Vascular Endothelial Growth Factor Receptor (VEGFR) and Latent Membrane Protein (LMP-1) Expression in Nasopharyngeal Carcinoma

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Background: Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and lining of the nasopharynx. NPC is a relatively rare malignancy in most parts of the world but it is endemic in many geographical regions, including Southern China, Southeast Asia and the Middle East/North Africa. In Indonesia in particular, the incidence is relatively high, ranking 10th of 10 large tumors of the body and ranks 1st in our department.

Objective: To study the relationship between the expression of LMP1 and VEGFR (Flt-4) proteins and the histopathological features of nasopharyngeal carcinoma (NPC) in the Indonesian population.

Materials and methods: A cross-sectional study with the exploitation of nasopharyngeal carcinoma (NPC) in Makassar, Indonesia from July 1st to August 30th, 2007. The expression of VEGFR (Flt-4) and LMP1 was evaluated.

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Vascular Endothelial Growth Factor Receptor (VEGFR Flt-4) and Latent Membrane Protein (LMP-1) Expression in Nasopharyngeal Carcinoma

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**Abstract:** Background: Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and line the nasopharynx. NPC is a relatively rare malignancy in most parts of the world but it is endemic in many geographical regions, including Southern China, Southeast Asia and the Middle East/North Africa. In Indonesia in particular, the incidence is relatively high, ranks 5\textsuperscript{th} out of 10 large tumors of the body and ranks 1\textsuperscript{st} in our department.

Objective: To study the relationship between the expressions of LMP1 and VEGFR (Flt-4) proteins compared with staging and histopathological features of nasopharyngeal carcinoma (NPC) in Indonesian population.

Materials and Methods: A cross sectional study with explorative approached was conducted in Makassar-Indonesia from July 2006 to August 2007. The expression of VEGFR (Flt-4) and LMP-1 proteins was examined by immuno histochemical with avidin-biotin methods staining in 45 NPC specimens.

Result: VEGFR (Flt-4) and LMP-1 were expressed in 100\% and 42,1\% of NPC specimens. No significant difference in correlation (p>0,05) between staging with VEGFR(Flt-4) and LMP-1 expression, these results indicated that VEGFR(Flt-4) and LMP-1 were expressed during early stage to prepare for enhancing metastatic capacity to the later stage of NPC. There was negative correlation (p<0,05) between histopathological classification with VEGFR(Flt-4) and LMP-1 expression, this indicated that the expression of VEGFR(Flt-4) and LMP-1 was much higher in WHO type II (well differentiated) than WHO type III (undifferentiated). WHO type II well-known as more less sensitive to radiotherapy than WHO type III, according to the prognostic value; WHO type III better than type II. There was strong positive correlation (r= 0,990, p<0,05) between LMP-1 with VEGFR(Flt-4) expression, thereby LMP-1 induces production or expression of VEGF. No significant correlation was found between staging and histopathological features, VEGFR(Flt-4) and LMP-1 expression with alcohol, smoking, betel leaves-araca nuts, air pollution (wood's fire stove, mosquito repellent's smoke) and preservative foods (salted fish, canned food and smoked meat).

Conclusion: These results suggest that both VEGFR (Flt-4) and LMP-1 expressions are valuable prognostic markers for prognostic prediction in NPC patients.

**Keywords:** Nasopharyngeal carcinoma (NPC), VEGFR(Flt-4), LMP-1, Indonesia.

**INTRODUCTION**

Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and line the nasopharynx. NPC is a relatively rare malignancy in most parts of the world but it is endemic in many geographical regions, including Southern China, Southeast Asia and the Middle East/North Africa [1-3]. Ho [1] reported that NPC is the third most common malignancy among men, with an incidence of between 50 per 100,000 in the Guangdong Province of Southern China. Incidence is higher in the Chinese and Tunisian populations. NPC in Indonesia ranks 5\textsuperscript{th} out of 10 large tumors of the body and ranks 1\textsuperscript{st} in our ENT department. Nations with high risk are Eskimo, Tunisia, Philippines, Malaysia, Algeria and Indonesia. Rarely found in Caucasian, India, and Japan [2-4]. In Indonesia the incidence to date is not known. Health department data in 1980 showed the prevalence was 4.7 in 100,000 or estimated 7,000 to 8,000 cases in a year [5]. Profile data of nasopharyngeal carcinoma in Hasanuddin University Hospital Makassar, Indonesia from period of January 2000 to June 2007 revealed that nasopharyngeal carcinoma covered 33\% malignancy of ear, nose, and throat. Majority in 4\textsuperscript{th} and 5\textsuperscript{th} decades of life, male to female ratio is 2:3:1, the main histopathology finding was anaplastic carcinoma (type III WHO) accompanied by high tendency of metastasis [6].

NPC is often overlooked due to variation of symptoms and sign as well as difficulty to examine nasopharyngeal space, especially in Rosenmuller fossa, which is taken from the inventor, a German anatomist, Johan Christian
(p<0.05), which means that the expression of VEGFR(Flt-4) and LMP-1 expression is higher on early stage, which is required for preparing metastasis. There were significant inverse relationship between histopathology and VEGFR(Flt-4) and LMP-1 expression (p<0.05), which means that the expression of VEGFR(Flt-4) and LMP-1 expression is higher in type II WHO (Figs. 3, 4) (good differentiation) compared to type III WHO (poor differentiation), where the prognosis of type II WHO based on tumor response against radiation therapy is poorer than type III WHO. There was strong relationship (p<0.05) between VEGFR(Flt-4) and LMP-1 expressions, which means that LMP-1 expression increased as the expression of VEGFR(Flt-4) increased, therefore LMP-1 may increase (strong regulator) production of VEGFR(Flt-4). There was no significant relationship (p>0.05) between clinical findings including staging, histopathology, VEGFR(Flt-4) and LMP-1 expression against alcohol, cigarette smoking, betel-quid chewing, pollutant (smoked mosquitoes repellent and wood smoke) and preserved food (salted fish, canned food, and smoked meat).

CONCLUSION

LMP-1 is a strong regulator to VEGFR(Flt-4), associated with the prognosis of NPC, marked with the expression on type II WHO compared to type III WHO. Although there were no correlation between clinical finding including staging, histopathology finding, VEGFR(Flt-4) and LMP-1 expression.

SUGGESTION

Wide research using larger sample covering various aspects that affect prognosis and multidisciplinary work. The expression of VEGFR(Flt-4) and LMP-1 expression can be considered as one predictor of NPC prognosis.

REFERENCES