Loss of SPINK1 Expression in Urothelial Carcinoma of the Bladder Is Associated with Unfavorable Outcome After Radical Cystectomy

Introduction and Objectives: We assessed the association of serine protease inhibitor Kazal type I (SPINK1) expression with clinico-pathologic outcomes in urothelial carcinoma of the bladder (UCB) patients treated with radical cystectomy (RC).
Material and Methods: Tissue microarrays comprising 438 consecutive UCB patients treated with RC between 1988 and 2003 and 62 cases of normal urothelium controls were stained for SPINK1. Semi-quantitative evaluation was performed by two pathologists blinded to clinical outcomes (loss of expression: <50% cells or intensity 0-2).
Results: In normal urothelium, SPINK1 expression was noted in umbrella cells of 32 of 62 controls (52%). There were 254 RC patients (57.9%) who exhibited loss of SPINK1 expression. Loss of SPINK1 expression was significantly associated with higher pathologic stages (p=0.002) and presence of lymph node metastasis (p=0.04). At a median follow-up of 130 months (IQR:98.4), loss of SPINK1 expression was associated with an increased risk of disease recurrence (p=0.02) and cancer-specific mortality (p=0.03). On multivariable analysis that adjusted for the effects of standard clinico-pathologic parameters, SPINK1 was not an independent predictor of disease recurrence (p=0.09) or cancer-specific mortality (p=0.12).
Conclusions: Over half of UCB patients treated with RC exhibit loss of SPINK1 expression. Loss of SPINK1 correlates with features of biologically aggressive UCB. Although SPINK1 expression did not have independent prognostic value in RC patients, it may serve as a biomarker for tumor staging and may be useful as an adjunct in clinical decision-making.