Is There Correlation between Infection with Human Papilloma Virus (HPV) and Primary Lung Squamous Cell Carcinomas?

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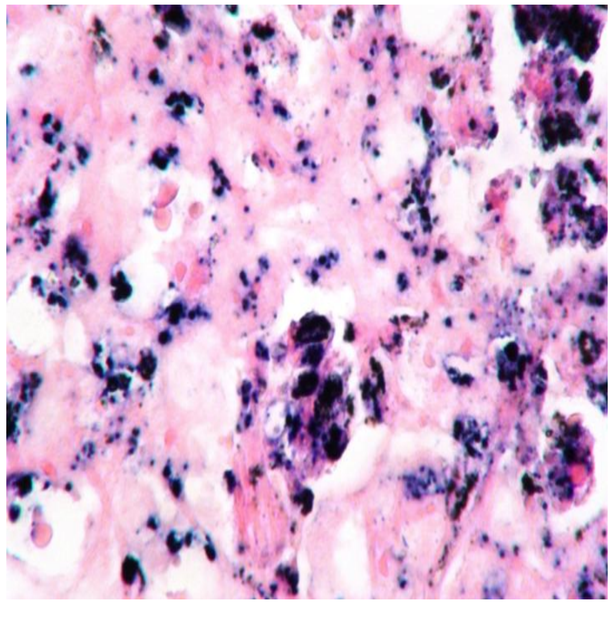
Introduction

Squamous cell carcinoma is a malignant epithelial tumor of the bronchial epithelium and is the second most common non-small cell lung cancer (NSCLC). We know that one of the main causes is smoking and the role of human papillomavirus (HPV) has not been demonstrated. The loss of p16INK4a gene function in lung carcinogenesis is known; it is located on chromosome 9p21 (CDKN2A locus) and encodes two tumor suppressor proteins: p16INK4a and p14ARF. P16INK4a suppressor protein (p16) inhibits cyclin D1 dependent kinases 4 and 6 (CDK4 / 6, cyclin D1), whose function is to regulate the activity of the retinoblastoma protein (Rb) by phosphorylation . The loss of p16 function generates an inactivation of Rb by hyperphosphorylation and therefore dysregulation and premature progression of the cell cycle, but the production of viral oncoproteins through the infection of human papillomavirus (HPV) has not been shown in lung squamous cell carcinoma.

Methods

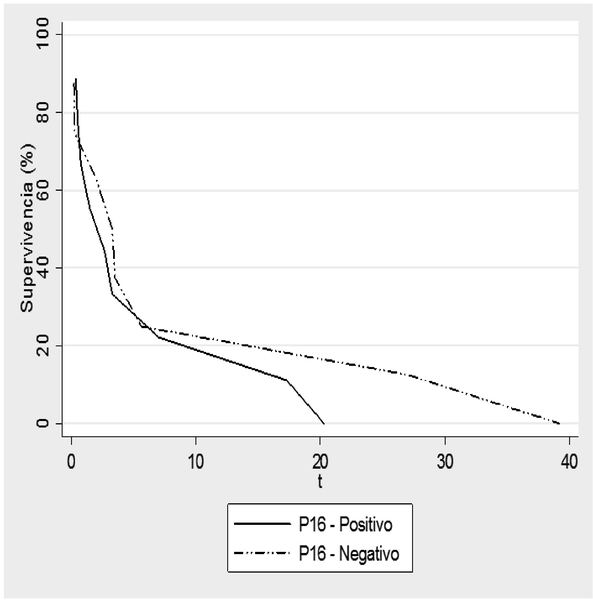
It is a retrospective descriptive study without intervention in 24 patients diagnosed with squamous lung cancer for the years 2009-2013 monitored in our center. Tumor tissue microarrays (TMAs) were performed, p16 protein was evaluated with the murine monoclonal antibody (Clone E6H4 ™) and performed with BenchMark Autostainer (Ventana®). The family 16 of Human Papillomavirus virus (HPV) was studied by in situ hybridization protocol HPVIII iView Blue + Inform in the BenchMark automated Autostainer (Ventana®).



Expression of HPV DNA family in tumor cells 16 by ISH technique

Results

The median age was 67 ± 14 years, with a predominance of males in 62.5%; 91.7% had a mass, 33.3% were cavitated, 50% located in the left lower lobe, 54.2% were smokers, 45.8% had hemoptysis and 75% received cancer treatment. 41.7% of the tumors were positive for p16 protein expression; of these, 53.85% were smokers. The study by in situ hybridization showed the presence of HPV in 4.1% of the tumors.



Graph 1: Kaplan Meier curve showing lower survival at 2 years in p16 positive patients

Conclusions

The presence of the overexpression of p16 protein in squamous cell lung cancer is related to genetic instability and cell cycle abnormalities. HPV infection studied by in situ hybridization can prove viral infection, suggesting that it might be one etiological factor and be related to the alteration in the cell cycle; increased growth / progression, genetic instability and the production of viral oncoproteins favoring the transformation oncogene, but unlike cervical cancer, it is not correlated with the expression alone of p16 protein and the presence of human papillomavirus (HPV), perhaps the presence of infection could be associated with sensitivity to antineoplastic drugs or punctual mutations.

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