohistochemistry stain for p16 in OSCC, 200x

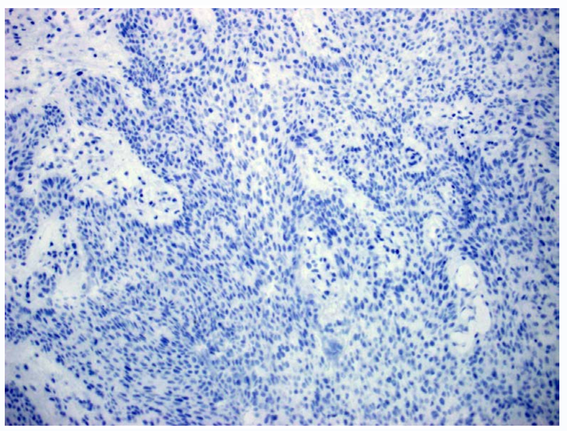

Figure 4: Negative immunohistochemistry stain for p16 in OSCC, 200x

CONCLUSION

Our study demonstrates that the majority of patients with HPV positive OSCC show a low p53 staining, in agreement with the known effect of viral E6 protein on cell cycle. Among the p16 positive patients, current smokers demonstrated the highest percentage of p53 overexpression.

In the p16 negative group, the highest level of p53 expression was in smokers (current and remote smoking history).

Our study brings strong evidence that p53 is increased in p16/HPV positive patients who are active smokers. The level of p53 expression is intermediary between p16 positive nonsmokers and p16 negative smokers. This difference may contribute to the previously described negative effect that smoking has on response to treatment and prognosis in HPV positive smokers.

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