Acta Neurologica Indonesia
Department of Neurology, Faculty of Medicine Universitas Indonesia
ISSN 3032-6303

Case Report

HEPATIC METASTATIC MENINGIOMA FOLLOWING REPEATED INTRACRANIAL REMOVAL SURGERIES

Tiara Aninditha[1], Audrey Clarissa[1], Eka Susanto[2], Kemal Fariz Kalista[3], David Tandian[4], Irma Savitri[1], Henry Riyanto Sofyan[1]

[1]Department of Neurology, Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, audreyclarissa@hotmail.com
[2]Department of Pathology, Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[3]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[4]Department of Neurosurgery, Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

ABSTRACT

Introduction: Meningioma is mostly benign. With appropriate management, it may have a good prognosis. However, it may reoccur and metastasize in <1% of all cases. Studies describing re-occurrences of meningioma and extracranial metastasis, especially to the liver, are limited.
Case Report: A 54-year-old female with secondary headache, cognitive impairment, blindness in the left eye, and paresis of the left facial nerve due to recurrent left spheno-orbital meningioma with scalp invasion had undergone four tumor removal surgeries. Previous histopathological findings were atypical meningioma (2017) and transitional meningioma (2023). A suspicion of a new primary tumor arose as an increase in transaminase and multiple liver nodules were observed despite being an asymptomatic patient. Histology and immuno-histochemistry from the intracranial tumor was an atypical meningioma, and cancer in the liver had a similar immunohistochemistry profile as the intracranial tumor, suggesting meningioma metastasis.
Discussion: Recurrences were more prevalent in higher histologic grading, which can lead to serial operations, higher complication rates, and morbidities. While the lungs are the most common site for metastasis, hepatic metastasis is thought to be underestimated as patients are often asymptomatic. Factors such as scalp and brain invasion, blood vessel proximity, meningioma recurrences, and subtotal resection increase the risk of metastasis. To date, there are no specific guidelines on metastasis treatment.
Conclusion: Meningioma can re-occur and metastasize to distant organs despite its usual benign characteristics. Aggressive tracking should be implemented in females with recurrent meningioma and scalp involvement.

Keywords: meningioma, metastasis, recurrence

INTRODUCTION

Meningioma is the most common benign primary central nervous system tumor, with a prevalence of 37.6% and female preponderance.[1] The tumors are mostly found in the convexity, parasagittal sinus, and the falx cerebri. Spheno-orbital meningiomas (SOM), as a subgroup of sphenoid ridge meningiomas, are also known as the en-plaque meningiomas. It accounts for 20% of intracranial meningiomas or the third most common location. Extension of SOMs into the cavernous sinus and involvement of the ocular musculature render gross total resection nearly impossible due to the risk of loss of visual function. Therefore, SOMs are notoriously known for exhibiting a high rate of recurrence, ranging from 35 to 50%. [2]

In 0.18% of the cases, extracranial metastatic meningiomas are reported. Metastasis will decrease the original good prognosis the patients had.[3] As the literature discussing meningioma metastasis to the liver is still limited, we report a metastatic meningioma to the liver following four intracranial removal surgeries.

CASE REPORT

A 54-year-old female was admitted due to a lack of communication 1 week prior to hospital admission. The patient had a history of worsening headaches and gradual visual loss before she was first diagnosed with atypical meningioma in 2017. The tumor was removed, but the patient refused radiation therapy. Meningioma re-occurs as a growing

Lump in the patient's forehead with bone invasion and further visual loss in the left eye.

Figure 1. Pre-operation clinical appearance

The tumor was removed, but recurrences complained, and a total of 4 removal surgeries were performed. Histopathological results from previous findings were atypical meningioma, CNS WHO grade 2 in 2017, and transitional meningioma, CNS WHO grade 1 in February 2023.

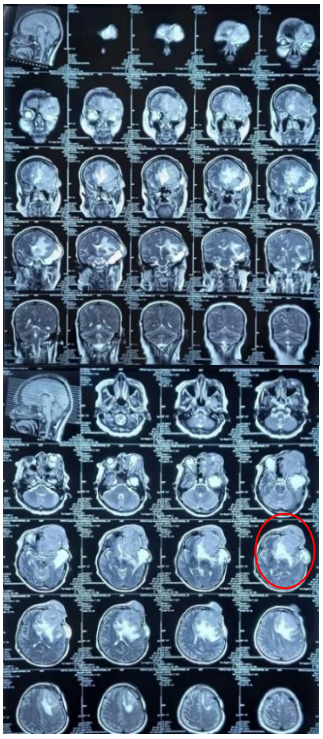

Figure 2. MRI of the patient before operation

In this hospitalization, the patient was diagnosed with secondary headache, cognitive impairment, left eye blindness, and central paresis of the left cranial nerve II due to recurrent left phenobarbital meningioma with scalp invasion. The patient was scheduled for a joint operation between a neurosurgeon, ophthalmologist, otolaryngologist, and plastic surgeon. However, an increase in the transaminase and multiple liver nodules were observed despite being an asymptomatic patient. Hence, the patient was thought to have a new primary tumor. The biopsy from the intracranial tumor was an atypical meningioma, CNS WHO grades 2, and the immunohistochemistry result of the liver is suggestive of meningioma metastasis, as the majority of tissue from the liver nodule had a similar immunohistochemistry profile as the intracranial meningioma.

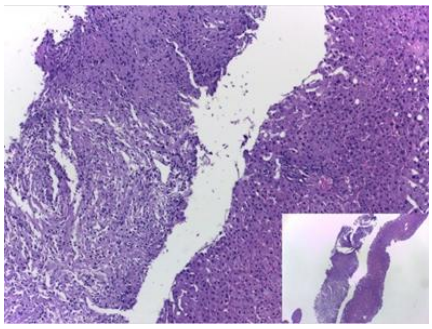

Figure 3. Liver tumor histology (left) compared to liver parenchymal (right). The patternless proliferation of atypical tumor cells was observed.

DISCUSSION

Meningioma and the brain

Meningioma arises from the meningiothelial cell of the meninges,

one of the coverings of the brain. The brain is covered by layers of skin, subcutaneous tissue, galea aponeurotic, loose connective tissue, and pericranium. The skin has blood supplies, along with venous and lymphatic drainage, while loose connective tissue is innervated by the cutaneous nerve. [4–7]

Based on the histology and cytomorphology, meningioma is classified into 3 WHO grades, where in benign or grade 1 meningioma, the prevalence is higher compared to the more aggressive grade 3 meningioma. The degree and extent of surgical removal is one of the predictors of patient survival.[4,8,9] Besides neuroimaging, histologic examination of the tissue, where pathognomic whorl with cytoplasmic intranuclear pseudo inclusion and psammoma bodies, can establish the diagnosis of meningioma.[4] The treatment of meningioma includes observation, operation, radiotherapy, and systemic therapy. Surgical removal is the practical treatment for symptomatic meningioma. However, gross total resection may be hard to achieve.[4,10]

Spheno-orbital meningiomas

Spheno-orbital meningiomas (SOM), a subtype of sphenoid ridge meningiomas (*en-plaque meningiomas)*, constitute 20% of intracranial meningiomas and are the third most common location for these tumors. These *en-plaque meningiomas*, extending into the orbit in 2-9% of cases, are diagnosed based on radiographic appearance rather than histological morphology.[2] SOMs, marked by a unique growth pattern and interosseous extension, exhibit a recurrence rate of 35 to 50%, often stimulating bone hyperostosis in surrounding skull bones disproportionately.[2] Female preponderance is observed, with main symptoms including proptosis, visual impairment, and retro-orbital pain.

Surgical approaches aim to address proptosis and optic nerve decompression, with gross total resection challenging due to potential visual function loss in cases involving the cavernous sinus or ocular musculature. Subtotal resection with postoperative radiation therapy is favored by some doctors, but consensus on radiation therapy's

utility, especially in cases with interosseous extension, remains elusive.

In a previous study of 22 patients undergoing surgery for spheno-orbital meningiomas, the pterional approach was predominantly employed. The surgical outcomes varied, with total resection achieved in 45.5% of cases, subtotal resection in 27.3%, and partial resection in 22.7%. Proptosis improvement was observed in 77.3% of patients, while 9.1% showed partial improvement, and 9.1% had no improvement at the 3-month follow-up.[2] The success of surgical resection and clinical regression of proptosis relied on meticulous drilling of the orbital walls and excision of intra-orbital soft tissue components. Challenges, such as hyperostosis extension, cavernous sinus invasion, and tumor adherence to orbital muscles, posed limitations on achieving total excision.

Recurrences of meningioma

Recurrence of meningioma was observed in 20% of grade 1 and 46% of grade 2 meningioma.[4,9,11] Factors that may increase the risk of meningioma recurrences are the location in the skull base, the extent of first surgical resection, histology grade evolution, Ki-67 proliferation, and expression of the progesterone receptor.[12,13] Additionally, there may be intratumoral heterogeneity, differences in the genomic, somatic variant frequency, and cell proliferation in meningioma, which can result in resistant meningioma.[14] Repeated operations can increase patients' morbidity, including a decrease in cognitive and performance status and higher complication rates.[15,16]

Metastasis meningioma

Extracranial metastases of meningioma are found in 0.18% of intracranial meningioma cases. Sites of metastasis include but are not limited to, lungs and pleura, mediastinum, axial bone, liver, and long bones. The preferred metastatic organ is the lung (61%), extracranial bone (26%), liver (19%), and soft tissue. The small number of hepatic metastases is thought to be underestimated, as many patients were asymptomatic.[8,17–19] Meningioma metastases are more commonly found in WHO grades 2

and 3. However, metastases are reported in all WHO grades. Factors that may predict meningioma metastasis are brain invasion, proximity to blood vessels, subtotal resection, recurrence of meningioma, histologic grading of tumor, mitosis rate, nuclear atypia, higher cellularity, focal necrosis, and anaplastic feature.[8] Garzon-Muzdi et al., reported that scalp invasion is the only significant predictive factor for metastasis.[16]

The hypothesized routes of metastasis in meningioma are hematogenous or lymphatic dissemination, cerebrospinal fluid (CSF) seeding, and drop metastasis. Tumor resection can lead to the spread of tumor cells to the lymphatic system and another vein. In addition, despite arising from the meninges and constant exposure to the CSF, fewer cases were reported compared to the hematogenous route.[8,17,18] Metastasis to the liver only, especially without the lung involvement, is rare, as hematogenous spread to the liver has to pass the lung before it reaches the liver tissue. If the lung is not involved as the site of metastasis, the tumor dissemination is suggested through the vertebral venous plexus with its anastomosis with an azygous vein.[20]

Patients with hepatic metastatic meningioma may present with hypoglycemia due to glycogen depletion as the tumor cells use excessive glucose, and liver parenchyma is replaced by tumor cells. Currently, a standard treatment protocol and prognosis are yet to be established for patients with hepatic metastatic meningioma. As meningioma is usually a slow-growing tumor, metastasectomy is suggested. Depending on the clinical symptoms, regular monitoring or chemoembolization may be proposed.[8,21]

CONCLUSION

Meningioma, as one of the most common primary nervous system tumors, is usually benign. Meningioma recurrences increase in accordance with the grade of the tumor, with factors such as skull base location, the extent of the surgical resection, histology evolution, progesterone receptor expression, and Ki-67 proliferation may increase the risk of the meningioma recurrence. The prevalence of

extracranial metastasis is <1%, in which the liver as the site of meningioma metastasis may be underestimated. Several factors, such as scalp invasion, subtotal resection, and meningioma recurrence, may increase the risk of metastasis. As the literature reporting meningioma is still limited, further studies are required to produce a standard of treatment for meningioma patients with hepatic metastasis.

ACKNOWLEDGEMENT

We extend our appreciation to the medical professionals involved in the care of the patient, contributing significantly to our understanding of this unique medical case. All parties acknowledged have provided explicit consent for recognition. Patient identities and specific details have been withheld to maintain confidentiality.

REFERENCE

1. Ostrom QT, Cioffi G, Gittleman H, et al.; CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012–2016. *Neuro-Oncol*. 2019 Nov;21(Suppl 5):v1–100.
2. Elborady MA, Nazim WM. Spheno-orbital meningiomas: surgical techniques and results. *Egypt J Neurol Psychiatry Neurosurg*. 2021 Dec;(57):18.
3. Vuong HG, Ngo TNM, Dunn IF. Incidence, risk factors, and prognosis of meningiomas with distant metastases at presentation. *Neuro-Oncol Adv*. 2021 Jun 25;3(1):vdab084.
4. Ogasawara C, Philbrick BD, Adamson DC. Meningioma: A Review of Epidemiology, Pathology, Diagnosis, Treatment, and Future Directions. *Biomedicines*. 2021 Mar 21;9(3):319.
5. Blumenfeld, Hal. Neuroanatomy through Clinical Cases. United States of America: Oxford University Press; 2022.
6. Agur, Anne M. R., Dalley, Arthur F. Moore's Essential Clinical Anatomy. United States of America: Wolters Kluwer; 2019.
7. Waxman, Stephen G. Clinical Neuroanatomy. United States of America: Mc Graw Hill; 2020.
8. Costea CF, Cucu AI, Bogdănici CM, et al.; The Myth of Prometheus in metastatic meningioma to the liver: from craniotomy to hepatectomy. Rom *J Morphol Embryol*. 2021;62(2):351–9.
9. Harter PN, Braun Y, Plate KH. Classification of meningiomas—advances and controversies. *Chin Clin Oncol*. 2017 Jul;6(Suppl 1):S2–S2.
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers. 2023.
11. Bender L, Somme F, Lhermitte B, et al.; High risk of recurrence for grade II meningioma: a 10-year multicenter analysis of prognosis factors. *Chin Clin Oncol*. 2021 Jun;10(3):26–26.
12. Lemée JM, Corniola MV, Meling TR. Benefits of re-do surgery for recurrent intracranial meningiomas. *Sci Rep*. 2020 Jan 15;10(1):303.
13. Bi WL, Zhang M, Wu WW, et al.; Meningioma Genomics: Diagnostic, Prognostic, and Therapeutic Applications. *Front Surg*. 2016 Jul 6;3:40.
14. Magill ST, Vasudevan HN, Seo K, et al.; Multiplatform genomic profiling and magnetic resonance imaging identify mechanisms underlying intratumor heterogeneity in meningioma. *Nat Commun*. 2020 Sep 23;11(1):4803.
15. Richardson GE, Gillespie CS, Mustafa MA, et al.; Clinical Outcomes Following Re-Operations for Intracranial Meningioma. *Cancers*. 2021 Sep 24;13(19):4792.
16. Garzon-Muvdi T, Maxwell R, Luksik A, et al.; Scalp Invasion by Atypical or Anaplastic Meningioma Is a Risk Factor for Development of Systemic Metastasis. *World Neurosurg*. 2020 Oct 1;142:e133–9.
17. Himič V, Burman RJ, Fountain DM, et al.; Metastatic meningioma: a case series and systematic review. *Acta Neurochir* (Wien) [Internet]. 2023 Jul 26 [cited 2023 Sep 18]; Available from: https://doi.org/10.1007/s00701-023-05687-3
18. Lee GC, Choi SW, Kim SH, et al.; Multiple Extracranial Metastases of Atypical Meningiomas. *J Korean Neurosurg Soc*. 2009 Feb;45(2):107–11.
19. Zhao L, Zhao W, Hou Y, et al.; An Overview of Managements in Meningiomas. *Front Oncol* [Internet]. 2020 [cited 2023 Sep 11];10. Available from: https://www.frontiersin.org/articles/10.3389/fonc.2020.01523
20. D'Aguanno V, Ralli M, Cerbelli B, et al.; Liver metastases from maxillary sinus sinonasal undifferentiated carcinoma: A case report. *Oncol Lett*. 2019 Jun;17(6):5811–4.
21. Obiorah IE, Ozdemirli M. Incidental Metastatic Meningioma Presenting as a Large Liver Mass. *Case Rep Hepatol*. 2018 May 7;2018:1089394.