Expression of Vascular endothelial growth factor (VEGF) and CD34 in different thyroid disorders

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Abstract

Background: Neovascularization/angiogenesis is crucial for the growth and metastatic spread of neoplasms. It is a key reaction to evaluate the growth potential of neoplasms, a multi-step process related to the modeling of the intercellular matrix, proliferation and migration of endothelial cells.

Aim: Study of the vascular density during Hashimoto's Thyroiditis (HT) and Papillary Thyroid Carcinoma (PTC) by immunohistochemical examination of angiogenesis activity: VEGF, CD34 markers.

Methods: The research database is retrospective and prospective tissue samples obtained from patients after total thyroidectomy, lobectomy or partial resection: HT (n=25), PTC (n =10) which studied histologically and immunohistochemically investigated.

Results: VEGF expression reduced as compare cases of HT than in PTC. There was no clear association between CD34 and thyroid pathology. Conclusion: VEGF is the most potent inducer of neovascularization, and its increased expression is associated with a poor prognostic outcome in many diseases. It is known that TTF-1 positively regulates VEGF. But it should be noted that, in terms of manifestation time, the action of VEGF is primarily than TTF1, and may be discussed as a predictor of dysplasia and malignant transformation. **(TCM-GMJ June 2024; 9 (1):P3-P6)**

Keywords: Hashimoto's Thyroiditis; Papillary Thyroid Carcinoma; VEGF; CD34; TTF-1

Introduction

Angiogenesis development of new blood vessels from the pre-existing vessels, although one of the crucial processes in normal physiology, is an important pathogenic link in both benign and malignant disease [1, 2]. Neoangiogenesis is a key reaction to evaluate the growth potential of neoplasms, a multi -step process related to the modeling of the intercellular matrix, proliferation and migration of endothelial cells [1-3].

Vascular endothelial growth factor (VEGF), which is a growth stimulator of microvessels endotheliocytes, can enhance their proliferation both in physiological and pathological conditions [4-6]. The biological effects of VEGF are mediated by two receptor tyrosine kinases (RTKs), VEGFR-1 and VEGFR-2, which are mainly expressed on endothelial cells [7, 8].

It should be noted that angiogenesis plays an important role in the development of goiter transformation of the thyroid gland. Endothelial cell proliferation has been described to precede thyrocyte hyperplasia in the follicles, leading to increased VEGF concentrations both in the blood serum and within the intrathyroidal vascular area, a phenomenon described in both Graves' and Hashimoto's autoimmune thyroiditis (HT) [9, 10].

According to researchers, immunomarkers CD34, CD31 are adequate indicators of the growth potential of thyroid parenchyma [11]. VEGF production is considered to be thyrotropin (TSH) induced, as TSH increases tissue VEGFmRNA protein content [10, 12].

VEGF is a specific mitogen for endothelial cells, main mediator function in angiogenesis in the thyroid gland has been established [10, 12, 13].

Under physiological conditions also in euthyroid goiter, angiogenesis is stable on the level given type of tissue. Vascular density is assessed during pathology by immunohistochemical examination of angiogenesis activity: VEGF, CD34 markers. The expression of these markers allows distinguishing between pseudoneoplastic hypertrophy and neoplasia [4-8, 11].

Based on the relevance of the issue, the aim of the study was defined: toinvestigatevascular endothelial growth factor (VEGF) and CD34 receptor activity in thyroid tissue samples during Hashimoto's thyroiditis (HT) and papillary carcinoma (PTC) – the most common

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thyroid disorders.

Vascular endothelial growth factor (VEGF) is a signaling protein of endothelial cells and can activate their growth in both physiological and pathological conditions [4-6].

The protein CD34 is interesting from the point of view that it's the main contributing factor to the proliferation of endothelial cells not only in nodular processes, but also in inflammatory processes, including autoimmune activity [11, 14].

Methods

The research database is both retrospective and prospective tissue samples obtained from patients of both sexes after total thyroidectomy, lobectomy or partial resection: HT (n=25), PTC (n =10). The age of the patients varied between 25-55 years. All clinical and diagnostic data of the mentioned cases were collected. Present study was reviewed and deemed exempt from written informed consent by the Ethics committee and Board of medical sciences at Tbilisi State University based on Helsinki - ethical principles declaration for medical research [15].

Surgically obtained thyroid tissue samples were stained with hematoxylin and eosin (H&E) after fixation in 10% buffered formalin. After selection, the material was prepared for immunohistochemical study.

Based on the main objective of the research, the tissue samples were studied using the following antibodies:

1. Human recombinant polyclonal anti-VEGF-165 antibody with dilution 1:50 (Biogenex, USA);
2. Ready-to-use monoclonal anti-CD34 (clone QBEnd/10, Novocastra, UK).

Each marker was studied on the material of 8-10 patients of a separate group. Immunohistochemical procedures were performed following the protocols of the antibody manufacturer (BioGenex, USA; Novocastra, UK).

Results and discussion

Positive cytoplasmic expression of VEGF was detected in both thyrocytes and vascular endothelial cells. Expression was focal and cytoplasmic, not diffuse or membranous. All tissue samples showing no or weakly positive VEGF expression were of benign origin. Increased thyrocyte staining was observed in PTC specimens compared with Hashimoto's thyroiditis (Fig. 1. a, b).

VEGF expression appears to be associated with behavioral aspects of thyroid carcinomas. Studies have shown that increased expression of VEGF in thyroid neoplasia is associated with a higher risk of recurrence and metastasis [16, 17].

As for the expression of CD34 in PTC - was low. In HT parenchyma CD34 expression is seen in basement membranes, not in follicular cells (Fig. 2 a).

According to a number of researchers, high expression of CD34 in PTC is associated with an increased risk of recurrence [18, 19]. However, there are studies to the contrary [19, 20], with their results that low expression of CD34 is characteristic of poorly differentiated cancers and is associated with high mortality.

In HT, there is a weakening of the VEGF and CD34 receptor status of thyrocytes, which creates a characteristic picture of angiogenesis and parenchymal function decline and hypothyroidism: low expression of thyroid-stimulating hormone (TSH) indicates not only inhibition of hormone-stimulating function, but also on the reduction of synthesis and activity of angiogenesis.

Conclusion

Thus, VEGF expression reduced as compare cases of HTthan in PTC. There was no clear association between CD34 and thyroid pathology. In general, neovascularization/angiogenesis is crucial for the growth and metastatic spread of neoplasms. Vascular endothelial growth factor (VEGF) is the most potent inducer of neovascularization, and its increased expression is associated with a poor prognostic outcome in many diseases.

It is known that TTF-1 positively regulates vascular endothelial growth factor (VEGF) [21]. We have studied Thyroid transcription factor 1 (TTF1) during HT and PTC as an indicator of follicular epithelial dysplasia [22, 23]. Morphological changes of follicular cells in HT may resemble changes developed during PTC. In the accordance of this hypothesis, the thyroid gland samples transform in two types of atypical cells: 1) immature follicular cells in cord-like structures and 2) solid basal cells. Both cell types maintain the follicular cells characteristic but expressedTTF1 intensively.It should be noted that, in terms of manifestation time, the action of VEGF is primarily than TTF1, and may be discussed as a predictor of dysplasia and malignant transformation.

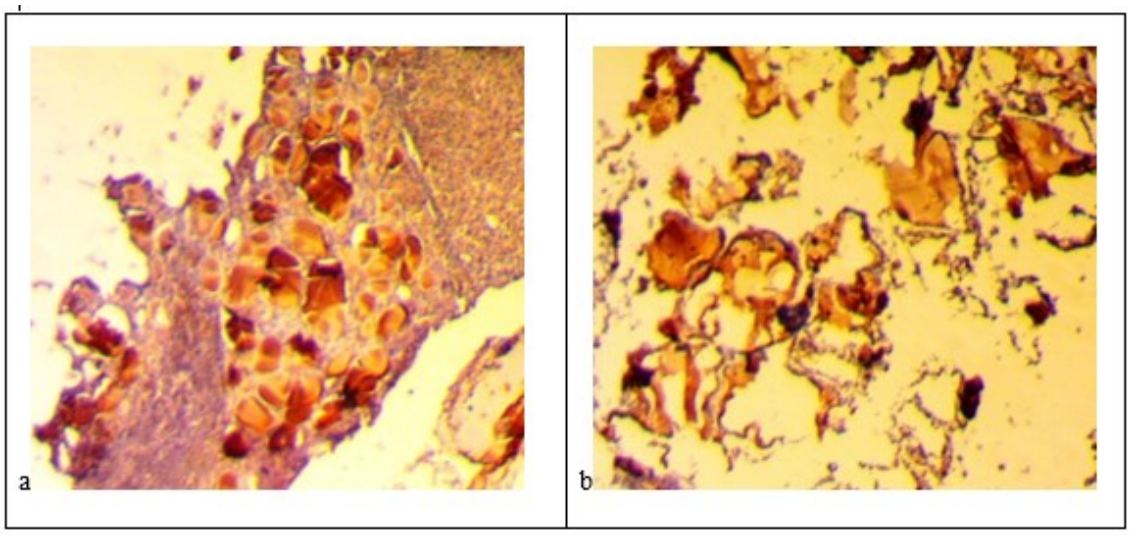

Fig. 1. a. HT, VEGF diffuse cytoplasmic expression in thyrocytes and vascular endothelial cells; b. PTC, increased VEGF thyrocyte staining. Immunoperoxidase reaction, X200.

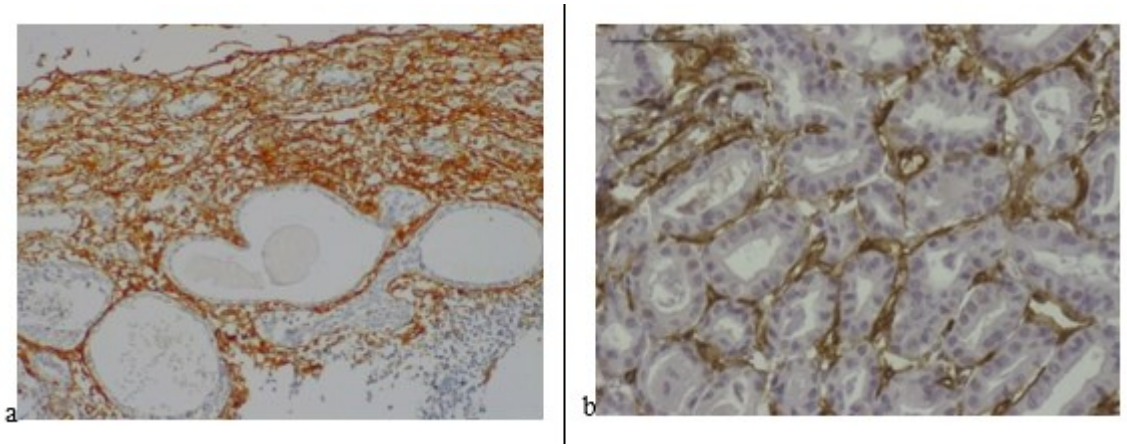

Fig. 2. a. HT, CD34 expressed in vascular basement membranes. X100; b.PTC, CD34 diffuse middle activity in interfollicular capillaries wall.X200. Immunoperoxidase reaction.

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