Monitoring PAI-1 and VEGF levels in 6 human squamous cell carcinoma xenografts during fractionated irradiation.

Abstract:
Previous studies have shown that the plasminogen activator inhibitor type-1 (PAI-1) and vascular endothelial growth factor (VEGF) are regulated by hypoxia and irradiation and are involved in neoangiogenesis. The aim of this study was to determine in vivo whether changes in PAI-1 and VEGF during fractionated irradiation could predict for radiation resistance. Six xenografted tumor lines from human squamous cell carcinomas (HSCC) of the head and neck were irradiated with 0, 3, 5, 10, and 15 daily fractions of 2 Gy. The PAI-1 and VEGF antigen levels in tumor lysates were determined by enzyme-linked immunosorbent assay kits. The amounts of PAI-1 and VEGF were compared with the dose to cure 50% of tumors (TCD(50)). Colocalization of PAI-1, pimonidazole (hypoxia), CD31 (endothelium), and Hoechst 33342 (perfusion) was examined by immunofluorescence. Human PAI-1 and VEGF (hVEGF) expression levels were induced by fractionated irradiation in UT-SCC-15, UT-SCC-14, and UT-SCC-5 tumors, and mouse VEGF (msVEGF) was induced only in UT-SCC-5 tumors. High hVEGF levels were significantly associated with radiation sensitivity after 5 fractions (P= .021), and high msVEGF levels were significantly associated with radiation resistance after 10 fractions (P=.007). PAI-1 staining was observed in the extracellular matrix, the cytoplasm of fibroblast-like stroma.
cells, and individual tumor cells at all doses of irradiation. Colocalization studies showed PAI-1
staining close to microvessels. These results indicate that the concentration of tumor-specific and
host-specific VEGF during fractionated irradiation could provide considerably divergent information for
the outcome of radiation therapy.

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