Combined mRNA expression levels of members of the urokinase plasminogen activator (uPA) system correlate with disease-associated survival of soft-tissue sarcoma patients.

Abstract:

Members of the urokinase-type plasminogen activator (uPA) system are up-regulated in various solid malignant tumors. High antigen levels of uPA, its inhibitor PAI-1 and its receptor uPAR have recently been shown to be associated with poor prognosis in soft-tissue sarcoma (STS) patients. However, the mRNA expression of uPA system components has not yet been comprehensively investigated in STS patients. The mRNA expression level of uPA, PAI-1, uPAR and an uPAR splice variant, uPAR-del4/5, was analyzed in tumor tissue from 78 STS patients by quantitative PCR. Elevated mRNA expression levels of PAI-1 and uPAR-del4/5 were significantly associated with clinical parameters such as histological subtype ($P = 0.037$ and $P < 0.001$, respectively) and higher tumor grade ($P = 0.017$ and $P = 0.003$, respectively). In addition, high uPAR-del4/5 mRNA values were significantly related to higher tumor stage of STS patients ($P = 0.031$). On the other hand, mRNA expression of uPA system components was not significantly associated with patients’ survival. However, in STS patients with complete tumor resection (R0), high PAI-1 and uPAR-del4/5 mRNA levels were associated with a distinctly increased risk of tumor-related death.
(RR = 6.55, P = 0.054 and RR = 6.00, P = 0.088, respectively). Strikingly, R0 patients with both high PAI-1 and uPAR-del4/5 mRNA expression levels showed a significant, 19-fold increased risk of tumor-related death (P = 0.044) compared to the low expression group. Our results suggest that PAI-1 and uPAR-del4/5 mRNA levels may add prognostic information in STS patients with R0 status and distinguish a subgroup of R0 patients with low PAI-1 and/or low uPAR-del4/5 values who have a better outcome compared to patients with high marker levels.