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Diagnosis and molecular targeting for individualized treatment of patients with pre-neoplastic lesions and locally advanced cervical cancer

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Background: The natural history of HPV infection and development of cervical intraepithelial neoplasia indicate that most lesions disappear without treatment in contrast to a significant proportion of high-grade lesions that progress to invasive cancer if not treated. Persistent infection with high-risk HPV may be necessary for the development of cervical cancer. The purpose of the study was make a retrospective molecular diagnosis that include detection of HPV16 variants, polymorphism Arg72Pro of P53, expression of anti-apoptotic markers such as IGF-1R and Survivin, and hypoxic markers and glycolytic as GLUT1 and CAIX and markers of progression as hTERT in samples invasive cancer and preneoplastic lesions taken in 2002 and 1986; the results may be useful to propose an appropriate therapeutic management.

Methods: From a prospective study of invasive squamous cell carcinoma of the cervix and predictive markers of response to radiotherapy published in 2012 (Moreno-Acosta et al.) of which the frequency of HPV 16 variants was reported, we study retrospectively some cases that present the Asian-American variant (AA). One of these cases correspond to a 43-year-old woman, whom in 1986 he took two biopsies of the transformation zone of the cervix, each at an interval of three months; the first biopsy was diagnosed as a high-grade lesion supports changes consistent with HPV infection, and the second biopsy was diagnosed as low-grade lesion. Gynecological medical board decided that the patient should be subjected to extended abdominal hysterectomy, being referred to another hospital. After 16 years of progression, in 2002, the patient returns to INC. In this year the presence of the Asian-American variant of subclass C of HPV 16 in a frozen biopsy tissue transformation zone was determined.

Results: HPV16 E6 E-r and AAc mixed variants were detected in samples took in 1986. A HPV16 E-r and AAc variant was detected in 2002, which indicate persistence of the infection. Polymorphism analysis of Arg72Pro p53 in 1986 and 2002 showed an Arg/Pro genotype. An increment of expression of IGF1R, Survivin, GLUT1, and CAIX was observed in biopsies taken in 2002 compared with the analysis done in biopsies of 1986; hTERT expression in pre-neoplastic lesions was detected at 100%. Conclusions: In the adequate therapeutic management of preneoplastic lesions and cervical cancer, the presence of the AAc-HPV16 could be used as a prognostic marker of persistent infection, progression and treatment, as well hTERT expression as tumor progression marker. The analysis of molecular profiles that include biomarkers prognostic, predictive as IGF1R expression and molecular targets, and employed in this work could ensure early diagnosis and better therapeutic management of cervical lesions and cervical cancer.

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