International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.13, pp 369-373, 2017

Fibroblast Growth Factor 2 (Fgf-2) Serum Related Relationship With The Degree Of Intracranial Meningiomas Patients In Haji Adam Malik Hospital, North Sumatera

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Abstract : Intracranial meningiomas are benign brain tumors derived from brain wrapping tissue. The growth of intracranial meningioma is influenced by growth factor. Fibroblast Growth Factor (FGF) has urgent angiogenesis and mitogenesis activity on the growth and process of intracranial meningioma tumorigenesis. FGF-2 levels and its relation to the degree of meningioma's classification in Indonesia, especially in North Sumatera, have not yet been studied. This study used cross sectional analytic methods to measure serum FGF-2levels in patients with intracranial meningioma and analyze of serum FGF-2 levels with WHO histopathology degree. The study was conducted at Haji Adam Malik General Hospital/Faculty of Medicine, Universitas Sumatera Utara, Medan from April 2013 until April 2014. Value of correlation between FGF-2and histopathology was p=0,4 (p> 0,05). There was no significant association between FGF-2 levels and histopathologic forms of intracranial meningioma. The correlation between FGF-2 an0.05d WH was p= 0.07(p>0.05). There was no significant association between FGF-2 and WHO levels.
Keywords : Intracranial meningioma, *FGF-2.*

Introduction

Intracranial meningiomas are benign brain tumors derived from meningens. The most commonly diagnosed primary brain tumor is meningioma with 33.8% of all primary brain tumors[1,2]. Intracranial meningioma are also highly variable. Many are benign, but some are very aggressive. The cause of this primary brain tumor has not been understood clearly[3].

Risk factors for intracranial meningioma are age, radiation, genetic and hormonal. Incidence of intracranial meningioma increases with age with peak at the age of 70 to 80 years. This tumor is very rare in children[4].

In addition, the growth of intracranial meningioma is also influenced by growth factor. Growth factor is a group of proteins with an important role in cell growth and proliferation. Some growth factor compounds that affect the growth of intracranial meningioma are Platelet Derived Growth Factor, Epidermal Growth Factor, Vascular Endothelial Growth Factor, and Fibroblast Growth Factor[5].

Until recently, twenty types of FGF have been found, and are named FGF-1 to FGF-20. FGF-2 also known as pro-angiogenic molecule and has been proven capable of stimulating angiogenesis in vivo[6]. There has been no study that states how much FGF-2 serum levels in patients with meningioma intracranial. Nor have there been any studies that suggest blood levels of FGF-2 at any degree of intracranial meningioma. In Indonesia, particularly North Sumatra, studies suggest that FGF-2 levels in patients with intracranial meningiomas do not exist.

Experimentals

This study was conducted using Cross Sectional analytic study to measure serum FGF-2 levels in patients with intracranial meningioma, followed by an analysis of the association between serum FGF-2 levels and WHO histopathology degree.

The study was conducted at HajiAdam Malik Hospital / Faculty of Medicine, UniversitasSumatera Utara, Medan. Sampling was done in patient care room and processed by Department of Clinical Pathology H. Adam Malik Medan. The study was conducted from April 2013 to April 2014.All samples were taken from patients suffering from intracranial meningiomas who came to the H. Adam Malik General Hospital Medan.

Once the patient and / or his family approves the data collection and has signed the consent form after notification, the blood is drawn approximately 5 cc. After the blood sample is taken, the sample is immediately coded in sequence, and submitted to the Clinical Pathology installation to be processed into serum. The stored serum will be melted at room temperature for about 5 minutes and FGF assay will be checked. The examination is a quantitative examination using the sandwich technique Enzyme Linked Immunosorbent Assay (ELISA).

To test for a correlation between serum FGF-2 values and WHO histopathologic degrees, it was determined that statistically significant values were either normal or abnormal curves using Kolmogorof-Smirrnov or Shapiro-Wilk (depending on the number of samples). If the distribution was normal, analysis using Pearson method will be used and if it has abnormal distribution, the correlation is assessed with Spearman's correlation test. P value of 0.05 is considered a significant relationship.

Results

The samples were taken from April 2013 to April 2014. A sample of 52 specimens were obtained from patients with intracranial meningiomas who had undergone tumor removal surgery at RSUP. H. Adam Malik Medan. After data collection and frequency distribution analysis were obtained, female sex samples were higher than male samples, whereas female samples were 38 persons (73.1%) and men were 14 (26.9%).

Tabel 1. Frequency Distribution by Gender

Gender	**N**	**%**
Male	14	26,9
Female	38	73,1
Total	52	100,0

Distribution Based on Histopathology

Based on histopathologic results, the highest frequency was found in Meningothelial Meningioma type of 23 cases (44.2%), followed by Fibroblastic meningioma 14 cases (26.9%), and Transitional meningioma 6 cases (11.5%).

Tabel 2. Frequency Distribution Histopathologically

Histopathology	**N**	**%**
Meningothelial	25	48,1
Transitional	6	11,5
Fibroblastic	14	26,9
Angiomatous	3	5,8
Psammomatous	1	1,9
Atypical	2	3,8
Anaplastic	1	1,9
Total	52	100.0

Relationship between FGF-2 with Histopathology Intracranial Meningioma

After a review of the data obtained, the relationship between FGF-2 and histopatholgi variables will be searched. The analysis will be done by using Kruskal - Wallis test.

Tabel 3. FGF 2 DistributionHistopathologically

Histopathology	n	Mean	Median	SD	Min	Max	P
Meningothelial	1	183,5	63,8	348,0	11,2	1366,2	
Transitional	3	98,9	36,2	162,5	0,0	422,0	
Fibroblastic		88,1	56,9	92,4	0,0	259,0	0,4*
Angiomatous		53,8	27,3	47,3	25,6	108,5	
Atypical		112,5	112,5	0,7	112,0	113,0	
Anaplastic		-	-	-	-	-	

**Kruskall-Wallis test*

Based on the above table, the correlation value obtained on the relationship between FGF-2 and histopathology was p = 0.4 (p> 0.05). This shows that there is no significant relationship between FGF-2 levels and histopathologic forms of patients with intracranial meningioma. In the above table anaplastic meningioma has no value count because it only has 1 sample only.

Relationship Between FGF-2 With Degree of WHO Intracranial Meningioma

After a detailed description of the data obtained, we will look for the relationship between FGF-2 and WHO degrees of intracranial meningioma. The analysis will be done by using Kruskal - Wallis test.

Tabel 4. FGF-2 Distribution FGF-2 Based on WHO Degree

Histopathology	n	Mean	Median	SD	Min	Max	p
WHO Grade 1		129,3	54,2	252,1	0,0	1366,2	0,07
WHO Grade 2		112,5	112,5	0,7	112,0	113,0	
WHO Grade 3		-	-	-	-	-	

**Kruskall-Wallis test*

The correlation value obtained on the relationship between FGF-2 and WHO levels was p = 0.07 (p> 0.05). This shows that there is no significant relationship between FGF-2 levels and WHO degrees of intracranial meningioma.

Discussion

Intracranial meningiomas are benign brain tumors derived from brain wrapping tissue or meningens. The most commonly diagnosed primary brain tumor is meningioma of 33.8% of all primary brain tumors[7]. Intracranial meningioma is an extra-axial benign tumor that grows from arachnoid cap cells with slow growth[8]. Intracranial meningioma occupies 15% to 20% of all primary intracranial tumors. Incidence increases with age. More common in women with male: female ratio equal to 1: 2 ratio[9].

In this study 52 samples of patients with intracranial meningioma who went to Haji Adam Malik Medan were obtained. Of the 52 samples were 38 female samples and 14 male samples. When comparisons of both sexes are obtained the comparison is; male: female equal to 1: 2,7. In 2012 Landriel through his study described the same thing, the incidence of women: men = 2.5: 1[3].

Common locations of primary meningiomas in the most frequent sequence are convexity, parasagital, sphenoid wing, cavernous, tubercullumsellae, lamina cribrosa, foramen magnum, torcular zone, tentorium cerebelli, serebelopontin angle, and sigmoid sinus[10,11].

The publications by Yi Wei suggest that FGF-2 levels are increasing as the degree of WHO classification increases. This is due to FGF-2 is a potential angiogenic growth factor that stimulates the

stimulation of endothelial cell proliferation of blood vessels and is involved in the angiogenesis of neoplasms of several tumors including meningioma[12].

The correlation value obtained on the relationship between FGF-2 and meningioma based on WHO classification was p = 0.07 (p> 0.05). This suggests that there is no relationship between FGF-2 levels and the degree of meningioma based on the WHO classification.

Based on statistics there is no relationship between FGF-2 and WHO classification. However, if we look at the median value at every degree of WHO classification, we will find different values of FGF-2 and tend to increase. At the 1st grade of WHO classification was found FGF-2 <100pg / ml, on grade 2 FGF-2> 100pg / ml, andFGF-2> 1000 pg / ml on grade 3. The absence of a meaningful relationship may be due to unheard of data normally.

The limitation of this study is the inhomogeneous of the used data and was not normally distributed. In addition, the comparison of the number of samples in each group in this study is not the same.

Conclusion

Based on the location of meningioma, the highest frequency was convexity meningioma (17 patients, 32.7%). Based on histopathology results, the highest frequency was found in Meningothelial meningioma type of 25 cases (48.1%). There was no association between FGF-2 levels and the degree of meningioma based on the WHO classification, p = 0.07 (p> 0.05).

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