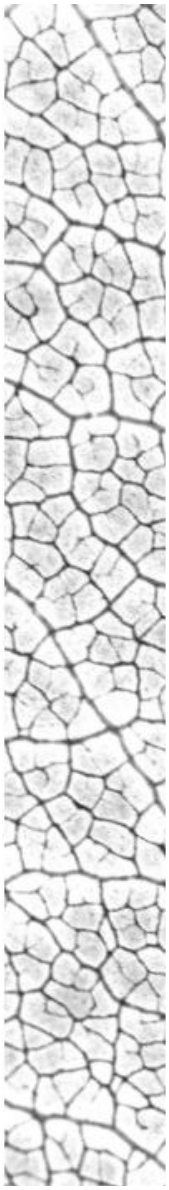

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The correlation between the vascular endothelial growth factor expressions and cervical lymphnodes on nasopharyngeal carcinoma

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Abstract

Background: In terms of its clinical characteristics, nasopharyngeal carcinoma (NPC) is easy to invade and metastasize. Therefore, it can cause locoregional recurrence and distant metastasis.The Prediction of the current NPC prognosis remains generally based on clinical stage assessments. In fact, patients with the same stage often get different therapeutic results. **Purposes:** This research aims to analyze the correlation between VEGF expressions and the enlarged cervical lymph nodes in NPC. **Methods:** This research utilized an observational analytic with the cross sectional approach. The samples employed 18 NPC patients with cervical lymph nodes from the criteria of N0 N1, N2, and N3, of type III WHO histopathology (undifferentiated carcinoma) who have never received any therapy. The data were analyzed using the Mann-Whitney U-test to determine the correlation between the increased VEGF expressions and the enlarged cervical lymph nodes with significance level (α) = 0.05. **Result:** From all samples, 83.33% of weak expressions were found, while moderate expressions amounted to 16.67%. The result of the Mann Whitney U-test indicated a p-value of 0.058. This fact suggested that the correlation between the increased of VEGF expressions and N had no significant differences. **Conclusion:** There are no correlations between VEGF expressions and the enlarged cervical lymph nodes.

Keywords: VEGF, nasopharyngeal carcinoma, cervical lymph nodes

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INTRODUCTION

In Indonesia, the incidence of nasopharyngeal carcinoma (NPC) ranks the first malignant case among others types of head and neck cancers. In terms of its clinical characteristics, nasopharyngeal carcinoma (NPC) is easy to invade and metastasize. Therefore, it can cause locoregional recurrence and distant metastasis. The prediction of the current NPC prognosis remains generally based on clinical stage assessments graded into primary tumor (T), cervical lymph nodes (N), and distant metastasis (M). In fact, patients with the same stage often get different therapeutic results. This phenomenon shows that staging is not sufficiently accurate to be used as a prognosis prediction. Therefore, it is important to look for new molecular biomarkers that can help clinicians improve their prognosis prediction and develop therapeutic interventions in people with NPC (Taweevisit, Keelawat, & Thorner, 2010. Li, et al. 2008).

Some research data indicate that angiogenesis plays an important role in the growth, development, invasion, and metastasis of a tumor. One of the important signal pathways involved in this complex process is vascular endothelial growth factor (VEGF). The increased VEGF expressions were found in metastatic colorectal cancer (CRC), renal cell carcinoma (RCC) and non-small cell lung cancer (NSCLL). The increased VEGF expressions were associated with an increased risk of recurrence, metastasis and death (Dimova, Popivanov, & Djonov, 2014; Senchi, & Malami, 2015).

A research on head and neck carcinomas showed that a high VEGF expression associated with N with a poor prognosis (Mineta, et al. 2000). Other researchers reported that there is no significant correlation between VEGF expressions and N in lung carcinoma (Zhan, et al. 2009). These facts indicate that there are still differences in perceptions regarding the correlation between VEGF expressions and N (Zhan, et al. 2009).

Based on this situation, the correlation between VEGF expressions and N in NPC should be discovered

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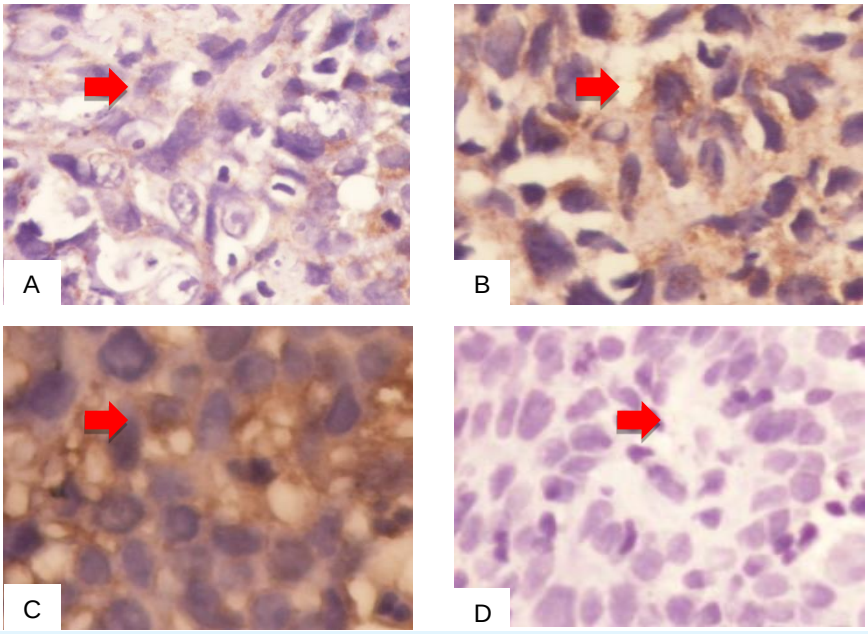

Fig. 1. The results of the VEGF expression examination using immunohistochemistry techniques. (A) Week expressions, (B) Moderate expressions, (C) Strong expression, (D) Negative expressions. For the negative expressions, there were no brown staining in in the cytoplasm of tumor cells (red arrows)

through research. This research aims to analyze the correlation between VEGF expressions using an analytic observational with a cross sectional approach with N on NPC.

METHOD

This research was conducted using an observational analysis with a cross sectional approach carried out at the Dept/SMF of Medical Sciences ENT-Head and Neck Faculty of Medicine - Universitas Airlangga- Regional Public Hospital Dr. Soetomo, Surabaya. The research started with the immunohistochemistry examination at the laboratory. This research was carried out from January to April 2013. The samples in this research were NPC patients with cervical lymph nodes from the criteria of N0 N1, N2, and N3 according to WHO type III histopathology (undifferentiated carcinoma) who have never received therapy.

The paraffin blocks used for the examination of VEGF expression was derived from nasopharyngeal biopsy material with sufficient tumor tissue and was applied using immunohistochemistry technique. The total samples amounted to 18 cases. The VEGF expressions were assessed using the immunohistochemistry examination (IHC) and rabbit polyclonal antibody Anti Human VEGF-A clone EP1176Y (Biocare Medical, LLC, USA). The assessment was carried out visually with a binocular light microscope by two independent anatomical pathology consultants.

The expression was considered positive when there was a brown staining of tumor cells on the membrane and cytoplasm. Otherwise, it was considered negative if there were no brown staining tumor cells on the membran and cytoplasmic tumor cells at the High Power Field (HPF) with 400-times enlargement. The VEGF expressions were assessed in 3 Power Fields, and its mean value was determined to gain the following scores: score – (weak) when the total of tumor cells was less than 25 cells/HPF, Score + (moderate) when the total of tumor cells was 25 – 50 cells/HPF, Score ++ (strong) when the total of tumor cells was between 51 and 75 cells/HPF, and Score +++ (very strong) when the total of tumor cells reached more than 75 cells/ HPF(Rossi, et al. 2010). The data were analyzed using the Mann-Whitney U-test to determine the correlation between the increased VEGF expressions and the enlarged cervical lymph nodes.

RESULT

The samples were 36 NPC patients who met the inclusion criteria with 9 samples for each of N0 N1, N2 and N3 cervical lymph nodes. The highest sex distribution was male with 22 patients (61.11%) and female with 8 patients (38.89%), resulting the ratio between men and women to be 1.5: 1. The highest age distribution was in the age range of 40-49 years with 19 cases in total (52.77%), followed by the age range of 30-39 years with 8 cases in total (22.22%) and 6 cases for the age range of 50–59 years (16.67%).The youngest age was 30 years old, whereas the oldest was 72 years old. The results of the VEGF expression examination are shown in **Fig. 1**.

Table 1. The Distribution of VEGF Expression Scores Based on the Enlarged Cervical Lymph Nodes

Score /Nodule	N0	N1	N2	N3	%
-	9	8	7	6	83.33
+	0	1	2	3	16.67
++	0	0	0	0	0.00
+++	0	0	0	0	0.00
Total	9	9	9	9	100.00

VEGF: vascular endothelial growth factor

Based on the enlarged cervical lymph nodes shown in **Table 1**, the distribution of obtained VEGF expression scores are as follows. Nine samples of N0 nodules and eight samples of N1 nodules showed week expressions, while 1 sample indicated moderate expressions in N1 nodule.

Week expressions in N2 nodule were found in seven samples, while moderate expressions in N2 were found in two samples. In the N3 nodule, week expressions were found in six samples, while moderate expressions were found in three samples. As much as 83.33% of the samples showed week expressions and 16.67% showed moderate expressions. There was an increase in the number of cells that showed moderate expressions at N0, N1, N2 and N3. The strong and the overly strong expressions were not found in this research. The Mann Whitney U-Test results obtained a p-value of 0.058, meaning that that the correlation between the increased of VEGF expressions and N had no significant differences. It can be concluded that there was no correlation between the VEGF expressions and the enlarged lymph nodes.

DISCUSSION

There was a tendency on the number of cells showing moderate expression at N0, N1, N2 and N3 to increase. Statistical test results proved that there was no correlation between the VEGF expressions and N. The results of this research differ from the research on carsinoma head and neck and the advance stages of NPC that showed that high expression is associated with N and poor prognosis (Li, et al. 2008. Mineta, et al. 2000).

Angiogenesis is an important stage in tumor growth and plays an important role in tumor invasion and metastasis. Tumors develop angiogenesis by secreting several growth factors to stimulate endothelial proliferation and migration. VEGF is the main stimulator for angiogenesis (Puspasari, et al. 2018. Pratiwi, Yuliati, & Ariani, 2017).

In vivo and in vitro research suggested that the increased VEGF expression is related to tumor growth and metastasis, while barriers in the VEGF expression result in the suppression of tumor growth and angiogenesis (Kyzas, Cunha, & Ioannidis, 2005). The different results might be caused by the analyzed sample size, the different stages, and the types of histopathology. This research only used WHO type III NPC without giving further consideration on the clinical and metastatic stages.

CONCLUSION

The samples size, the different stages, and the types of histopathology affect the results obtained. This research shows that there is no corelation between the VEGF expression and the enlarged cervical lymph nodes.

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