

Case Report**Early Term Pregnancy in a Patient with Brain Tumor****Achmad Rivaldi¹, Bernadus Dirgantoro²**¹General Practitioner²Department of Obstetrics and GynecologyAji Muhammad Parikesit General Hospital Kutai Kartanegara
Tenggarong**Abstract****Objective:** To investigate the association between patient's current pregnancy and a suspected meningioma brain tumor along with how to its management.**Methods:** Case Report.**Case:** A 45-year-old pregnant woman at 37 weeks of gestation, showed signs of intermittent left-sided headaches accompanied by vision loss and difficulty hearing which occurred gradually over the past 2 years. The patients has a history of a brain tumor. During pregnancy, there were no worsening neurological deficits such as seizures or loss of consciousness. A Imaging test evaluation during pregnancy revealed a brain tumor, suggestive for meningioma, measuring from 4.6 cm x 5.6 cm x 3.7 cm to 5.2 cm x 5.6 cm x 4.4 cm after 2 years. Based on the result of all examinations, the patient was diagnosed with early term pregnancy with brain tumour, preeclampsia, diabetes mellitus, anemia, and IUGR. The decision was made to terminate the pregnancy via cesarean section. The patient's postoperative recovery was uncomplicated and the baby was born female, BW 1980 gram, BL 43 cm, APGAR 8/9. Then the patient was planned for tumor excision.**Conclusion:** In this case, there is no association was found between the patient's current pregnancy and the brain tumor, suspected to be meningioma. In pregnancies with brain tumors that do not exhibit progressive neurological deficits, pregnancy termination can be performed until term, before subsequently undergoing tumor surgery. A multidisciplinary approach involving various fields is necessary to manage pregnancies with brain tumor and comorbid diseases to reduce maternal and neonatal morbidity and mortality rates.**Keywords:** brain tumor, meningioma, pregnancy, termination.**Correspondence Author.** Achmad Rivaldi. Aji Muhammad Parikesit General Hospital. Kutai Kartanegara.
Email; achmadrivaldi53@yahoo.com. Telp: +6282185358597**INTRODUCTION**

As reported by the Central Brain Tumor Registry of the United States (CBTRUS), the occurrence of central nervous system tumors from 2016 to 2020 was 24.83 per 100,000 people per year. Meningioma is the predominant primary brain tumor, Contributing to 40.8%, and over 95% of cases are benign.¹ Meningioma is an extra-axial brain tumor originating from meningotheial cells (arachnoidal cap cells).² Meningiomas are predominantly located in the cerebral convexity, sagittal sinus, cranial base, cerebellum, and spinal cord.^{2,3} Meningioma rates escalate with advancing age, with 43.6% occurring in individuals over 40 years old. Women have a higher prevalence of

meningioma compared to men, exhibiting a ratio of 2:1.^{1,4}

Brain tumors in pregnancy are rare, with an estimated incidence of approximately 1 in 1000-2000 pregnancies.⁵ The incidence of meningioma in pregnancy is even more rare compared to non-pregnant women in the same age group.⁶ However, meningioma is tightly linked to sex hormones, resulting in accelerated tumor growth during pregnancy.^{6,7}

The clinical symptoms of meningioma depend on the tumor's location. Neurological deficits arise due to cortical irritation, compression of surrounding brain tissue and cranial nerves, and vascular injury.⁸ Some common symptoms include headaches, cranial nerve deficits, seizures, altered

cognitive function, and asymptomatic cases.³ The increased vascularity and hormonal shifts during pregnancy may contribute to the progression of these symptoms.⁷

The approach to managing brain tumors during pregnancy must be thoughtfully organized. Surgical intervention for a brain tumor while pregnant carries considerable risk for both the mother and the unborn child.⁹ There is limited evidence regarding whether a brain tumor must be addressed during pregnancy or after pregnancy termination, including the timing and method of delivery.

We present the case of a pregnant patient with a suspected intracranial meningioma, in which elective cesarean section was performed before planning the excision of the brain tumor. We aim to contribute our case to the existing literature to further enrich the current knowledge on this subject.

CASE

A 45-year-old pregnant woman, gravida 3 para 2 abortus 0, at 37 weeks of gestation with a brain tumor suspected to be meningioma, presented to the Obstetrics and Gynecology Clinic for pregnancy monitoring. The patient complained of intermittent left-sided headaches, unable to see, and has difficulty hearing, which has gradually developed over the past 2 years. Throughout the pregnancy, the patient has not experienced projectile vomiting, unilateral weakness, loss of consciousness, or seizures. However, the patient did experience a loss of consciousness and recurrent seizures before pregnancy and at that time, the patient was advised by the doctor to undergo surgery to remove the tumor, but the patient refused because the operation had a high risk. The patient has a history of using hormonal contraceptive injections every 3 months containing progesterin for 2 years prior to the brain tumor diagnosis. Due to her high-risk pregnancy, the patient received routine antenatal care from general practitioners and obstetrician-gynecologist. The obgyn's recommendation is to continue to have routine pregnancy check-ups and undergo the birth process using the cesarean section method in hospital.

Upon physical examination, the blood pressure was measured at 150/90 and other vital signs were within normal limits. The patient scored E4V5M6 on the Glasgow Coma Scale (GCS) and was conscious and oriented. Visual

examination of both eyes revealed a visual acuity of 0 with isocoric pupils, measuring 5 cm/5 cm, with negative pupillary reflexes. Fundoscopy revealed papilledema (optic disc swelling) in both eyes. There were no signs of neck stiffness, pathological reflexes, or abnormal physiological reflexes. Motor and sensory examinations were within normal limits.

An ultrasound examination showed an Estimated Fetal Weight (EFW) of 2,278 grams, which falls below the 10th percentile. Cardiotocography (CTG) revealed a normal fetal heart rate pattern. Laboratory showed Hb level 10.7 g/dL, leucocyte 9.900/ μ L, PLT 283.000/ μ L, HbA1C 6.5%, a positive protein result in urine analysis, negative HBsAg, and non-reactive HIV antibodies. Two years ago, the patient had a CT scan performed on the head which suggested a Space Occupying Lesion (SOL), suspected to be meningioma with measuring in cranio-caudal (CC), anterior-posterior (AP), lateral-lateral (LL) orientation are 4.6 cm x 5.6 cm x 3.7 cm (Figure 1A, B). Furthermore, an evaluation using MRI at 35-36 weeks of gestation displayed an isointense lesion on T1 and T2-weighted images (Figure 2A, B) with contrast enhancement on T1+C (Figure 2C). The lesion appeared oval-shaped with well-defined borders, measuring at AP 5.2 cm x CC 5.6 cm x LL 4.4 cm in the left temporal region, accompanied by edema causing narrowing and compression of the left lateral ventricle and the third ventricle, with midline shifting to the right. The lesion seemed attached to the convexity of the left temporal bone, showing characteristics of an extra-axial mass, suspected to be a meningioma. The differential diagnosis of brain tumours in this case includes hemangiopericytoma, glioblastoma, and schwannoma which are also accompanied by other diseases such as preeclampsia, diabetes mellitus, anemia, and IUGR.

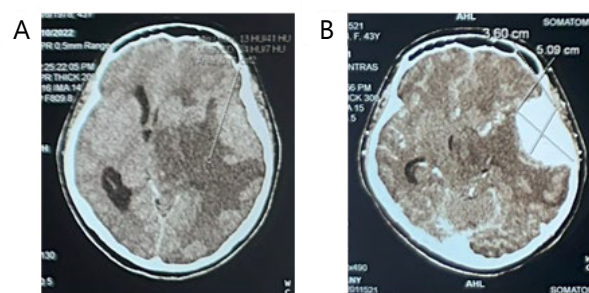


Figure 1. CT scan of the head before pregnancy, measuring AP 4.6 cm x CC 5.6 cm x LL 3.7 cm, horizontal view. (A) without contrast. (B) with contrast.

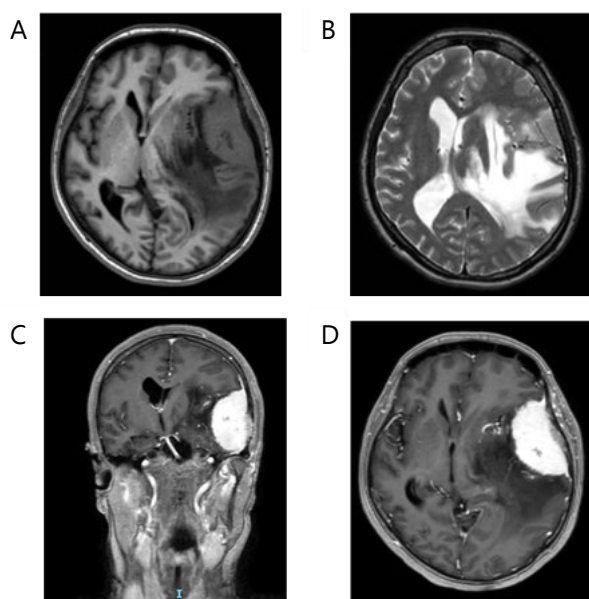


Figure 2. MRI of the head during pregnancy at 35-36 weeks, measuring AP 5.2 cm x CC 5.6 cm x LL 4.4 cm. (A) T1-weighted, horizontal section. (B) T2-weighted, horizontal section. (C) T1+Contrast, coronal section. (D) T1+Contrast, horizontal section.

The patient was scheduled for elective cesarean section surgery and Method of Operation for Women (MOW)/ Tubectomy due to indications related to her condition, age, gestational age, and brain tumor. Subsequently, the patient was consulted to the departments of neurosurgery, neurology, internal medicine, cardiology, and anesthesia to receive appropriate therapy for the existing disorders as part of the preparation before the cesarean section operation. The patient received antihypertensive and diabetes medications from the cardiologist and internist. The neurologist suggested the administration of phenytoin. Steroid administration included dexamethasone, was recommended by the neurosurgeon. It was also suggested to perform emergency tumor excision if the patient experienced a loss of consciousness. However, if the condition remained stable, tumor excision would be planned after pregnancy termination. The anesthesiologist decided to perform cesarean section surgery with spinal anesthesia. The cesarean section surgery proceeded smoothly, and a baby girl was born weighing 1,980 grams and measuring 43 cm in length was born. Apgar scores at the first and fifth minutes were 8/9. The postoperative period was uneventful and the mother was admitted to a regular inpatient ward after the surgery. The patient was freed from the hospital after a three-day stay after delivery, with plans for tumor excision in the future.

DISCUSSION

Based on the case description, it is noted that the patient is a 45-year-old woman. Several studies have demonstrated that meningiomas are more commonly found in women than in men, with a ratio exceeding 2:1.¹ The incidence of meningiomas in women increases post-puberty and peaks during the reproductive years.^{4,10} This implies a correlation between female sex hormones and the likelihood of developing meningiomas.⁷ The patient's history revealed the use of 3-month injectable contraceptives for 2 years. This type of contraception is a hormonal method containing a single hormone, progestin. Several studies have discussed the correlation between exogenous progesterone hormone and the risk of meningioma occurrence.¹¹ The administration of exogenous progesterone influences the expression of progesterone receptors (PR), leading to the inactivation of the Neurofibromatosis-2 (NF-2) gene. NF-2 serves as a direct indicator of the meningioma-specific tumor suppressor in the etiology of meningiomas. A case-control study found in a hospital in Indonesia indicates that prolonged administration of exogenous progesterone results in diminished expression of PR and NF2 in serum, increasing the risk of meningioma.¹² Another study reveals that the utilization of hormonal contraceptives for over 10 years heightens the risk of meningioma to 18 times greater, whereas use for less than 10 years increases the risk by 5 times.¹³

Pregnancy does not affect the incidence of brain tumors, but in certain types of brain tumors, faster growth is observed during pregnancy. Throughout pregnancy and the luteal phase of the menstrual cycle, meningioma growth accelerates and can become symptomatic.¹⁴ The mechanism behind tumor growth during this period is still controversial. On the other hand, there was a tumor size regression and symptom improvement in postpartum meningioma patients.¹⁵ This is associated with a close connection with sex hormones which increase through gestation and the luteal segment of the menstrual cycle, such as progesterone, estrogen, and prolactin.¹¹ Approximately 70-95% of meningiomas have progesterone receptors on their cell membranes and fewer estrogen receptors.¹⁶ Additionally, there is an increase in vascularity during pregnancy, leading to hemodynamic changes in tumors such as intratumoral hypervascularization,

edema, spontaneous bleeding, or necrosis.¹⁴ On average, meningiomas grow less than 1 cm per year.¹⁷ In contrast, this study found no influence of pregnancy on meningioma, either in terms of tumor size growth (the mass increase less than 1 cm in 2 years from 4.6 cm x 5.6 cm x 3.7 cm to 5.2 cm x 5.6 cm x 4.4) or worsening of clinical symptoms compared to the pre-pregnancy condition.

In this case, the fetus experienced Intrauterine Growth Restriction (IUGR) with an EFW below the 10th percentile (2,278 grams). Previous studies have indicated that intracranial tumors can affect pregnancy outcomes for both the mother and the fetus. Intracranial tumors, including meningiomas, occurring during pregnancy increase the risk of premature birth (23%), cesarean section delivery (56%), and maternal mortality (19%). The impact of intracranial tumors on pregnancy can also be linked to the risk of IUGR, possibly due to the administration of brain tumor therapies (e.g., antiepileptic drugs, chemotherapy) during pregnancy.¹⁸ However, in this case, the patient did not take any medication during pregnancy because the neurological deficits in the patient were non-progressive, such as a lack of loss of consciousness or seizures. Therefore, the possible causes of IUGR in this case are related to the patient's age (45 years) and chronic diseases, namely anemia, diabetes, and hypertension.

In this case, the patient had clinical symptoms such as headache, blindness, and hearing disorder and had been diagnosed with a brain tumor, suspected to be meningioma, before the pregnancy. Meanwhile, diagnosing a brain tumor during pregnancy presents its own challenges. Clinically, signs of increased intracranial pressure may mimic early pregnancy symptoms, hyperemesis gravidarum, or preeclampsia/eclampsia. However, symptoms that warrant attention include severe localized headaches accompanied by forceful vomiting, particularly in the second or third trimester. Changes in mental status, abnormal fundoscopy, focal seizures with secondary generalization, unilateral motor or sensory deficits, and visual field defects, especially in the first trimester, must be monitored.^{19,20} If metabolic disorders and preeclampsia/eclampsia have been ruled out, imaging will help identify SOL such as abscesses, tuberculomas, neurocysticercosis, bleeding, or brain tumors. In diagnostic investigations, radiological imaging should be avoided as much as possible in the early stages of pregnancy. MRI is the preferred

method for accurate diagnosis because it involves no exposure to ionizing radiation compared to a CT scan. Although contrast-enhanced MRI can pass through the placenta, no studies have reported abnormalities in the fetus.¹⁹

For this particular case, elective cesarean section termination of pregnancy was performed with spinal anesthesia, and the planned tumor excision was scheduled after childbirth. The management strategy for intracranial tumors during pregnancy must be grounded in the patient's physical status, tumor location, gestational age, and other predisposing factors.⁹ If there is an indication for tumor excision surgery and it is emergent, tumor excision is performed regardless of gestational age. However, if it is elective, termination of pregnancy can be done at a minimum gestational age of 34 weeks to avoid adverse effects on the pregnancy especially for neonates because the survival rate before 24 weeks is around 20% to 30%.^{18,21} As is the case with tumors in the gynecological area such as ovarian cancer with slow or moderate progress of disease, the pregnancy should be allowed to proceed until term.²² In this patient, no signs of early herniation or progressive neurological deficits such as loss of consciousness or seizures were found, so pregnancy termination was performed at the earliest term gestational age to obtain better maternal and fetal outcomes.

Cesarean section was chosen as the termination method to avoid increased ICP during vaginal delivery and the immaturity of the cervix in preterm pregnancies. General anesthesia is recommended for cesarean section in patients with brain tumors accompanied by signs of increased ICP to avoid the risk of brain herniation pertaining to regional anesthesia.⁹ Other studies indicate that regional anesthesia with spinal anesthesia is safe for pregnant patients with brain tumors undergoing cesarean section, provided there are no new neurological symptoms (Exacerbating headaches, changes in vision, seizures, or diminished consciousness), the lesion typically enlarges or changes during pregnancy, without imaging signs of significant mass effect with or without midline shift, no indications of hydrocephalus, and no clinical or imaging evidence suggesting increased intracranial pressure (ICP).^{23,24} In this patient, none of these signs were found, although clinically and in imaging, there was an increase in ICP, albeit non-progressive, as compensation had already occurred.

CONCLUSION

In this case, the patient did not experience a deterioration of neurological status or significant growth of tumor size during pregnancy. Therefore, it can be concluded that there was no association between the current pregnancy of the patient and brain tumor. In pregnancies with brain tumors that do not exhibit progressive neurological deficits, pregnancy termination can be performed until term, before subsequently undergoing tumor surgery. A multidisciplinary approach involving various fields is necessary to manage pregnancies with brain tumor and comorbid diseases to lessen the incidence of illness and death in mothers and infants.

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REFERENCES

- Ostrom QT, Price M, Neff C, Cioffi G, Waite KA, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary brain and other central nervous system tumor diagnosed in the United States in 2016-2020. *Neuro-Oncol.* 2023; 25(12 Suppl 2):iv1-iv99. doi: 10.1093/neuonc/noad149.
- DeAngelis LM, Wen PY. Primary and Metastatic Tumors of the Nervous System. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's LM, Wen PY. Primary and Metastatic.* 19th ed. New York: McGraw-Hill Education. 2015.
- Ogasawara C, Philbrick BD, Adamson DC. Meningioma: a review of epidemiology, pathology, diagnosis, treatment, and future directions. *Biomedicine.* 2021; 9(3): 319-342.
- Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. *Future Oncol.* 2018;14(21):2161-2177.
- Verheeecke M, Halaska MJ, Lok CA, Ottevanger PB, Fruscio R, Dahl-Steffensen K, Kolawa W, Gziri MM, Han SN, Van Calsteren K, Van den Heuvel F, De Vleeschouwer S, Clement PM, Menten J, Amant F; ESGO Task Force 'Cancer in Pregnancy'. Primary brain tumours, meningiomas and brain metastases in pregnancy: report on 27 cases and review of literature. *Eur J Cancer.* 2014;50(8):1462-71.
- Pettersson-Segerlind J, Mathiesen T, Elmi-Terander A, Edström E, Talbäck M, Feychting M, Tettamanti G. The risk of developing a meningioma during and after pregnancy. *Sci Rep.* 2021;11(1):9153.
- Michaud DS, Gallo V, Schlehofer B, Tjonneland A, Olsen A, Overvad K, et al. Reproductive factors and exogenous hormone use in relation to risk of glioma and meningioma in a large European cohort study. *Cancer Epidemiol Biomarkers Prev.* 2010; 19(10): 2562-2569.
- Hallinan JT, Hegde AN, Lim WE. Dilemmas and diagnostic difficulties in meningioma. *Clin Radiol.* 2013 Aug; 68(8):837-44.
- Shiro R, Murakami K, Miyauchi M, Sanada Y, Matsumura N. Management Strategies for Brain Tumors Diagnosed during Pregnancy: A Case Report and Literature Review. *Medicina (Kaunas).* 2021 Jun 12; 57(6): 613.
- Dresser L, Yuen CA, Wilmington A, Walker M, Vogel TJ, Merrell RT, et al. Estrogen hormone replacement therapy in incidental intracranial meningioma: a growth-rate analysis. *Sci Rep.* 2020; 10(1): 17960.
- Schildkraut JM, Calvocoressi M, Wang F, Wrensch M, Bondy ML, Wiemels JL, et al. Endogenous and exogenous hormone exposure and the risk of meningioma in men. *J Neurosurg.* 2014; 120(4): 820-826.
- Supartoto A, Sasongko MB, Respatika D, Mahayana IT, Pawiroranu S, Kusnanto H, et al. Relationships Between Neurofibromatosis-2, Progesterone Receptor Expression, the Use of Exogenous Progesterone, and Risk of Orbitocranial Meningioma in Females. *Front Oncol.* 2019; 8: 651.
- Nakamura M, Roser F, Michel J, Jacobs C, Samii M. The natural history of incidental meningiomas. *Neurosurgery.* 2003;53(1):62-70-71.
- Lusis EA, Scheithauer BW, Yachnis AT, et al. Meningiomas in pregnancy: a clinicopathologic study of 17 cases. *Neurosurgery.* 2012; 71(5): 951-961.
- Shitara S, Nitta N, Fukami T, Nozaki K. Tuberculum sellae meningioma causing progressive visual impairment during pregnancy. Case report. *Neurol Med Chir.* 2012;52(8):607-11.
- Laviv Y, Ohla V, Kasper EM. Unique features of pregnancy-related meningiomas: lessons learned from 148 reported cases and theoretical implications of a prolactin modulated pathogenesis. *Neurosurg Rev.* 2018;41(1):95-108.
- Nakamura M, Roser F, Michel J, Jacobs C, Samii M. The natural history of incidental meningiomas. *Neurosurgery.* 2003; 53(1).
- Girault A, Dommergues M, Nizard J. Impact of maternal brain tumours on perinatal and maternal management and outcome: a single referral centre retrospective study. *Eur J Obstet Gynecol Reprod Biol.* 2014;183:132-6.
- Goyal S, Yadav A, Madan R, Chitkara A, Singh R, Khosla D, Kumar N. Managing brain tumors in pregnancy: The oncologist's struggle with maternal-fetal conflict. *J Cancer Res Ther.* 2022;18(1):5-18.
- Kurdoglu Z, Cetin O, Gulsen I, Dirik D, Bulut MD. Intracranial Meningioma Diagnosed during Pregnancy Caused Maternal Death. *Case Rep Med.* 2014;2014:158326.
- Ocviyanti D, Putri RA. Biopsychosocial Aspect of Pregnant Women Suspected Brainstem Death. *Indones J Obstet Gynecol.* 2021; 9(2):107-10.
- Aditanzil H, Mahendra B, Suwiyoga K. Management of Pseudomyxoma Peritonei Syndrome during Pregnancy. *Indones J Obstet Gynecol.* 2013; 1(3):161-5.

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23. Wlody DJ, Gambling DR, Griffiths TL. Anesthesia for neurosurgery in the pregnant patient. In: Cottrell JE, Patel P, eds. Cottrell and Patel's Neuroanesthesia. 6th ed. New York. Elsevier. 2017.
 24. Hirs I, Grbcic P. Cesarean section in spinal anesthesia on a patient with mesencephalic tumor and ventriculoperitoneal drainage-a case report. Korean J Anesthesiol. 2012; 63(3): 263-5.