

[Clin Exp Metastasis](#). 2000;18(4):313-9.

Tumor specific activation of the VEGF/KDR angiogenic pathway in a subset of locally advanced squamous cell head and neck carcinomas.

[Giatromanolaki A](#), [Koukourakis MI](#), [Sivridis E](#), [Thorpe PE](#), [Brekken RA](#), [Konstantinos S](#), [Fountzilas G](#), [Gatter KC](#), [Harris AL](#).

Source

Department of Pathology, Democritus University of Thrace, Alexandroupolis, Greece.

Abstract

Vascular endothelial growth factor (VEGF) and its receptors, Flt-1 and flk-1(KDR), constitute an important angiogenic pathway which, under hypoxic conditions, is up-regulated in many solid tumours. We used the monoclonal antibody 11B5, specific for recognizing VEGF expression and the 'VEGF/flk-1(KDR) complex' on tumour endothelium, to assess free VEGF protein expression and VEGF/receptor activated microvessel density (aMVD) in a series of 104 inoperable locally advanced squamous cell carcinomas of the head and neck, treated with chemo-radiotherapy. High VEGF expression in cancer cells was strongly associated with high VEGF/receptor expression in the vasculature. The high VEGF expression and the aMVD were not associated with the standard microvessel density (sMVD), as assessed with the monoclonal antibody anti-CD31 and, were not detected in normal tissue. An increased sMVD, however, was significantly related with the expression thymidine phosphorylase (TP), and also with the nuclear accumulation of the oncoprotein p53, but neither p53 nor TP was associated with VEGF expression by cancer cells or VEGF/receptor complex aMVD. In 35% of cancer cases examined, more than 20% of the microvessels assessed with anti-CD31 also expressed the VEGF/KDR complex. The vasculature of the normal head and neck mucosa did not express the VEGF/KDR complex. There was no association between VEGF expression or VEGF/receptor complex aMVD and response to chemo-radiotherapy or patient's survival. It is concluded that activation of the angiogenic pathway VEGF/flk-1(KDR) is tumor specific in a subgroup of locally advanced squamous cell carcinomas of the head and neck. Selective destruction of this type of vasculature, using immunoconjugates directed against the VEGF/receptor complex, may prove therapeutically useful for patients with a high tumoral VEGF/flk-1(KDR) activated microvessel fraction.