Expression of VEGF in breast cancer

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Abstract---Background: To evaluate the expression of Vascular Endothelial Growth Factor in breast cancer patients. Materials & methods: A total of 40 patients were enrolled. Mean age of the patients was 47.5 years. Biopsy specimens were obtained and were subjected with H and E staining. For VEGF marker, IHC staining was done. 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 and were analysed using SPSS software. Results: A total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p-value. Positive family history of cancer and mean tumour size were also significant. Conclusion: Breast cancer patients are associated with enhanced expression of VEGF.

Keywords---breast cancer, VEGF.

Introduction

Breast cancer is the most frequent type of cancer among women worldwide, with increasing incidence rates in the majority of countries. In Thailand, breast cancer is also the most common type of cancer among women. 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).

Vascular endothelial growth factor (VEGF), a potent angiogenic factor, plays a critical role in tumor growth and metastasis. 5,6 VEGF signaling in cancer cells is responsible for their resistance to apoptotic stimuli and their migration and invasion. 7 VEGF is highly up-regulated in breast cancer. Compared with normal or benign breast tissues, breast cancer showed higher levels of VEGF transcripts. 8 Approximately 72–98% of breast cancer is positive for VEGF by immunohistochemistry (IHC). 9 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. 10 In animals, anti-VEGF therapy inhibits the growth of breast tumors, reduces tumor microvessel density, and limits the infiltration of tumor-associated macrophages. 11 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. 12 Increased VEGF expression is implicated in acquired anti-estrogen resistance in vitro. 13 Hence, this study was conducted to evaluate the expression of Vascular Endothelial Growth Factor in breast cancer patients.

Materials & methods

A total of 40 patients were enrolled. Mean age of the patients was 47.5 years. Biopsy specimens were obtained and were subjected with H and E staining. For VEGF marker, IHC staining was done. 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 and were analysed using SPSS software.

Results

A total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p-value. Positive family history of cancer and mean tumour size were also significant.
Table 1: Associative factors

| Variable                        | VEGF Positive | VEGF negative | p-value |
|---------------------------------|---------------|---------------|---------|
| Mean age (years)                | 46.3          | 48.8          | 0.14    |
| Mean BMI (Kg/m²)                | 25.3          | 25.8          | 0.78    |
| Positive Smoking history (n)    | 20            | 2             | 0.001*  |
| Positive family history of cancer | 15           | 5             | 0.01*   |
| Mean tumour size (cm)           | 6.2           | 2.8           | 0.01*   |

*: significant

Discussion

The correlation of VEGF with established pathological markers for breast cancer prognosis has been reported. However, little is known about whether VEGF is differentially expressed by intrinsic subtypes of breast cancer. The analysis of plasma VEGF levels in metastatic breast cancer patients receiving bevacizumab demonstrated that VEGF levels >32.6 pg/ml were associated with shorter time-to-progression. The evaluation of VEGF in a randomized control trial on HER2-negative metastatic breast cancer revealed that the pretreatment plasma concentration of VEGF was correlated with a greater treatment effect. In addition, patients with higher VEGF concentrations exhibited lower hazard ratio (bevacizumab + docetaxel vs. placebo + docetaxel). In this study, a total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p-value. Positive family history of cancer and mean tumour size were also significant.

A study by Sa Nguanraksa D et al, showed that Vascular endothelial growth factor (VEGF), the key modulator of angiogenesis, has been implicated in breast cancer susceptibility and aggressiveness. VEGF expression was determined 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.

Another study by Liu Y et al, they showed by using immunostaining of tissue microarray sections, VEGF expression was determined in 1,788 primary invasive breast cancers identified from the Nurses’ Health Study cohort. Overall, 72.5% of breast cancers were positive for VEGF. VEGF expression was correlated with
intrinsic subtypes (P < 0.0001), with higher frequency in luminal B, HER2, and basal-like types versus luminal A type. Although VEGF expression was not significantly related to worse survival when all cases were considered together, it was significantly associated with increased risks for breast cancer-specific mortality (BCSM) (HR = 1.41, 95% CI = 1.01, 1.97) and distant recurrence (HR = 1.49, 95% CI = 1.07, 2.07) among women with luminal A tumors. In 262 women untreated systemically, VEGF expression was significantly associated with BCSM (HR = 5.58, 95% CI = 1.17, 26.66). In 902 women receiving adjuvant hormonal therapy, VEGF expression did not significantly predict clinical outcomes. The VEGF-associated increased risk of BCSM is limited to luminal A tumors. VEGF expression is a prognostic but not predictive marker of hormonal response in non-metastatic invasive breast cancer. 17

**Conclusion**

Breast cancer patients are associated with enhanced expression of VEGF.

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