39°CBU

MYC COPY NUMBER ALTERATIONS IN PENILE SQUAMOUS CELL CARCINOMA

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Introdução e Objetivo

Penile Squamous Cell Carcinoma (PSCC) is a rare malignancy; however, the incidence is higher in developing countries. In Brazil, the state of Maranhão is assumed to have the highest reported incidence of PSCC worldwide.The c-myc gene locus (8q34) is described as an important HPV integration site, commonly resulting in c-myc overexpression. Since this gene is involved in numerous mechanisms of cell regulation, dysregulation in its expression may promotes carcinogenesis. The present study aimed to analyze the copy number alterations (CNA) and protein expression of *c-Myc* in 40 PSCC samples from patients treated at three referral hospitals in Maranhão, Brazil.

Método

Tumor DNA was extracted and HPV detection was carried out using the nested-PCR (PGMY09/11 and GP5+/6+). Copy number (CN) analysis was performed by qPCR using TaqMan copy number assays for *c-Myc*. CN analysis results were defined as gain (3 copies) and amplification (≥ 4 copies). The *c-Myc* protein expression assay was performed by immunohistochemistry (IHC) using the monoclonal anti-myc antibody (clone EP121). Staining in ≥ 40% of invasive PSCC was considered positive (overexpression). Categorical variables were analyzed using chi-square or fisher's exact tests.

Figuras

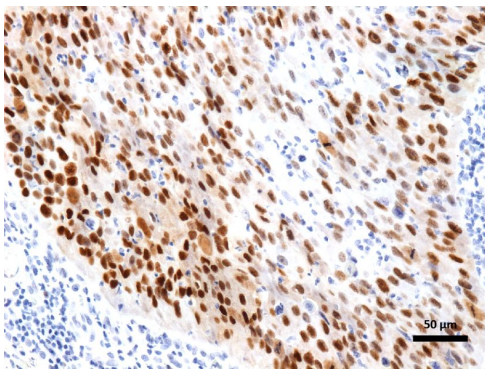

Figure 1 - Immunohistochemistry of *c-Myc* protein showing over expression in invasive PSCC.

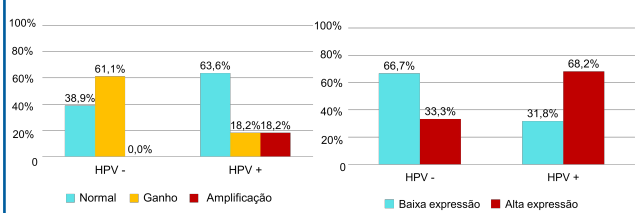

Figure 2 - Comparison between CNA (left) and gene expression (right) results in HPV-positive and HPV-negative PSCC.

Resultados

The patients had a mean age of 59.6 ± 15.0 years, a low level of education (77.5%), were alcohol consumers (75.0%), smokers (45.0%), and exhibited phimosis (55.0%). The lesions were predominantly located on the penile glans (52.5%) with sizes ranging from 2.1 to 5.0 cm (57.5%). Histologically, the majority of tumors were usual (52.5%), poorly differentiated (75.0%), with the presence of koilocytosis (65.0%), at pT3/pT4 stage (50.0%), stage II (62.5%), and exhibited metastasis (50.0%). Angiolymphatic invasion and perineural invasion were observed in 37.5% and 50.0% of cases, respectively. The presence of HPV was detected in 55.0% of the cases. IHC results showed high-expression in 52.5% of cases. MYC gain and amplification were identified in 37.5% and 10% of PSCC samples, respectively. The overexpression of *c-Myc* was statistically significant for HPV infection (P=0.028). Advanced pathological stage (P=0.027) and the absence of koilocytosis (P=0.049) were associated with CN alterations. Interestingly, HPV was detected more frequently in samples without CN alterations in *c-myc* (P=0.007).

Conclusão

In this study, we observed an increased MYC overexpression in HPV-positive samples. However, it may not be directly associated with HPV integration in the MYC locus or MYC gains/amplifications. Therefore, our study group is currently conducting RT-qPCR assays and HPV genotyping to elucidate this association.

Referências

MASFERRER, Emili et al. MYC copy number gains are associated with poor outcome in penile squamous cell carcinoma. **The Journal of urology**, v. 188, n. 5, p. 1965-1971, 2012.
PETER, M. et al. MYC activation associated with the integration of HPV DNA at the MYC locus in genital tumors. **Oncogene**, v. 25, n. 44, p. 5985-5993, 2006.
SHEN, Congle et al. Long-distance interaction of the integrated HPV fragment with MYC gene and 8q24. 22 region upregulating the allele-specific MYC expression in HeLa cells. **International journal of cancer**, v. 141, n. 3, p. 540-548, 2017.