ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 12, pp.8745-8747, December, 2019

DOI: https://doi.org/10.24941/ijcr.37406.12.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

RELATIONSHIP OF MATRIX METALLOPROTEINASE-9 EXPRESSION AND KI-67 LABELLING INDEX IN SUBJECT WITH MENINGIOMA IN ADAM MALIK GENERAL HOSPITAL 2017-2018

Prawira Buntara Putra*, Ridha Dharmajaya and Adril Arsyad Hakim

Department of Neurosurgery, Faculty of Medicine, Universitas Sumatera Utara, H. Adam Malik Hospital Medan, Indonesia

ARTICLE INFO

Article History:
Received 24th September, 2019
Received in revised form
18th October, 2019
Accepted 07th November, 2019
Published online 30th December, 2019

Key Words:
Meningioma,
MMP-9, Li Ki-67,
Mitosis,
Proliferation.

ABSTRACT

Introduction: Meningiomas are benign brain tumors in the brain wrapping tissue or meningens. The primary brain tumor most commonly diagnosed is meningioma, which is 33.8% of all primary brain tumors. Total resection of meningioma cases increases life expectancy and improves the prognosis of patients with these cases, in high grade meningioma total resection is not possible and another modality is needed to prevent tumor recurrence, including administering drugs to block the expression of genes that effect tumor growth.Initial studies show enzymes such as cysteine protease, metalloproteinase (MMP) and serine protease are closely related to growth and invasion of tumors. The Ki-67 antigenswere found in each active cell cycle (G1, S, G2 and M) but were not found in resting cells (G0). The expression of the Ki-67 protein is associated with the proliferative activity of the intrinsic cell population in malignant tumors, thus allowing its use as a marker of tumor aggressiveness. **Method:** This study is a cross sectional analytic observational research study in patients diagnosed as meningiomas in Adam Malik Hospital in the periods of January 2017 - December 2018.Inclusion criteria includes confirmed cases of meningioma by pathological examination and the patient's age is over 17 years. Exclusion criteria are based on medical record data, found other systemic diseases such as chronic obstructive pulmonary disease, arthritis, atherosclerosis, tubulointestial kidney disease and suffering from other tumors on the body.The sampling technique used is total sampling with a total sample of 33 samples. All meningioma paraffin block specimens that had previously been treated with hematoxylin-eosin base staining and confirmed as a meningioma had MMP-9 and Ki-67 immunohistochemical staining. After staining, overexpression of MMP-9 and Ki-67 labeling index (LI) were calculated. **Result**s: The division of meningioma patient by gender is 23 women (69.7%) and 10 men (30.3%). The highest incidence of meningioma is in the age group of 40 - 49 years and equal to 18 cases (54.5%). While the least frequency of occurrence was found in the age group 60-69 namely 1 case (3%). the highest frequency is grade I meningioma in 24 (84.8%) cases, followed by grade II as many as 4 cases (12.1%) and grade III as much as 1 case (3%). The relationship between SI staining of MMP-9 and LI Ki-67, with Chi square analysis results with p value of 0.393. **Conclusion:** There is no significant relationship between MMP-9 overexpression with LI Ki-67

Copyright © 2019, Prawira Buntara Putra et al. *This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.*

Citation: Prawira Buntara Putra, Ridha Dharmajaya and Adril Arsyad Hakim. **2019.** "Relationship of matrix metalloproteinase-9 expression and ki-67 labelling index in subject with meningioma in adam malik general hospital 2017-2018", *International Journal of Current Research*, 11, (12), 8745-8747.

INTRODUCTION

Meningiomas are benign brain tumors in the brain wrapping tissue or meningens. The primary brain tumor most commonly diagnosed is meningioma, which is 33.8% of all primary brain tumors (Wiemels, 2010). Some risk factors for meningioma are age, radiation, genetic and hormonal (Barnholtz-Sloan, 2007). Total resection of meningioma cases increases life expectancy and improves the prognosis of patients with these cases.

Corresponding author:* **Prawira Buntara Putra,
Department of Neurosurgery, Faculty of Medicine, Universitas Sumatera Utara, H. Adam Malik Hospital Medan, Indonesia.

But in high-grade meningiomas, the location is difficult to achieve or the size is too large, total resection is not possible so that another modality is needed to prevent and reduce the possibility of tumor recurrency. One modality that can be done is by administering drugs to block the expression of genes that effect tumor growth (Verma, 2007). Malignancy from meningiomas depends on the ability of tumor cells to pass through the histological barrier of the basement membrane, invasion of interstitial stroma to surrounding tissue, rapid cell proliferation, and release of growth factors from the tumor. Initial studies show enzymes such as cysteine protease, metalloproteinase (MMP) and serine protease are closely

related to growth and invasion of tumors (Tummalapalli, 2007). The Ki-67 antigens discovered by Scholzer and Geldes in 1980 were antigens found in each active cell cycle (G1, S, G2 and M) but were not found in resting cells (G0). The expression of the Ki-67 protein is associated with the proliferative activity of the intrinsic cell population in malignant tumors, thus allowing its use as a marker of tumor aggressiveness (Li, 2015).

MATERIALS AND METHODS

This study is a cross sectional analytic observational research study in patients diagnosed as meningiomas in Adam Malik Hospital in the periods of January 2017 - December 2018. Inclusion criteria includes confirmed cases of meningioma by pathological examination and the patient's age is over 17 years. Exclusion criteria are based on medical record data, found other systemic diseases such as chronic obstructive pulmonary disease, arthritis, atherosclerosis, tubulointestial kidney disease and suffering from other tumors on the body. The sampling technique used is total sampling with a total sample of 33 samples. This study was approved by the Health Research Ethics Commission of the Faculty of Medicine, University of North Sumatra / H. Adam Malik Hospital. All meningioma paraffin block specimens that had previously been treated with hematoxylin-eosin base staining and confirmed as a meningioma had MMP-9 and Ki-67 immunohistochemical staining. After staining, overexpression of MMP-9 and Ki-67 labeling index (LI) were calculated.

RESULTS

The data collection of research samples shows that the division of meningioma patient by gender is 23 women (69.7%) and 10 men (30.3%) (Table 1).

Table 1. Distribution based on gender

Gender	n	%
Male	10	30,3
Female	23	69,7
Total	33	100.0

Table 2. Distribution based on ages

Age	n	%
20 – 29	2	6,1
30 – 39	8	24,2
40 – 49	18	54,5
50 – 59	4	12,2
60 – 69	1	3,0
Total	33	100.0

Table 3. Distribution based on WHO Grading

WHO Grading	n	%
I	24	84,8
II	4	12,1
III	1	3,0
Total	33	100.0

In table 2, it was found that the highest incidence of meningioma is in the age group of 40 - 49 years and equal to 18 cases (54.5%). While the least frequency of occurrence was found in the age group 60-69 namely 1 case (3%). Classification of meningioma by WHO grade (table 3) shows that the highest frequency is grade I meningioma in 24 (84.8%) cases. Then followed by grade II as many as 4 cases (12.1%) and grade III as much as 1 case (3%). Based on table 4 below, an analysis of the relationship between SI staining of MMP-9 and LI Ki-67 is computerized with Chi square statistical tests with significance limits $p < 0.05$. Chi square analysis results obtains p value of 0.393. This shows that there is no significant relationship between MMP-9 overexpression with LI Ki-67. The cross tabulation table for analyzing the data is shown in the table below.

DISCUSSION

From the results of this study, it was found that meningiomas were found more in the female gender group at 69.7% compared to the male group at only 30.3%. This study obtained a comparison of the incidence of meningiomas around 2: 1 between the sexes of women and men. This is also the case with epidemiological studies that show that meningiomas are more common in the female sex group than men in a ratio of 2: 1. This study shows that there is a higher incidence of meningioma in women compared to men (Wiemels, 2010). In this study, the highest incidence of meningioma was found in the age group of 40-49 years, amounting to 18 people with a percentage of 54.5%. Based on other studies, the incidence of meningioma increases with age where the peak incidence is between the ages of 40-60 years (Al-Hadidy et al., 2007). In this study it was found that grade I meningioma based on WHO classification was the most common type of meningioma, which was 84.8% of the total sample studied, followed by grade II at 12.1% and grade III at 3%. In this study an analysis of the relationship between over expression of MMP-9 with LI Ki-67 is computerized with the Chi square statistical test with a significance limit of $p < 0.05$. The results of a computerized Chi square analysis obtained $p = 0.393$. This shows that there is no significant relationship between over expression of MMP-9 with LI Ki-67.

This is certainly not in accordance with the initial hypothesis proposed by the author. Sandberg's research revealed that high MMP-9 expression correlated with cell density, mitosis and necrosis in meningioma tumors.[7] This might be caused because the samples in this study do not have the same number of ratios between grades I, II, and III because the incidence of grade II and III meningiomas is very small. In addition, researchers were also unable to homogenize the study sample from other mitotic factors such as Insulin Growth Factor (IGF), Fibroblast Growth Factor (FGF), Vascular Endothelial Growth Factor (VEGF), Platelet Derified Growth Factor (PDGF) and estrogen receptors.

But the results of this study showed no difference with the results of previous studies. For this reason, it is recommended to conduct further studies by comparing the same amount in grade I, II, and III meningiomas and examining other variables such as IGF, FGF, VEGF, PDGF and estrogen receptors so as to get a more minimal bias and cofounding factors that are less. In addition, research can also be done to homogenize other disease factors that can cause overexpression of MMP-9 such as cancer metastases, rheumatoid arthritis, osteoarthritis, decubitus ulcers, gastric ulcer, corneal ulceration, periodontal disease, brain damage and neuroinflamation. Research that has been done only adheres to the medical record and does not further examine the disease in existing patient objects.

Table 4. *Crosstabulation* of MMP-9and Ki-67

		KI-67		Total	p*
		Positive (n%)	Negative (n%)		
MMP-9	Positive (n%)	8 (24,2)	8 (24,2)	16	0,393
	Negative (n%)	6 (18,1)	11 (33,3)	17	
Total		14	19	33	

REFERENCES

Al-Hadidy, A.M., Maani, W.S., Mahafza, W.S., Al-Najar, M.S., Al-Nadii, M.M. 2007. Intracranial Meningioma. *J Med J* 41 (1): 37-51.

Barnholtz-Sloan, J.S., Kruchko, C., 2007. Meningiomas: causes and risk factors. *Neurosurg Focus* 23 (4): E2.

Li, L. T., Jiang, G., Chen, Q., Zheng, J. N., 2015. Ki67 is a promising molecular target in the diagnosis of cancer (Review). Molecular Medicine Reports 11: 1566-1572.

Nordqvist, A.S., Peyrard, M., Pettersson, H., Mathiesen, T., Collins, P., Dumanski, J.P. et al., 1997. A high Ratio of Insulin-like Growth Factor II/Insulin-like Growth Factor Binding Protein 2 Messenger RNA as a Marker for Anaplasia in Meningiomas. *Cncer Res* 57: 2611-2614.

Tummalapalli, P., et. al. 2007. RNAi-mediated abrogation of cathepsin B and MMP-9 gene exoression in a malignant meningioma cell line leads to decreased tumor growth, invasion and angiogenesis. International Journal of Oncology 31: 1039-1050.

Verma, R.P. and Hansch, C. 2007. Matrix metalloproteinases (MMPs): chemical–biological functions and (Q) SARs. Bioorganic & medicinal chemistry, 15(6), pp.2223-2268.

Wiemels, J., Wrensch, M., Claus, E.B., 2010. Epidemiology and etiology of meningioma. *J Neurooncol* 99 (3): 307-314

****