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THE ROLE OF CD34-POSITIVE CELLS IN THE ANGIOGENESIS OF MALIGNANT TISSUES

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ABSTRACT — Development of methods for targeted treatment aimed at inhibiting angiogenesis in malignant tissues is of great importance for modern oncology. The features of expression of CD34-positive cells at the border of the tumor and malignant tissue were studied. High expression of CD34-positive cells in small and large vessels during malignancy and is in correlation with the size of the tumor and the age of the disease. A promising target for targeted treatment is VEGF, as the main regulator of angiogenesis during tissue malignancy.

KEYWORDS — angiogenesis, CD34, Vascular endothelial growth factor (VEGF), malignancy, vessels, targeted treatment, inhibition of angiogenesis

RELEVANCE

High mortality due to insufficient understanding of carcinogenesis in general and the role of angiogenesis mechanisms in the pathogenesis of malignant tissues in particular, indicate the undoubted relevance of studies aimed at solving these issues. Angiogenic factors that are significant in the physiological vascularization of structures also play an important role in ensuring cellular interactions during the malignancy of various tissues. [1]. The question of a targeted conservative effect on tumors with the use of angiogenesis inhibitors in the zone of malignancy remains open. As previously noted in 2012, Eleftherios P. Diamandis, Robert C. Bast, Jr. PhilGold [2], and at the present stage, despite the emergence of powerful genomic, proteomic, epigenomic, metabolomic, microarray and other technologies, the efficiency of timely diagnosis and target treatment of tumors remains low [3, 4, 5]. Improving targeted treatment methods aimed at key morphological substrates that support carcinogenesis is of great importance in predicting outcomes.[6, 7, 8]. The issues of pathogenetically substantiated induction and inhibition of angiogenesis in human tumor tissue and prevention of cancer cell metastasis remain poorly understood.

Objective

To study the expression of CD34-positive precursors of endothelial cells, as well as VEGF-positive, secreting endothelial vascular growth factor in the tissue at the border with the tumor and directly in the tumor.

MATERIAL AND METHODS

The paper analyzes and discusses the results of our own studies of biopsy specimens from tumor tissues in 11 patients obtained in accordance with the order of the Ministry of Healthcare of the Russian Federation dated 04.29.94 N82 "On the procedure for conducting pathological autopsies", according to the rules of the regulating instructions on the procedure for autopsy Committee of FEFU.The control group consisted of 4 patients who died as a result of traumatic brain injuries incompatible with life, presumably without somatic pathology at the age from 24 to 56 years. Using the methods of immune histochemistry, a quantitative analysis of vascular endothelial growth factors and CD34 expression in tumor tissue and at the border of unchanged tissue with a tumor was carried out. The biopsy material was recorded according to the appropriate protocols to prepare for histological studies immediately after collection. The exclusion of possible artifacts is based on the data obtained by Yu.I. Pigolkin. (1995), indicating that when corpses are kept at a temperature of 4–7° C for 4–6 hours, no microscopically visible changes are observed in the morphology of various organ systems, except for a slight decrease in the intensity of specific reactions to enzymatic activity. We used classical histological research methods with staining with hematoxylin and eosin to obtain a general morphological picture, as well as the method of immune histochemistry to identify the expression of CD34 and VEGF. Analysis of preparations and production of illustrations were performed using an Olympus Bx52 microscope and a DP25 digital camera.

RESEARCH RESULTS AND DISCUSSION

We found that cells expressing CD34 were identified in all normal tissues of control vascular samples by pronounced and continuous staining. At the same time, VEGF was not expressed in normal unaltered tissues of various organs. It is known that vascular endothelial growth factor (VEGF) and VEGF receptors — VEGFR1 and VEGFR2 signaling are powerful activators of angiogenesis. The percentage of VEGFR-positive tumor cells was quantified in brain tumors. The density and diameter of microvessels was also analyzed using immune histochemistry for VEGF and CD34 expression. Although it was originally thought that the expression of VEGFR1 and VEGFR2 is limited to endothelial cells, now from Clara C.A., Marie S.K., de Almeida J.R. et al. (1914) it is known that both receptors can also be expressed in tumor cells [9]. In addition, we, based on the work of Jung S., Moon K.S., Jung T.Y., et al. (2006), it was considered that expressing CD34 cells are co-expressing the receptor VEGF2 [10]. Analysis of our own data and presented in the available literature Golab-Janowska M., Paczkowska E., Machalinski B., et al. (2018) showed that VEGFR — positive brain tumor cells provide an increased regulation of VEGF signaling on VEGFR [11]. We have noted a higher content of VEGFR1 and VEGFR2 — positive tumor cells than in tissues with thermal injuries. Higher mobilization of cells expressing CD34 occurs in trauma, respectively. It was also noted that CD34 is expressed not only in small, but also in larger vessels of tumors, which is consistent with the results of the study by TamuraR., SatoM., MorimotoY., (2020) [5]. We noted that the level of VEGF expression significantly correlated with the activity and expression of CD34. The analysis showed that there are no significant statistically significant differences in the expression of VEGF and CD34 in the age aspect, which is in correlation only depending on the size of the tumor and the age of the disease. Vascular endothelial growth factor, VEGF, is considered the main regulator of angiogenesis in tissue malignancy and in various tumors [12].Intratumoral hemorrhage, as one of the pathogenetic links in the development of complications in various tumor conditions, occurs mainly in malignant tumors. Recent studies have shown that overexpression of vascular endothelial growth factor (VEGF) may play a role in the loss of vascular integrity and subsequent bleeding [13]. In our opinion, bleeding can be associated with both imperfection of the vascular wall and the absence of pericytes in the membrane of small vessels, which play not only the role of regulators of the vascular tone of small vessels and capillaries of the microvasculature, but also inhibitors of the proliferative activity of endothelial cells. The spectrum of influence of various factors on tumor development in the nervous tissue is complemented by a role in angiogenesis, neuroinflammation and cerebral ischemia performed by matrix metalloproteinases and tissue inhibitors of metalloproteinases[14, 15]. With physiological immaturity of the endothelium, there are no transport enzymes, such as alkaline phosphatase, which corresponds to the high ability of the immature endothelium to diffuse blood from the lumen of the vessels into the surrounding tissue under conditions of malignancy. This explains the high expression of CD34-positive cells during malignancy against the background of the lack of specialization of endothelial precursor cells in the tumor tissue.

CONCLUSION

Strategies for the normalization of vascular histophysiology, aimed at improving the trophic supply of the structures of the tissues surrounding the tumor due to the full trophic supply with a decrease in hypoxia, are treatment methods that can improve the outcome in cancer patients undergoing rehabilitation treatment after surgery by inducing an increase or inhibition of gene expression. responsible for the secretion of proteins VEGF and CD34.

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