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AN IMMUNOHISTOCHEMICAL ANALYSIS OF VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR 1 IN HIGH GRADE T1 BLADDER CANCER WITH CONCOMITANT CARCINOMA IN SITU

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Vascular endothelial growth factor receptor 1 (VEGFR1) reduces the angiogenic activity of vascular endothelial growth factor (VEGF), acting like decoy receptor for VEGF and limiting its availability for genuine angiogenic receptors. The purpose of this study was to establish the significance of VEGFR1 expression in high grade T1 (HGT1) bladder cancer with concomitant carcinoma in situ (CIS) and to determine possible immunohistochemical marker helpful in the follow-up of "unpredictable" HGT1 bladder cancer patients. The analysis included 137 HGT1 bladder cancer samples. Concomitant CIS was diagnosed in 21 (15.33%) of these patients. Sections of 137 formalin-fixed, paraffin-embedded materials were incorporated in tissue micro-arrays and then stained with a rabbit monoclonal antibody against VEGFR1 (N-term: Y103/-Epitomics, diluted 1:250). Immunohistochemical reaction was scored as following: negative if ≤ 10% of cells were stained and positive if > 10% were stained. We considered both membranous and cytoplasmic expression and staining intensity was scored using a scale of 0 to 3 (0, no staining; 1, weak; 2, moderate; and 3, intense). After a mean follow-up of 50 months, in 137 patients diagnosed with HGT1 urothelial bladder cancer, we found that patients who had concomitant CIS had worse overall survival ($p < 0.05$), furthermore, those tumour samples had weakly expressed VEGFR1 ($p < 0.05$). Patients with positive VEGFR1 had longer disease-free ($p < 0.01$) and overall survival ($p < 0.01$). Present investigation has revealed that the estimation of VEGFR1 expression could be diagnostic supplement, selecting the HGT1 bladder cancer patients that would require more intensive follow-up, especially if accompanied with CIS.

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Key words: *angiogenesis, VEGFR1, bladder cancer, carcinoma in situ*