PROGNOSTIC VALUE OF IMMUNOPHENOTYPING LYMPHOID SUBPOPULATIONS IN INVASIVE VULVA CARCINOMA

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INTRODUCTION: Vulvar invasive carcinoma (VICA) represents 3-5% of malignant neoplasia of female genital tract. Its pathogenesis comprises a pathway related to mutations on TP53 gene, mainly in older women, and another one related to infection with human papillomavirus (HPV) in younger patients. In both mechanisms, carcinoma is preceded by precursor lesions (vulvar intraepithelial neoplasia - VIN). A worrisome increase in incidence of VICA in younger women has been attributed to the increase in HPV infections. Approximately one third of patients with vulvar carcinoma are diagnosed in advanced stages, resulting in shorter disease free survival, and poorer prognosis. Surgery is the standard method for the treatment of vulvar carcinoma. However, in advanced stages, surgery may be extensive and present mutilating effect. The repercussion of radical conventional treatment highlights the need for less aggressive alternative methods, such as immunotherapy. This approach has proven a promising strategy in conjunction with other methods in the treatment in other cancer types. Thus, it could generate more efficient clinical responses and survival benefits with less harm for patients with VICA. Therefore, it is important to recognize the role of inflammation in tumor progression, a matter that has been scarcely addressed in this tumor type. **HYPOTHESIS:** Characterization of tumor associated inflammatory infiltrate and its correlation with clinicopathological data could provide useful information to support future prevention and treatment strategies for patients with vulvar carcinoma. Therefore, it is our aim to characterize and evaluate the prognostic value of inflammatory infiltrate in vulvar carcinoma. **METHODS:** Formalin fixed paraffin embedded tissue samples were retrospectively selected from the files of the Anatomic Pathology Department in A C Camargo Cancer Center, Sao Paulo, Brazil, between 1980 and 2013. Forty-four patients with VICA were studied: 40 usual squamous type, 4 basaloid type and 1 verrucous type. Peri- and intratumoral (VICA P and VICA I) hotspot regions were evaluated for each tumor. Inflammatory cell phenotyping was accomplished by immunohistochemistry, using monoclonal antibodies to CD3, CD4, CD8, CD20 and FOXP3. Quantification of the reactive cells was performed using the APERIO® system. **RESULTS:** High expression of CD3 was associated with lower invasion depth (p=0.004) in VICA I. Strong expression of CD8 was associated with lower invasion depth (p = 0.037) in VICA P. High expression of FOXP3 was associated with absence of vascular invasion (p = 0.016) in VICA P and lower invasion depth (p = 0.011), absence of vascular invasion (p=0.030) and of perineural invasion (p = 0.026) in VICA I. Moreover, higher expression of CD3 and FOXP3 was associated with increased specific cancer survival and disease-free survival of patients with VICA. In opposition, low CD4 expression intensity associates with increased overall survival in VICA patients. Evaluation of these lymphoid markers may be of prognostic value in patients with vulvar carcinoma.

Key words: vulvar carcinoma; tumor associated inflammatory infiltrate; tumor immunology; immunohistochemistry; lymphoid subpopulations; prognosis.