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The Cancer Control Challenge:
Better Understanding It to Better Face It

IMMUNOHISTOCHEMICAL EXPRESSION PROFILE OF *P16* AND *P53* IN SAMPLES FROM PATIENTS WITH VULVAR CANCER

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Introduction: Vulvar cancer (VC) is a rare malignant gynecological neoplasm, often associated with persistent infection by human papillomavirus (HPV). It presents distinct clinical behaviors and prognoses depending on its molecular subtype. Evaluating the biomarkers *p16* and *p53* has proven useful in the clinicopathological stratification of these tumors. **Objectives:** To analyze the association between the immunohistochemical expression of *p16* and *p53* markers and the clinical and epidemiological data of patients with VC. **Methods:** This is a retrospective study that analyzed 132 medical records of patients diagnosed with VC who were treated between 2013 and 2023 at three oncology referral hospitals in the state of Maranhão, Brazil. Clinical and epidemiological information was extracted from medical records. Immunohistochemical expression of *p16* and *p53* proteins was evaluated in a subsample of 25 patients. These cases were selected based on the availability and integrity of paraffin-embedded tissue blocks from invasive and in situ squamous cell carcinomas. Only samples with adequate preservation and sufficient tumor tissue for analysis were included. The subsample was reviewed to ensure it reflected the clinical and epidemiological characteristics of the broader cohort. The study was approved by the Research Ethics Committee of the University Hospital of the Federal University of Maranhão, under approval number 7.344.280. **Results:** The majority of patients were in their sixties (59.5%), of mixed race (73.3%), retired (28.6%), had low educational levels

(45.5% were illiterate or had incomplete primary education), and resided predominantly in the northern region of Maranhão (68.9%). Immunohistochemical analysis showed *p16* positivity in 76.9% of the evaluated samples, with a statistically significant association between *p16* expression and histopathological features consistent with HPV infection ($p < 0.001$). Evaluation of *p53* immunostaining revealed that the wild-type *p53* pattern was significantly associated with *p16* positivity, whereas the mutated *p53* pattern was observed in *p16*-negative cases ($p = 0.011$). Furthermore, significant associations were found between *p53* expression and a vertical growth pattern ($p = 0.019$), suggesting deeper tissue invasion and a greater potential for metastasis. **Conclusion:** The correlation between *p16* and *p53* expression patterns and clinical characteristics underscores the relevance of molecular classification in VC. HPV-independent tumors (*p16*-negative/mutated *p53*) may be associated with greater tumor aggressiveness and potential treatment resistance, indicating a poorer prognosis. In contrast, HPV-related tumors (*p16*-positive/wild-type *p53*) tend to exhibit better therapeutic response and, consequently, a more favorable prognosis. The combined use of these biomarkers represents an important tool for prognostic stratification and for guiding individualized therapeutic approaches for patients with VC.

Keywords: Immunohistochemistry; Human Papillomavirus; Vulvar Neoplasms