Expression of VEGF in breast cancer

[1]Dr.Divya J, [2]Dr.Prathipaa R, [3]Dr.Keerthini G
[1-3]Assistant Professor, Department of Pathology, A.C.S Medical College and Hospital, Velappanchavadi, Chennai, India
Correspondence: Dr.Prathipaa R
Assistant Professor, Department of Pathology, A.C.S Medical College and Hospital, Velappanchavadi, Chennai, India

ABSTRACT

Background: The present study was conducted for evaluating the expression of VEGF in breast cancer patients.
Materials & methods: A total of 50 patients with confirmed diagnosis of breast cancer. Biopsy specimens were obtained and were subjected H and E staining. IHC staining was also done for VEGF marker. Segregation of subjects was done on the basis of VEGF expression. Univariate analysis was done for assessing the factors associated with positive expression of VEGF in breast cancer.
Results: Positive expression of VEGF was observed in 80 percent of the patients with breast cancer. Majority of the patients of the present study were of postmenopausal status. Positive family history of cancer, mean tumour size and positive smoking history were found to be significant associative factor for VEGF.
Conclusion: Breast cancer patients are associated with enhanced expression of VEGF.

Key words: VEGF, Breast cancer
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INTRODUCTION

Being characterized by six major hallmarks, carcinogenesis might occur in every cell, tissue, and organ, leading to the pathological alternations that result in a vast number of cancers. The major mechanisms that enable its progression include evasion of apoptosis, limitless capacity to divide, enhanced angiogenesis, resistance to anti-growth signals and induction of own growth signals, as well as the capacity to metastasize.[1-3]

Vascular endothelial growth factor (VEGF), a potent angiogenic factor, plays a critical role in tumor growth and metastasis. VEGF signaling in cancer cells is responsible for their resistance to apoptotic stimuli and their migration and invasion. VEGF is highly up-regulated in breast cancer. Compared with normal or benign breast tissues, breast cancer showed higher levels of VEGF transcripts. Approximately 72–98% of breast cancer is positive for VEGF by immunohistochemistry (IHC). VEGF expression in breast tumors is correlated with large size, high histologic grade, estrogen receptor (ER) negativity, progesterone receptor (PR) negativity, human epidermal growth factor receptor-2 (HER2) over-expression, and lymph node metastasis. In animals, anti-VEGF therapy inhibits the growth of breast tumors, reduces tumormicrovessel density, and limits the infiltration of tumor-associated macrophages. Anti-VEGF therapy with bevacizumab, a humanized monoclonal antibody against VEGF, shows an improvement in progression-free survival in combination with chemotherapy for women with metastatic breast cancer. Increased VEGF expression is implicated in acquired anti-estrogen resistance in vitro.[4-6]Hence; the present study was conducted for evaluating the expression of VEGF in breast cancer patients.

MATERIALS & METHODS

The present study was conducted for evaluating the expression of VEGF in breast cancer patients. A total of 50 patients with confirmed diagnosis of breast cancer. Biopsy specimens were obtained and were subjected H and E staining. IHC staining was also done for VEGF marker. Segregation of subjects was done on the basis of VEGF expression. Univariate analysis was done for assessing the factors associated with positive expression of VEGF in breast cancer. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

RESULTS

Mean age of the subjects was 49.2 years. Mean BMI of the patients was 26.3 Kg/m^2. Positive expression of VEGF was observed in 80 percent of the patients with breast cancer. Majority of the patients of the present study were of postmenopausal status. Positive family history of cancer, mean tumour size and positive smoking history were found to be significant associative factor for VEGF.

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Table 1: Associative factors

Variable	VEGF Positive	VEGF negative	p- value
Mean age (years)	48.3	50.1	0.12
Mean BMI (Kg/m^2)	26.1	26.9	0.84
Positive Smoking history (n)	25	2	0.00 (Significant)
Positive family history of cancer	18	3	0.01 (Significant)
Mean tumour size (cm)	6.5	3.2	0.00 (Significant)

DISCUSSION

Breast cancer is the most frequent type of cancer among women worldwide, with increasing incidence rates in the majority of countries. Genetic alteration is one of the key factors involved in breast cancer initiation and progression. Human epidermal growth factor receptor 2 (HER2), an oncogene that is amplified and overexpressed in breast cancer, has been correlated with more aggressive characteristics, including negative estrogen receptor (ER) and progesterone receptor (PR) status, higher histological grading, lymph node involvement and resistance to chemotherapy.In addition to oncogene alterations, angiogenesis, the formation of new blood vessels, is of particular significance in the process of cancer growth, invasion and metastasis (3,4). The most important key modulator in this complex process is vascular endothelial growth factor (VEGF). The expression of VEGF has been correlated with the presence of higher microvessel density (MVD), lymphovascular invasion (LVI) and shorter disease-free survival (DFS) and overall survival (OS).[6-9]Hence; the present study was conducted for evaluating the expression of VEGF in breast cancer patients.

Mean age of the subjects was 49.2 years. Mean BMI of the patients was 26.3 Kg/m^2. Positive expression of VEGF was observed in 80 percent of the patients with breast cancer. Majority of the patients of the present study were of postmenopausal status. Adams J et al examined for the first time both plasma (VEGFp) and serum (VEGFs) VEGF concentrations in 201 blood samples from pre- and postmenopausal healthy controls and from patients with benign breast disease, localized breast cancer, breast cancer in remission, or metastatic breast cancer and related these to other clinicopathological markers. VEGFp but not VEGFs concentrations of patients with localized disease were significantly elevated compared with normal controls ($P = 0.016$). Patients with metastatic disease had higher VEGFp and VEGFs levels than normal controls ($P < 0.001$, $P = 0.044$ respectively), and higher VEGFp, but not VEGFs, than patients with benign disease ($P = 0.009$) and patients with localized disease ($P = 0.004$). However, the highest VEGFp and VEGFs concentrations were seen in patients in remission compared with normal controls ($P < 0.001$ and $P = 0.008$, respectively). VEGFp concentrations in patients in remission were also higher than in patients with benign disease ($P = 0.01$) or patients with localized disease ($P = 0.005$). Tamoxifen treatment was significantly associated with higher circulating and platelet-derived VEGF levels. Circulating VEGF did not correlate with any clinicopathological factor, including MVD or VEGF expression. VEGF expression was significantly correlated with estrogen receptor status and inversely correlated with tumor grade.[10]

In the present study, positive family history of cancer, mean tumour size and positive smoking history were found to be significant associative factor for VEGF. Sa-Nguanraksa D et al, in their study, determined the expression of VEGF in 99 breast cancer tissue samples using reverse transcription-polymerase chain reaction and the human epidermal growth factor receptor 2 (HER2) status was determined by immunohistochemistry. Subsequently, the associations of VEGF, HER2 and hormone receptor status with clinicopathological data were evaluated. High VEGF expression was found to be significantly correlated with the presence of lymphovascular invasion. In hormone receptor-positive/HER2-positive, HER2-positive and triple-negative breast cancer, high VEGF expression was correlated with the presence of axillary nodal metastasis and lower overall survival rates. Therefore, the assessment of the VEGF status along with the hormone receptor and HER2 status may help identify high-risk patients who may benefit from anti-VEGF treatment.[11]

CONCLUSION

Breast cancer patients are associated with enhanced expression of VEGF.

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