Review Article

POSSIBLE ASSOCIATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR WITH GRADES OF BREAST CANCER

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ABSTRACT
Background: This study aimed to assess the significance of vascular endothelial growth factor (VEGF) and its possible correlation with tumor grade in female patients with breast cancer. **Subjects and Methods:** The present investigation was performed over a period from December 2011 to June 2012. A collection of 20 paraffin-embedded blocks from patients with breast cancer were included in current study. In addition to 15 paraffin-embedded blocks from patients with benign breast lesions (fibroadenoma) were included as a comparative group. Slides from both groups were stained with VEGF by immunohistochemistry. **Results:** The expression of VEGF was considered as positive in (16 patients) 80%. While VEGF overexpression of the marker has been noticed in benign breast tissue sections in only 2 patients (13%), with significant difference from that of malignant patients ($P<0.05$). There was a negative association between VEGF the grade of tumor ($P<0.05$). **Conclusion**: Based upon the findings of current study, it may be concluded that VEGF may play an important role in the pathogenesis of breast cancer and supports the evidence of its role in development, angiogenesis and cell survival of this aggressive tumor.

Keywords: VEGF, Breast cancer, Immunohistochemistry.

INTRODUCTION
Breast cancer is the commonest malignant tumor with annual death of more than one million worldwide[1]. In Iraq, breast cancer is one of the most common malignant tumors[2]. Vascular endothelial growth factor (VEGF), is thought to be a key mediator of angiogenesis which may play a role in local tumor growth and metastasis in many solid tumors, including breast cancer[3]. Preclinical experiments indicate that over-expression of VEGF may mediate the biologically aggressive phenotype of breast cancer[4, 5].
Several anti-angiogenic drugs have been developed and are being tested in clinical trials for different types of cancer. Because VEGF plays a key role in angiogenesis, reliable measurements of this factor are of crucial importance from both a clinical and a biological point of view.
Therefore the current study try to find the possible association between VEGF and histological types of breast cancer, as a possible explanation for the aggressive behavior of this tumor and hence whether such relation could be used as an objective tool for the early management of these patients with this type of breast cancer patients.

MATERIALS AND METHODS
This retrospective study included 20 paraffin embedded tissue blocks, collected from patients with breast cancer incvolved in this study. All the cases were collected from Al-Kadhimiya Teaching Hospital and private laboratories in Baghdad. A group of 15

patients with benign fibroadenoma breast lesions were included as a comparative group. Labeled Streptavidin-Biotin method was used for immunohistochemical detection of VEGF. All malignant tissue biopsies were classified, according to the modified WHO classification, into three grades: grade I, grade II and grade III. The results were statistically tested by Chi-squared test SSPS software.

RESULTS

Vascular endothelial growth factor (VEGF) was positive in 16 patients (80%) of malignant group (table 1). Furthermore there was positive VEGF in 2 (13%) in benign (fibroadenoma) breast tissue sections with significant difference from that of malignant cases (P<0.05). Immunohistochemical analysis in relation to grade of tumor revealed that, there was significant difference between VEGF overexpression and the tumor grade (P<0.05) as the expression was higher in low grade tumors and reduced as the tumor grade advances (table 2).

DISCUSSION

Overexpression of VEGF which is a central regulator of angiogenesis, suggesting that the aggressive breast cancers may be in part attributable to increased angiogenesis. The role of VEGF was established in many other solid tumors as in bladder cancer[6] and colorectal adenocarcinoma[7]. Moreover, its expression was also revealed in chronic lymphocytic leukemia[8].

The result of the current study showed that there was limited expression of VEGF in benign breast lesions in compare to malignant sections. This observation was expected hence VEGF expression could be a landmark in the malignant breast tissue, and may have a limited role in the benign breast lesions. This result was similar to the study presented by Al-Khafaji et al in 2010[9] as they showed 70% of breast cancer patients were positive for VEGF by immunohistochemistry. The current study revealed that tumor grade showed reverse expression of VEGF and this was shown by Konecny et al in 2004[10] as they revealed that there was low expression of VEGF in invasive breast tumor. This can be explained that, VEGF plays an important role in the early stages of the tumor as angiogenesis is important for early tumor, but later on the expression could be reduced due to introduction of other angiogenic factors like Platelet-derived endothelial growth factor (PDGF) and transforming growth factor (TGF), that both expressed in advanced breast cancer and they have an important angiogenic activity.

This expression of VEGF can be used as predictive marker for prognosis as the reduction of its expression may indicate advanced tumor. It can be also be targeted as treatment for early tumor in the therapy of breast cancer.

Table 1: The expression of VEGF in malignant breast cancer

VEGF expression	Positive	Negative	Total
Malignant	16 (80%)	4 (20%)	20 (100%)
Benign	2 (13%)	13 (87%)	15 (100%)

P<0.05

Table 2: The expression of VEGF according to tumor grade

Tumor grade	Positive VEGF	Negative VEGF	Total
Grade I	4 (80%)	1 (20%)	5 (100%)
Grade II	5 (71%)	2 (29%)	7 (100%)
Grade III	4 (50%)	4 (50%)	8 (100%)

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