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2007-06-01

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**Expression of Vascular Endothelial Growth Factor Subtypes in Mammary Invasive Ductal Carcinoma and their Relationship to Tumor Progression**

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**Context:** Multiple genes and proteins have been shown to be important in treatment and prognosis of breast cancer, including the estrogen and progesterone receptors and Her-2 neu. Vascular endothelial growth factor (VEGF) subtypes have been shown to be associated with lympho-vascular invasion, lymph node metastases and prognosis in multiple types of cancer, including colon cancer, gastric cancer and breast cancer. The goal of this project was to observe and quantify the protein expression of VEGF subtypes in human breast cancer, then correlate this with known clinicopathologic information.

**Design:** Ninety grade three (high grade) invasive ductal carcinomas received over a four year period (1997-2001) were selected from our files. Immunohistochemistry was performed on formalin fixed paraffin embedded tissue of both primary tumor and lymph node metastasis when applicable using VEGF-A, VEGF-C, VEGF-D and VEGF-R (the VEGF receptor) antibodies. The staining was graded from zero (no expression) to 3+ (high expression). These expression profiles were then compared via Chi-Square test to known information about the patients and tumors including lympho-vascular invasion (LVI), lymph node metastases (LNM), stage of the tumor at diagnosis and cancer recurrence.

**Results:** A high level (3+) of VEGF-A, VEGF-D and VEGF-R expression was seen in 43 (47.8%), 32 (35.6%), and 24 (26.7%), cases respectively; expression of VEGF-C was seen in 7 (7.8%) of cases. Normal residual breast tissue was either negative or showed 1+ to 2+ staining. A high level of VEGF-A expression and the presence of VEGF-C expression were both associated with tumor recurrence ( $p < 0.2$ ). In addition, a high level of VEGF-R expression was associated with LVI, LNM, and higher TNM stage at diagnosis ( $p < 0.5$ ). No correlation was seen between high levels of VEGF-D expression and LVI, LNM or tumor recurrence.

**Conclusions:** In high grade invasive ductal carcinoma, strong VEGF-A, VEGF-C and VEGF-R protein expression was associated with adverse prognostic factors, including lymph node metastases, higher TNM stage and cancer recurrence. These results imply that further study of these proteins and their quantification in tissue samples may help in predicting long-term prognosis of patients with breast cancer.

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