Human Papilomavirus infection and Ki-67 expression in Penile Cancer: Do they relate?

Ana Ferreira[1], Marisa Vilela[1,2], Edgar Tavares Silva[3,4,5,6], Vasco Quaresma[3], Rui Almeida[2], Maria Fátima Silva[1,2], Paulo Teixeira[1,2], Diana Martins[1,4,5,6], Fernando Mendes[1,4,5,6,7*]

[1] Polytechnic University of Coimbra, Coimbra Health School, UCPCBL, Rua 5 de Outubro - SM Bispo, Apartado 7006, 3046-854, Coimbra, Portugal
[2] Pathology Department, University Hospital Center of Coimbra, Coimbra, Portugal
Coimbra Institute for Clinical and Biomedical Research (iCBR) Area of Environment Genetics and Oncobiology (CIMAGO), Biophysics Institute of Faculty of Medicine, University of Coimbra, Coimbra, Portugal..
[3] Department of Urology and Renal Transplantation, Centro Hospitalar E Universitário de Coimbra (CHUC), Coimbra, Portugal.
[4] Center for Innovative Biomedicine and Biotechnology (CIBB), University of Coimbra, Coimbra, Portugal.
[5] Clinical Academic Center of Coimbra (CACC), Coimbra, Portugal.
[6] Coimbra Institute for Clinical and Biomedical Research (iCBR) Area of Environment Genetics and Oncobiology (CIMAGO), Biophysics Institute of Faculty of Medicine, University of Coimbra, Coimbra, Portugal.7[8] European [7]Association fo Biomedical Scientists, B-1000, Brussels, Belgium

** fjmendes@estesc.ipc.pt*

Introduction: Squamous cell carcinoma (SCC) of the penis is a rare but devastating neoplasm for the patient. Human Papillomavirus (HPV) infection can induce penile carcinogenesis and may contribute to 30 to 50% of penile cancer (PeCa) cases. The overexpression of $P16^{INK4a}$ can be used as a surrogate marker for active HPV infections, although the correlation between HPV infection in PeCa still is controversial. Ki-67 is a cell proliferation marker and disease aggressiveness. **Aim:** Our aim was to evaluate the expression and prevalence of $P16^{INK4a}$ and Ki-67 in PeCa and its correlation with disease prognosis. **Methods:** A retrospective study was conducted from 2010 to 2020, including 48 patients with PECa. Immunohistochemical analysis of $P16^{INK4a}$ and Ki-67 was performed from paraffin-embedded tissues. **Results:** We observed 12 cases (25%) PeCa with $P16^{INK4a}$ positive expression. The expression of $P16^{INK4a}$ was not associated with any histological characteristics, except the AJCC stage and the Ki-67 expression. A high Ki-67 expression was identified in $P16^{INK4a}$ positive patients, and a higher survival rate was observed in patients with low Ki-67 expression. The multivariate cox progression analysis showed that only stage N and age were significant predictors of SCC. We observed also a significant high number of penectomies, and deaths associated to PeCa. **Conclusion:** Our study showed a lower incidence of HPV compared to what is described in the literature. A correlation between Ki-67 and $P16I^{NK4a}$ and a cell cycle deregulation mediated by high-grade HPV infection was confirmed. Overexpression of Ki-67 contributes to the prognosis of PeCa patients.

Keywords: Penile Neoplasms; Alphapapillomavirus; Prevalence; $P16^{INK4a}$; Diagnosis; Ki-67.

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