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A Case Report : Modality Treatment With Mineralcorticoid And Radikal Reseksi To Total Reseksi In Pediatric Brain Tumor

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ABSTRACT

Brain tumor are the second most common neoplasm and the most common solid tumor in children. Fifty percent to 60% of childhood brain tumors originate in the posterior fossa. These include medulloblastomas, cerebellar astrocytomas, and fourth ventricle ependymomas. The remaining 40% to 50% of childhood brain tumors are supratentorial and include astrocytoma, hypothalamic and optic pathway tumors, and craniopharyngiomas. A 19 year old child came to the hospital emergency room with complaints of dizziness. Dizziness is accompanied by headaches that dissapearing. Complaints have been felt since about half a year but have worsened for one week before at emergency room. While being treated at the hospital, the patient experienced a seizure once, when the seizure was felt for 2 minutes, it was a whole body type of seizure. Patients also experience nausea and decreased appetite. Consciousness is still fully conscious. In this case, patien can be treatment IVFD Ringer Lactate 135 cc/hour, Metamizole 250 mg/1 ml /8 hour IV, Diphenhidramin 5 mg /12 hour IV, Dexamethasone 5 mg /8 hour IV, Piracetam 500 mg/12 hour IV. In this case, Dexamethasone therapy is given which is the corticosteroid of choice in these patients because of its low mineralocorticoid activity and only reduces the symptoms caused optimally. The goal is to reduce neurological symptoms but with a dose that is lowered slowly. The main treatment is still tumor resection with neurosurgeon.

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INTRODUCTION

Brain tumor are the second most common neoplasm and the most common solid tumor in children. Recent advances in diagnostic capabilities, surgical instrumentation allowing for aggressive surgical intervention, and modifications in radiation and chemotherapy have increased the long-term survival rates for many of these children (Ostrom et al., 2019).

Fifty percent to sixty percent of childhood brain tumors originate in the posterior fossa. These include medulloblastomas, cerebellar astrocytomas, and fourth ventricle ependymomas. The remaining forty to fifty of childhood brain tumors are supratentorial and include astrocytoma, hypothalamic and optic pathway tumors, and craniopharyngiomas (Zhao et al., 2014).

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Alterations in chromosome 17 have been associated with medulloblastoma and astrocytoma and loss on chromosome 10 has been associated with glioblastoma. Common pediatric brain tumors, symptoms at diagnosis, and treatment are outlined (Zhao et al., 2014). Unlike adult gliomas, several pediatric low-grade gliomas are genetically transmissible (Johnson et al., 2014). An example is the predisposition of patients with the neurocutaneous syndrome neurofibromatosis type-1 (NF1) to develop low-grade gliomas, particularly pilocytic astrocytomas of the optic or hypothalamic pathways (Albright, 1993; Robertson, 1998; Udaka & Packer, 2018). The occurrence of pilocytic astrocytomas in patients with NF1. The NF1 gene encodes the tumor suppressor protein, neurofibromin that acts through its GTP-ase activating domain to downregulate the MAPK cascade causing growth arrest of astrocytic cells (Liu et al., 2021).

Tuberous sclerosis complex, due to germline mutations in TSC1 and TSC2, is associated with subependymal giant cell astrocytomas (SEGAs) in 5-15% of cases (Lombardi et al., 2015). SEGAs are intraventricular circumscribed astrocytic gliomas located near the foramina of Monro (Lombardi et al., 2015). They are driven by dysregulation of the serine or threonine kinase, which has a role in cell growth and metabolism (Lukas et al., 2019). Symptomatic tumors can be resected (Mallick, Benson, Hakim, & Rath, 2016). Targeted therapy with the mTOR inhibitors everolimus or sirolimus (Rapamycin), macrocyclic lactones, have been effective in treating SEGAs, though they have side effects including immunosuppressive activity (Mondal, Kumari Singh, Panda, & Shiras, 2017).

CASE ILLUSTRATION

A 9 year old child came to the hospital emergency room with complaints of dizziness. Dizziness is accompanied by headaches that dissapearing. Complaints have been felt since about half a year but have worsened for one week before at emergency room. While being treated at the hospital, the patient experienced a seizure once, when the seizure was felt for 2 minutes, it was a whole body type of seizure. Patients also experience nausea and decreased appetite. Consciousness is still fully conscious.

Examination of vital sign obtained are blood pressure 118/82 mmHg, heart rate 70x/i, respiratori rate 20x/l, and temperature 36,50C. Patien can be treatment IVFD Ringer Lactate 135 cc/hour, Metamizole 250 mg/1 ml /8 hour IV, Diphenhidramin 5 mg /12 hour IV, Dexamethasone 5 mg /8 hour IV, Piracetam 500 mg/12 hour IV.

Table 1. Laboratorium Examination Results

HEMATOLOGI		
Lekosit	12,7	3,6-11 (10^3/uL)
Eritrosit	5,68	3,80-5,20 (10^6/uL)
Hemoglobin	15,1	11,7-15,5 (g/dL)
Hematokrit	46,6	35-47 (%)
INDEX ERITROSIT		
MCV	82	80-100 (fL)
MCH	26,6	26-34 (pg)

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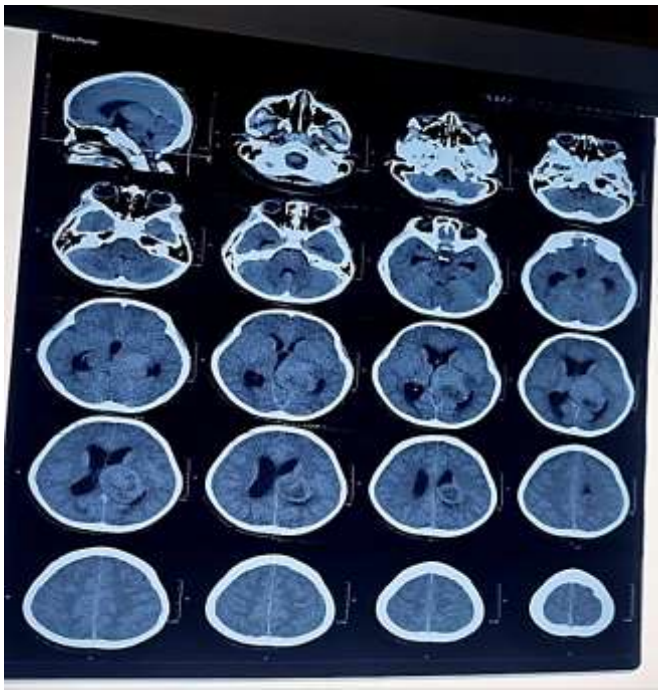
HEMATOLOGI		
MCHC	32,4	32-37 (g/dL)
Trombosit	357	150-450 (10^3/uL)
RDW-CV	13,2	11,5-14,5 (%)
PDW	9,9	fL
MPV	9,4	fL
P-LCR	19,9	%
PCT	0,34	%
Diff Count		
NRBC	0,00	
Neutrofil	73,6	0-1 %
Limfosit	19,2	53-75 %
Monosit	6,10	25-40 %
Eosinofil	0,50	2-8 %
Basofil	0,60	2,00-4,00 %
IG	0,40	0-1 %
Rasio N/L	3,8	<3,13 %
KIMIA KLINIK		
Ureum	34,6	0-31 mg/dL
Creatinin	0,66	0,50-0,90 mg/dL

Result Head CT Scan Examination



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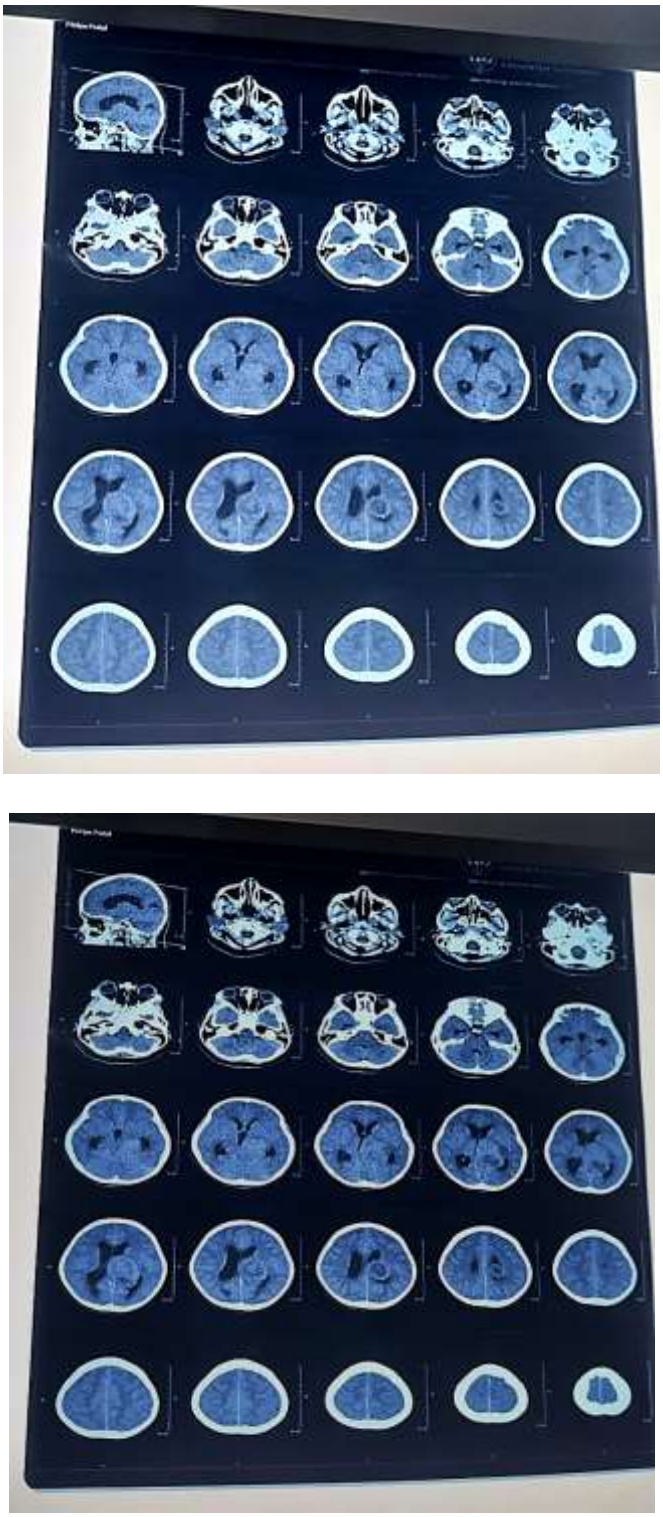

Figure 1. Head CT Scan

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The Expertise

The sulci and silvian fissure are narrow, the white matter and gray matter base is firm, a solid, round mass appears with a few cystic areas in the subependymal area around the left thalamus, the boundaries of the thalamus and the mass cannot be separated on non-contrast CT, the size of the mass is 5.4x4.6x4, 7 cm density 22-36 HU, no calcification, with perifocal edema in the left internal capsule. The CPA and sella tursica did not appear abnormal, the SPN and air cellulae mastoidea appeared normodense. The impression is of a rounded solid mass with a few cystic areas, in the subependymal area around the left thalamus at the border of the thalamus and the mass cannot be separated on non-contrast CT. Mass size lk 5.4x4.6x4.7 cm, density 22-36 HU, no calcification, with perifocal edema in left internal capsule differential diagnosis of left thalamic glioma and choroid plexus papilloma. The mass causes midline deviation to the laterodextra as far as 12 mm and mild left transtorial downward herniation, the mass narrows the posterior left lateral ventricle and the posterior left lateral ventricle and third ventricle, and begins to show dilatation of the right lateral ventricle with transependymal edema of the posterior right (starting to show signs ICT improvements).

RESULTS AND DISCUSSION

The diagnosis of a brain tumor is often difficult to establish. The presenting symptoms of a childhood brain tumor may be vague or similar to the symptoms of many common childhood illnesses (Mrugala, 2013). Signs and symptoms vary depending on the location and growth rate of the tumor and the age and development of the child (Omuro, 2013). Tumors with short history usually days to several weeks and acute onset of symptoms tend to be more aggressive or malignant, those with a long, vague history of symptoms are often slower growing or benign (Opoku-Darko, Amuah, & Kelly, 2018). Commonly associated with an increase in intracranial pressure (Ozdemir-Kaynak, Qutub, & Yesil-Celiktas, 2018). This may be because of pressure caused by the tumor mass itself or by the tumor obstructing the normal flow of CSF (Posti et al., 2015). Ataxia, nystagmus, and other symptoms of cerebellar dysfunction are other common symptoms of posterior fossa tumors. Cranial nerve deficits and hemiparesis are usually associated with brain stem involvement (Sasmita, Wong, & Ling, 2018).

Supratentorial tumors are commonly associated with a hemiparesis, hemisensory loss, seizures, visual field changes, and intellectual prob lems. Midline tumors, such as those in the hypothalamic or pituitary region, are associated with visual changes, endocrinopathies and increased intracranial pressure secondary to hydrocephalus (Seidlitz et al., 2015).

The intracranial pressure inside the skull is dependent on the volumes and pressures exerted by three components are blood, brain, and CSF (Silantyev et al., 2019). After the sutures have fused, the skull forms a solid container with a fiied volume capacity (Stoyanov et al., 2018). An increase in intracranial volume may be compensated for with a shifting of the intracranial contents to accommodate the increase in volume. Large increases in intracranial components, such as tumor growth, results in the child becoming symptomatic. Tumor growth can block the normal flow of CSF with hydrocephalus resulting. There is a

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compensatory mechanism within the brain that handles small increases in intracranial volume by shifting the intracranial contents, usually by reduction in blood or CSF volume. When that fails, brain parenchyma is then compressed by the expanding tumor (Tan et al., 2020).

The most common symptoms of increased intracranial pressure include headache, nausea, vomiting, ataxia, decline in academic functioning, and blurred or double vision. These symptoms, if not treated, progress into a decline in level of consciousness and, ultimately, coma (Thakkar et al., 2014). Changes in vital signs are a late sign of increased intracranial pressure and include a decrease in pulse with an increase in blood pressure and a widening pulse pressure. Respiratory patterns become irregular. Pupillary changes can also occur with increasing pressure. Open sutures in the infant and young child allow the bony structure to expand with an increase in intracranial pressure. Increasing head circumference, a full fontanelle, irritability, and poor feeding are the most common symptoms associated with increased intracranial pressure in this group of children (Wilson, Karajannis, & Harter, 2014).

Increased intracranial pressure in childhood brain tumors occurs from the tumor mass itself and or from hydrocephalus. Surgical treatment of increased intracranial pressure involves removal of the lesion, if possible. A ventricular drain may be placed to temporarily remove CSF as a method of reducing intracranial pressure. Ventriculoperitoneal shunts are used for the treatment of hydrocephalus that does not resolves after tumor removal (Wirsching, Galanis, & Weller, 2016; Witthayanuwat et al., 2018).

After radiological confirmation of a tumor, the child is seen by a neurosurgeon and evaluated for surgery. Surgical intervention is the primary treatment for all newly diagnosed brain tumors. Removal or debulking of the tumor, with a reduction in its overall size, allows for greater efficacy of additional treatment modalities. It has been shown across studies that a gross total removal of malignant tumors is predicative of a longer progression free survival. Surgery also provides the opportunity for tumor samples to be collected and sent to the pathologist for a tissue diagnosis. The development of pediatric neurosurgery as a subspecialty has occurred in the past two decades. Surgeons who devote the majority of their practice to children are committed to providing the most aggressive surgical approach to the tumor in an attempt at a cure. It is optimal for a child diagnosed with a brain tumor to have surgery performed by a pediatric neurosurgeon. Advanced surgical technology, including the operating microscope, ultrasonic surgical aspirator, CO, laser, ultrasound and intraoperative electrocortocography, and sensory and motorevoked potentials has permitted radical resection of many tumors with decreased surgical morbidity. Tumors of the hemispheres and posterior fossa are readily accessible, allowing for gross total surgical resections (Wilson et al., 2014). Surgical removal of part, or all of the tumor in areas of the third ventricle, hypothalamus, optic nerve, and pituitary. Surgery is not indicated in children with diffuse intrinsic brain stem tumors in which the surgical risks outweigh the benefits of a radical resection and in which the overall prognosis is not changed with surgery. The exception is the tumor that is isolated to the medulla or cervical medullary junction. Staged surgical procedures and second-look operations are also now feasible given the decreased surgical morbidity. Deep tumors, such as hypothalamic lesions, can be approached from two different angles at two separate surgeries for maximal tumor resection. This is useful for tumors whose

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histology is low grade or slow growing. A 95% tumor removal would result in no further active treatment or deferring chemotherapy or radiotherapy and the late effects associated with those treatments. Secondlook operations after a specific treatment modality has been administered can be used to remove tumor still present on scan after treatment, thus rendering the patient free of disease. They also provide an opportunity for the oncologist to evaluate the tumor for changes that may have occurred as a result of treatment (Wirsching et al., 2016; Witthayanuwat et al., 2018).

Surgical therapy is the initial modality carried out after the patient is diagnosed with intracranial tumor. This approach includes consideration of extensive surgical resection of tumor tissue even though the entire tumor cannot be removed. Tumor resection when possible should follow the aggressiveness of the tumor characterized by infiltration into surrounding tissues and extensive vascularization of the tumor. The maximal resection performed is aimed at eliminating the mass effect, achieving cytoreduction. Based on the literature, non-surgical or non-surgical types of glioblastoma tumors have a very poor prognosis with a 5-year survival rate in 4-5% of cases, and a 2-year survival in 26-33% (Wilson et al., 2014).

Overall, the average survival is 15 months. Most patients die less than one year from the date of diagnosis. Patients with tumor masses can present with different signs and symptoms, which are produced by three mechanisms: first, the direct effect of brain tissue damage due to necrosis that causes symptoms such as focal nerve deficits (40-60%) and cognitive impairment. The signs and symptoms caused by malignancy depend on the region of the brain affected by the tumor. For example, patients who show hearing and vision problems indicate that the tumor is located in the area of the temporal lobe, while 20-40% of patients present with personality changes as a consequence of the tumor located in the frontal lobe, thus impairing cognitive function. If the tumor is large with a significant mass, it can cause an imbalance in gait and incontinence (Wilson et al., 2014).

With a secondary effect of increased intracranial pressure, which is a direct consequence of a gradual increase in the size of the tumor and an increase in edema around the tumor, which causes a shift in intracranial contents, resulting in headaches that are characteristic in 30-50% of patients of glioblastoma multiforme type. Headaches are usually unilaterally localized with progressive severity and do not have a specific pain pattern. These headaches can also be associated with vomiting and papyl edema, which are now rarely seen due to detection of the disease at an earlier stage (Wirsching et al., 2016; Witthayanuwat et al., 2018).

Depending on the location of the tumor, 20-40% of cases may also present with seizures usually with focal onset, which can be simple, partially complex, or generalized partial seizures. Clinical manifestations that appear mostly arise due to spatial pressure mechanisms, so that these manifestations can be directed to diagnose intracranial tumors. Currently, the main diagnostic methods for detecting gliomas rely on neurological tests and neuroimaging methods, which are carried out when the disease is already at an advanced stage. Over the past 20 years, magnetic resonance imaging (MRI) has become the standard in brain tumor imaging to determine lesion boundaries including tumor size, shape, and location.

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Effective supportive care requires the management of various signs and symptoms of the disease, consisting of the management of cerebral edema, seizures, gastrointestinal tract disorders, osteoporosis, venous thromboembolism, cognitive impairment and mood disorders. Neurological symptoms are significantly reduced upon administration of corticosteroids, but due to their substantial side effects, they are usually lowered gradually at the beginning of the treatment regimen. Dexamethasone, is usually the corticosteroid of choice in these patients due to its low mineralocorticoid activity. In patients with seizures, Levetiracetam is often prescribed due to its low toxicity profile and no drug-drug interactions with chemotherapeutic agents.

Specific therapeutic management involves surgical or surgical resection of the tumor along with radiation and concomitant temozolomide adjuvant therapy (TMZ). The standard initial approach for most primary central nervous system tumors is maximally safe surgical resection, which allows accurate histological diagnosis, tumor genotype, and tumor volume reduction. Typical treatment for intracranial tumors involves surgical resection of the tumor mass, followed by radiotherapy and chemotherapy treatments. However, such therapies often prove ineffective, given the high recurrence rate, the emergence of general tumor resistance over time, coupled with serious neurological damage to patients.

The prognosis of adult patients with GBM remains poor; However, complete surgical resection and adjuvant treatment improve progression-free and overall survival.

In this case, patien can be treatment IVFD Ringer Lactate 135 cc/hour, Metamizole 250 mg/1 ml /8 hour IV, Diphenhidramin 5 mg /12 hour IV, Dexamethasone 5 mg /8 hour IV, Piracetam 500 mg/12 hour IV. In this case, Dexamethasone therapy is given which is the corticosteroid of choice in these patients because of its low mineralocorticoid activity and only reduces the symptoms caused optimally. The goal is to reduce neurological symptoms but with a dose that is lowered slowly. The main treatment is still tumor resection with neurosurgeon.

CONCLUSION

In this case, patien can be treatment IVFD Ringer Lactate 135 cc/hour, Metamizole 250 mg/1 ml /8 hour IV, Diphenhidramin 5 mg /12 hour IV, Dexamethasone 5 mg /8 hour IV, Piracetam 500 mg/12 hour IV. In this case, Dexamethasone therapy is given which is the corticosteroid of choice in these patients because of its low mineralocorticoid activity and only reduces the symptoms caused optimally. The goal is to reduce neurological symptoms but with a dose that is lowered slowly. The main treatment is still tumor resection with neurosurgeon. The prognosis of adult patients with Glioblastoma remains poor. However, complete surgical resection and adjuvant treatment improve progression-free and overall survival.

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