EEG changes in patients with intracranial tumors and seizures symptom at Mohammad Hoesin Hospital Palembang

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Abstract. This study was conducted to determine the EEG changes in intracranial tumor patients with symptoms of seizures and the correspondence between the location of tumor by the location of the EEG abnormality. This is a cross-sectional descriptive study using primary and secondary data. Samples were collected consecutively over a period of 1 year. Of the 35 samples, abnormal EEG in patients with primary intracranial tumors obtained 68.2%, whereas in metastatic intracranial tumors obtained in 84.6%. From the abnormal EEG, in primary intracranial tumors description focal slowing in 60.0%, epileptic activity 20.0%, accompanied focal epileptic activity and focal slowing in 13.3%. Whereas in patients with intracranial tumor metastasis overview the form of a focal slowing in 36.4%, epileptic activity in 18.2%, and deceleration focal epileptiform activity accompanied by 45.5%. Presence of the EEG abnormality locations in tumor area 23.1%, non-tumor area by 38.5%, tumor and non-tumor area area by 38.5%. In this study, most patients have an abnormal EEG which more common in the form of a focal slowing compared epileptic activity, and some abnormalities are located in non-tumor areas. This indicates that the seizures that occur may be more due to irritation lesions than for the formation of epileptic focus.

1. Introduction
Intracranial tumors are one type of tumor that has a moderately high incidence of 18.71% per year. Based on statistical reports from the United States Central Brain Tumor Registry (CBTRUS), more than 200,000 people in the United States are diagnosed with primary or metastatic brain tumor each year [1]. In patients with intracranial tumors, one of the common symptoms are seizures, approximately 20-40% of patients with intracranial tumors develop seizures. The most common types of seizures occur secondarily generalized seizures by 51%, and simple partial seizures by 27% [2]. One of the investigations that are non-invasive with relatively low cost that can be used in cases of seizures with intracranial tumor is electroencephalography (EEG) [3]. Based on the results of a study, in 117 patients with intracranial tumors, there were 92 patients with abnormal EEG. Although in line with technological advances there is a CT-scan and MRI of the head, but the EEG is still often used to supplement the examination and evaluation of the functional condition of the patient [4]. This study was conducted to determine EEG in patients with intracranial tumors with symptoms of seizures in RSUP DR Mohammad Hoesin Palembang.
2. Methods
This study is a descriptive cross section using primary and secondary data.

3. Results
In the span of March 1, 2017 to March 31, 2018. There were 55 patients with tumor intracranial EEG recording done at RSUP Dr Mohamad Hoesin Palembang, of the 55 patients there were 35 samples that met the inclusion criteria and did not meet the criteria for exclusion. In this study, the average age of patients in both groups: primary intracranial tumors and metastatic intracranial tumors almost the same, namely 45.8 years in the group of primary intracranial tumors and 46.3 years in the group of intracranial tumor metastasis.

In the variable gender, the prevalence of women as much as 9 (40.09%), and men were 13 (59.09%) in primary intracranial tumors, whereas in the group of metastatic intracranial tumors the prevalence of women as much as 4 (37.2%) and men as much as 9 (69.23%).

Based on the main complaint, seizures are the most common primary complaints or symptoms in the group of primary intracranial tumors were 12 (54.5%), followed by headache 4 (18.2%), blurred vision 3 (13.6%), the weakness on one side of the body 2 (9.1%) and loss of consciousness as much as 1 (4.5%). Whereas in the group of metastatic intracranial tumors or headache are the main symptoms of the most common complaints that cause the patient came to the hospital, as many as seven (53.8%), followed by convulsions 4 (30.8%) and loss of consciousness as much as 2 patients (15.4%).

Table 1. Characteristics of patients by type of intracranial tumors.

| Characteristics                  | Primary (N = 22) | Metastasis (N = 13) |
|----------------------------------|-----------------|---------------------|
| Age (years)                      |                 |                     |
| Average                          | 45.8            | 46.3                |
| SD                               | 15.23           | 9.52                |
| 18-45                            | 8               | 6                   |
| 46-60                            | 13              | 6                   |
| > 60                             | 1               | 0                   |
| Gender                           |                 |                     |
| Man                              | 13 (15.09%)     | 9 (40.9%)           |
| Woman                            | 9 (69.23%)      | 4 (3.2%)            |
| Main complaint                   |                 |                     |
| convulsions                      | 12 (54.5%)      | 4 (30.8%)           |
| headache                         | 4 (18.2%)       | 7 (53.8%)           |
| The weakness on the one side of the body | 2 (9.1%)   | 0 (0.0%)           |
| Blurred vision                   | 3 (13.6%)       | 0 (0.0%)            |
| Loss of consciousness            | 1 (4.5%)        | 2 (15.4%)           |

Based on the type of seizures, the primary intracranial tumor was found that generation became secondarily generalized partial seizures become the most common type, ie as many as 10 patients (45.5%), whereas in the group of intracranial tumors metastases obtained generalized tonic clonic seizure is the most common type of as many as 10 patients (76.9%).

Based on the EEG, in patients with primary intracranial tumors most patients had abnormal EEG as many as 15 (68.2%), where the primary intracranial tumors, it was shown in the form of focal slowing as much as 9 (60.0%). No different from the results obtained in the group of intracranial tumor metastases wherein abnormal EEG was found in 11 patients (84.6%) where the tumor metastasis mostly in the form of a slowdown abnormal picture focal epileptiform activity with as many as five patients (45.5%). In primary intracranial tumors, the overall obtained epileptiform activity in the form of a sharp surge in 5 patients (100%), whereas in 7 patients with intracranial tumor metastases, showed more varied that there are 5 (71%).
Based on the appearance of abnormalities location, description focal slowing in the tumor area was found in 5 (11.5%) patients, non-tumor areas obtained in 3 (11.5%) patients, tumor and non-tumor areas in the area of 5 (19.2%). Overview epileptiform activity in the tumor area was found in 1 (3.8%) patients, non-tumor areas in 3 (11.5%), tumor and non-tumor areas in the area 1 (3.8%). While the slowdown picture obtained with epileptiform activity on non-tumor areas 3 (11.5%), in the area of tumor and non-tumor area 4 (15.4%), and the tumor area was not obtained 0 (0.0%), slowing background obtained in 1 (3.8%) patients in the non-tumor area.

Table 2. Type of epileptic seizures by type of intracranial tumors.

| Type of seizure | Type of tumor | Total |
|-----------------|---------------|-------|
| simple partial  | Primary       | 4 (18.2%) |
| complex partial | Primary       | 6 (27.3%) |
|                | Metastasis    | 0 (0.0%)  |
| Become partial  | Primary       | 10 (45.5%) |
| generalized     | Primary       | 1 (4.5%)  |
| tonic           | Primary       | 1 (4.5%)  |
|                 | Metastasis    | 2 (15.4%) |
| Slowing         | Primary       | 1 (4.5%)  |
| activity        | Metastasis    | 0 (0.0%)  |
| Slowing         | Primary       | 10 (76.9%) |
| accompanied     | Metastasis    | 10 (76.9%) |
| focal           |               | 13 (100%) |
| epileptiform     |               | 13 (100%) |

Table 3. EEG based on the type of intracranial tumors

| Type of tumor | EEG | Total |
|---------------|-----|-------|
|               | Normal | Abnormal | 22 (100%) |
| Primary       | 7 (31.8%) | 15 (68.2%) |
| Metastasis    | 2 (15.4%) | 11 (84.6%) |

Table 4. Description of abnormal EEG based on the type of intracranial tumors

| Abnormal EEG | Type of tumor | Total |
|--------------|---------------|-------|
| Slowing focal epileptiform activity | Primary | 9 (60.0%) |
| Slowing accompanying focal epileptiform activity | Metastasis | 4 (36.4%) |
| Slowing background | Primary | 3 (20.0%) |
|                 | Metastasis | 2 (18.2%) |
|                 |               | 2 (13.3%) |
|                 |                 | 5 (45.5%) |
|                 |                 | 0 (0.0%)  |
|                 |                 | 11 (100%) |

Table 5. Types of epileptiform activity by type of intracranial tumors

| Type of epileptiform activity | This type of tumor | Total |
|------------------------------|--------------------|-------|
| Wave spikes                  | Primary            | 0 (0.0%) |
| Sharp waves                  | Metastasis         | 2 (28.5%) |

4. Discussions

Characteristic variables obtained at a mean age in the group of metastatic tumors was slightly higher than the group of primary intracranial tumors. And the primary intracranial tumor, the age range is 46-60 years of age who suffered most intracranial tumors, intracranial tumor metastasis while the age range of 18-60 years had the same incidence. In line with the results of a study published by Cancer Research UK in 2018 explained that in theory it reflects the accumulation of DNA damage increased. The cause of DNA damage can be derived from biological processes or exposure to risk factors.
While at an older age, tumor incidence decreased, likely due to the health condition of the patient is generally decreasing so the diagnosis or suspicion towards tumors also decreased [5].

**Table 6. Overview Abnormal EEG Based on Location Emergence Abnormality**

|                     | Focal Slowing | Epileptiform activity | Slowing accompanied focal epileptiform activity | Slowing background | Total |
|---------------------|---------------|------------------------|-------------------------------------------------|--------------------|-------|
| Tumor area          | 5 (19.2%)     | 1 (3.8%)               | 0 (0.0%)                                        | 0 (0.0%)           | 6 (23.1%) |
| Non-tumor area      | 3 (11.5%)     | 3 (11.5%)              | 3 (11.5%)                                       | 1 (3.8%)           | 10 (38.5%) |
| Tumor and non-tumor area area | 5 (19.2%) | 1 (3.8%)               | 4 (15.4%)                                       | 0 (0.0%)           | 10 (38.5%) |
| Total               | 13 (49.9%)    | 5 (19.1%)              | 7 (26.9%)                                       | 1 (3.8%)           | 26 (100%) |

In the gender variable obtained men with intracranial tumors found more than women. Based on research published in the journal Cellular and MolecularLife Science in 2015, men also have a poorer response to therapy, so the overall figure is also lower survival [6]. The British study concluded that the prevalence of intracranial malignant tumor in men is higher than women, but the benign intracranial tumor prevalence in women is higher than men, it is unclear why this is so [7].

Symptoms seizures are common symptom that most frequently appear in patients with primary intracranial tumors, the ability of tumors to induce excitability of neuronal affected by the type and degree of growth, the tumors are low grade and slow growing, the incidence of seizures is quite high because the pathophysiology, tumors of the many lead changes both in morphology biochemistry, neurotransmitters and ph in the surrounding area, causing functional changes in neurons. Unlike the primary intracranial tumor, headaches are more often as the main symptom of the metastatic intracranial tumors. Based on the growth, metastasis tumor infiltrating brain parenchyma was not extensive as the primary tumor, so the ability to biochemically to produce neuronal excitability are also more rare [8].

Of variable type of seizure, it is in line with research conducted by Kerkhof.m et al in 2013, which states that focal seizures with or without disturbances of consciousness and seizures secondarily generalized focal become the most frequent symptom. Focal seizures with impaired consciousness was found in 50% -70% of patients with tumors of neuroglial, whereas the focal seizures secondarily generalized obtained more that 70% in patients with low-grade gliomas [9].

Explanation of abnormal EEG in patients with intracranial tumors either primary or metastatic intracranial tumors, based on the theory that the newly developing tumors or early stage tumor where there has been no disruption or change of the structure of nerve cells metabolism then the EEG can be normal. In tumor that is located in and away from the cortex can also provide images normally, because the recording is done on the scalp is more sensitive in recording the electrical activity in the cerebral cortex, it looks at the results of this study that most of the picture abnormal EEG occurs in tumors located supratentorial, and there is only one infratentorial tumor patients who have abnormal EEG [10].

For an overview abnormality EEG, on the theory that the tumor itself is a structure that electrically 'silent', the changes recorded in the EEG is the result of the electrical activity of the brain are affected, the disorder can be caused by direct pressure due to the development of tumors or disruption to the flow of CSF. Meanwhile, changes in the electrical activity of the brain which is then recorded on the EEG varies, can be either focal or general slowing and epileptic activity or a combination of both that emerged in response to the disruption of normal brain function [10].

Based on the location of the emergence of an idea abnormal EEG, mostly abnormalities arise in the area of the tumor and a few undergoing expansion in the area of non-tumor, but there are some patients where the abnormality EEG arrives in the non tumor, in the pathophysiology of this is
possible because the mechanism that causes the wave abnormal and epileptiform activity is multifactorial. In addition, the literature also mentions some of the hypotheses related to the biochemical, microstructural and electrical activity outside the area of tumor that causes epileptogenesis. The evidence available today indicates that a slow growing tumor can affect the electrical connectivity in areas outside of the tumor, mengkibatkan malfunctioning of neurons and increases the risk of seizures. Instead of high-grade tumor will induce seizures through damage of brain tissue (ischemia, edema, mass effect and necrosis). This indicates that the seizures or EEG abnormalities appear not merely because of the tumor itself, but changes in the physiology of neurons in an area outside of the tumor can also cause the occurrence of abnormalities on EEG recording [11].

5. Conclusion
In this study, most patients had abnormal EEG in the form of focal slowing, epileptiform activity or a combination of both. Abnormal picture appearing partly on the tumor area, but some appear on non-tumor areas, these findings indicate that in addition to the tumor itself, beyond the many other factors that can induce tumor epileptogenesis, which in turn increases the risk of seizures.

6. References
[1] Maschio M. Brain Tumor-Related Epilepsy. Current Neuropharmacology. 2012;10(2):124-133.
[2] Sharanreddy M, Kulkarni PK. Can EEG Tests Help in Identifying Brain Tumor?. World Academy of Science, Engineering and Technology International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering.2013;7(11):703-708.
[3] You G, Zhiyi S,Tao J. The Pathogenesis of Tumor-Related Epilepsy and Its Implications for Clinical Treatment. British Epilepsy Association.2012;21:153-159.
[4] Small JG, Bagchi BK, Kooi KA. Electro-clinical Profile of 117 Deep Cerebral Tumors. Electroencephalography and Clinical Neurophysiology.1961;13(2):193-207.
[5] Brain, other CNS and intracranial tumours statistics ... [Internet]. [cited 2018Aug20]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/brain-other-cns-and-intracranial-tumours
[6] Sun T, Plutynski A, Ward S, Rubin JB. An integrative view on sex differences in brain tumors. Cellular and Molecular Life Sciences. 2015;72(17):3323–42.
[7] Mckinney PA. Brain tumours: incidence, survival, and aetiology. Journal of Neurology, Neurosurgery & Psychiatry. 2004Jan;75(suppl_2):ii12–ii17.
[8] Brain Neoplasms: Practice Essentials, Background, Pathophysiology [Internet]. Background, Pathophysiology, Etiology. 2018 [cited 2018June20]. Available from: https://emedicine.medscape.com/article/779664-overview
[9] Kerkhof M, Vecht CJ. Seizure characteristics and prognostic factors of gliomas. Epilepsia. 2013;54:12–7.
[10] Bagchi B, Lam R, Kooi K, Bassett R. EEG findings in posterior fossa tumors. Electroencephalography and Clinical Neurophysiology. 1952;4(1):23–40.
[11] Giulioni M. Epilepsy associated tumors: Review article. World Journal of Clinical Cases. 2014;2(11):623.

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