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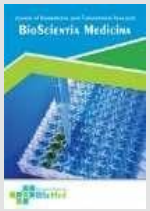

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Expression of Estrogen Receptor and Progesterone Receptor in Meningioma Patients

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A B S T R A C T

Background: Meningioma is a primary intracranial benign tumor that is affected by the balance of the estrogen and progesterone hormones. This study aimed to assess the relationship between estrogen receptor (ER) expression and progesterone receptor (PR) expression in meningioma conditions. **Methods:** Analytical observational research with a cross-sectional study design. The number of samples is 25 meningioma patients who performed ER and PR examinations. The research was performed at Dr. Kariadi General Hospital Semarang. Statistical test using Spearman test. **Results:** Relationship of ER and PR to degree of meningioma is p = 0.181 (r = -0,276) and p = 0,056 (-0,387). **Conclusion:** There is no correlation between estrogen receptor (ER) and progesterone (PR) receptor to the degree of meningioma

1. Introduction

Meningiomas are the most common primary intracranial benign tumors found in health facilities. These tumors originate from the pia mater and arachnoid tissue covering the brain.[1] There are about 25% of intracranial tumors in America diagnosed as meningiomas.[2] Meningiomas are asymptomatic, located intracranially, so they can be life-threatening.[3–5]

The prevalence of meningiomas is estimated at 97.5 in 100,000 people, and about 138,000 Americans are diagnosed with meningiomas.2 Data from the Central Brain Tumor Registry of the United States that the Age-Adjusted Incidence Rate (per 100,000 people) is 6.59 per 100,000 per year, with the incidence in women 2 times higher than in men. The results of the analysis from the National Cancer Data Base reported 2-5 years survival rates of meningioma patients between 81% and 69%.[3] According to the journal Epidemiology of Intracranial Meningiomas, there was no significant difference in incidence in Caucasian, African, American, and Hispanic races.[2]

Meningiomas are more common in adults and old age. Meningiomas are also associated with Body Mass

Index (BMI). This is associated with high activity of estrogen, progesterone, androgen, and insulin-like growth factor.[4] The risk of meningioma increases in women who have a history of giving birth more than 3 times and also in women who have not reached the age of menopause. This situation is probably due to increased levels of progesterone and estrogen, so it can be concluded that the incidence of meningiomas is influenced by steroid hormones. Previous studies have explained that the incidence of meningiomas is associated with exposure to hormones, namely estrogen and progesterone hormones. This study aimed to assess the relationship between estrogen receptor (ER) expression and progesterone receptor (PR) expression in meningioma conditions.

2. Methods

This study is an observational study that has been approved by the medical research and ethics committee of Dr. Kariadi General Hospital Semarang. The subjects of this study were meningioma patients who had been diagnosed clinically and histopathologically and had been treated at Dr. Kariadi Semarang period January 2017 – completed. A consecutive sampling method was used in the study. All subjects who met the inclusion and exclusion criteria were included in the study until the number of samples was met. A total of 24 patients diagnosed with clinical and histopathological meningioma were included in the study sample.

Patients who have given consent to be sampled in the study must meet several inclusion criteria: (1) Patients diagnosed with meningioma based on clinical signs in the form of signs of intracranial enhancement, head CT scan with contrast showing homogeneous contrast enhancement images, and histopathological examination. The exclusion criteria were; (1) There are diseases associated with significant levels of reproductive hormones (Klinefelter syndrome, Turner syndrome, CAH, testicular agenesis); (2) The block preparations are damaged, have run out, and cannot be stained with immunohistochemistry; (3) The patient dies.

Data collection for ER and PR immunohistochemical examination was carried out at the Anatomical Pathology Laboratory, Faculty of Medicine, Universitas Diponegoro/Dr. Kariadi General Hospital was observed by two observers blindly. The data obtained from observer 1 and observer 2 were not much different (consistent). The collection of data on the examination of meningioma patients was carried out at the polyclinic, neurosurgery ward, Dr. Kariadi General Hospital, and home visits in the Semarang area.

Analysis of the data using SPSS Windows version 17. Before testing the hypothesis, the collected data was first carried out by editing, coding, entry, and cleaning data processes. Then statistical test analysis was carried out based on the type of data used, namely a numerical scale. The Spearman test was performed to see the relationship between ER and PR variables and the meningioma degree.

3. Results

In this study, there was a total sample of 25 patients, with 24 female samples and 1 male sample with the highest frequency in the age range of 41 years - 50 years. From the histopathological examination of meningioma, 64% were diagnosed with grade I meningioma, and no grade III meningioma was found in the sample. Examination of the estrogen receptor (ER) partially contained 22 patients with negative results, and there were no samples with strong ER (+) results. As for the progesterone receptor (PR) examination, there were 19 samples with a strong (+) PR and 2 samples with a PR (-) result.

Table 1. Characteristics of patients

Characteristics	F	%
Gender		
Male	1	8
Female	24	92
Total	25	100
Age (years)		
20 – 30	1	4
31 – 40	8	32
41 – 50	14	56
51 – 60	2	8
Total	25	100
Meningioma grading		
Meningioma grade 1	16	64
Meningioma grade 2	9	36
Meningioma grade 3	0	0
Total	25	25
Estrogen receptor (ER) intensity		
Negative	22	88
Mild positive	2	8
Moderate positive	1	4
Strong positive	0	0
Total	25	100
Progesterone receptor (PR) intensity		
Negative	2	8
Mild positive	0	0
Moderate positive	4	16
Strong positive	19	76
Total	25	100

Table 2. Characteristics of ER, PR, and the degree of meningioma

Meningioma Grading	ER				PR			
	Negative	Mild	Moderate	Strong	Negative	Mild	Moderate	Strong
I	13	0	1	0	0	0	2	14
II	9	2	0	0	2	0	2	5
III	0	0	0	0	0	0	0	0
Total	25				25			

Table 3. Relationship of ER and PR with the degree of meningioma

Variable	Meningioma		Description
	P value	r	
ER	0,181	-0,276	No significance
PR	0,056	-0,387	No significance

The results above show insignificant results to assess the relationship between estrogen receptor (ER) expression and progesterone receptor (PR) expression with the degree of meningioma (p-value <0.05).

4. Discussion

The prevalence of meningiomas is mostly experienced by women with an age range of 40 years to 50 years. In previous research conducted at H. Adam Malik General Hospital, it turns out that 60% of meningioma patients are female, and 30% are male.6 Research on 24 meningioma patients who had surgery at Naraya Medical College, India, between 2013 and 2016, found 20 cases with female gender and 4 cases with the male gender. Anaplastic is mostly experienced by men.[4-7] The prevalence of meningioma has increased from the age of 40 years to 49 years. Previous research explained that patients diagnosed

with meningioma were mostly women aged 40 to 50 years.[8,9]

According to the existing theory, there are 3 grades of meningiomas, namely grade I meningiomas, grade II meningiomas, and grade III meningiomas. Previous research stated that in 30 meningioma patients, there are 27 patients with grade I (benign) Ioma.[10] Previous studies showed that of the 78 patients studied. There were 63 patients suffering from grade I (benign) meningioma, 10 patients suffering from grade II meningioma (Atypical), and 5 patients suffering from grade III (anaplastic) meningioma. Another study showed that 90% of patients were diagnosed with benign meningioma, 0.9% with atypical meningioma, and 10.6% with anaplastic type.[11] This indicates that most cases are grade I (benign) meningioma.

The progression and proliferation of meningioma types can be identified by examination of the estrogen receptor (ER) and progesterone receptor (PR). Tumor cells with ER (+) have a high mitotic index, high recurrence rate, and poor prognosis. The results of PR (+) are weak, and ER (+) is strong in meningiomas that tend to be necrotic and have high mitotic power.[9] ER (-) or low ER levels in meningiomas patients mostly have high chromosome 14 and chromosome 22, respectively. De novo tumors tend to have aggressive characteristics of tumor cell mitosis and tend to have a high recurrence rate.[10]

On the other hand, the results of the meningioma examination with PR (+) tend to have a good prognosis. Naima et al. showed that the PR (+) positive progesterone receptor was found significantly in grade I (benign) meningiomas. Meningiomas with PR (+) tend to recur very little. This is associated with lower mitotic activity in tumor cells with PR (+). The progesterone receptor (PR) has 2 lysosomes, namely PR-B and PR-A, which have different biological functions and have their own DNA and ligand-binding. PR-A has a function as a negative transrepressor, while PR-B is a strong trans-activator. In most meningiomas, PR-A levels are more dominant than PR-B, resulting in different tumor cell characteristics. With PR-A being more dominant, the rate of mitosis and tumor aggressiveness decreases.[11,12] Tumor cells with PR(+) have a better prognosis than tumor cells with PR(-).[13,14] Results of PR(+) increase cell sensitivity. meningiomas to undergo mitosis. There are other studies that state that there is no significant relationship between PR status and the type of meningioma. Detection of PR (+), in most cases of meningiomas, provides an opportunity for the administration of anti-progesterone drugs. Mifepristone, an antiprogesterone agent that is useful in the treatment of breast cancer, may be given in cases of meningioma.[15-18]

5. Conclusion

There is no correlation between estrogen receptor (ER) and progesterone receptor (PR) to the degree of meningioma.

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