Iranian Journal of NEUROSURGERY
2022, Volume 8

Case Report:
Metastasis of Malignant Intracranial Meningioma to the Lung: Report of a Case and Review of the Relevant Literature

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Citation Sungkaro K, Sae-heng S. Metastasis of Malignant Intracranial Meningioma to the Lung: Report of a Case and Review of the Relevant Literature. Iran J Neurosurg. 2022; 8:E9. http://dx.doi.org/10.32598/irjns.8:9
http://dx.doi.org/10.32598/irjns.8.9

Article info:
Received: 17 Mar 2022
Accepted: 25 Apr 2022
Available Online: 13 Jun 2022

Keywords:
Meningioma, Brain Neoplasms, Neoplasm Metastasis

ABSTRACT

Background and Importance: Distant extracranial metastasis of meningioma is rare, and the pathophysiology of metastasis in meningioma remains a topic of debate. This study aimed to describe a patient who suffered from multiple pulmonary metastases of meningioma.

Case Presentation: This report introduced a rare case of a 47-year-old female who presented with right hemiparesis. Cranial Computed Tomography (CT) demonstrated a homogeneously enhanced tumor in the left temporal lobe. The patient underwent tumor resection; the pathological result was found to be World Health Organization (WHO) grade I meningothelial meningioma. Recurrence of the tumor transpired after two years and a second operation was performed. WHO grade II atypical meningioma was diagnosed. Subsequently, the patient developed a chronic cough and her chest x-ray showed multiple lung masses. CT-guided biopsy of the right lung mass was performed. Finally, pulmonary metastatic meningioma was diagnosed.

Conclusion: Distant extracranial metastasis and malignant transformation of meningioma involve the genetic alteration of a tumor, which should be studied further.

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Highlights

- Most forms of meningioma are benign, and distant metastatic meningioma is uncommon.
- Distant extracranial metastasis of meningioma should be a concern in malignant types of tumors.

Plain Language Summary

Tumor spread to other organs is an uncommon presentation in meningioma. The authors described a patient who suffered from meningioma that transformed into malignancy and spread to the lung.

1. Background and Importance

Extracranial metastasis of meningioma has a low incidence rate [1, 2]. A few cases have been reported in the literature. The pathophysiology of metastasis in meningioma is still being debated. The authors described a patient who suffered from multiple pulmonary metastases of meningioma. This case also highlights the malignant transformation of the World Health Organization (WHO) grade I meningioma.

2. Case Presentation

A 47-year-old female was admitted to a provincial hospital due to hemiparesis on the right side. Cranial Computed Tomography (CT) demonstrated a homogeneously enhanced tumor at the left temporal lobe measuring 5.7x5.0x4.0 centimeters (Figure 1A). Consequently, the patient underwent an operation at the provincial hospital involving a left craniotomy with partial tumor removal, after which she was transferred to our hospital. At our hospital, she was still not fully conscious and had a motor weakness. The postoperative cranial CT revealed a residual tumor that was 5.0x4.1x3.5 centimeters in size. Therefore, the patient underwent a decompressive craniectomy with total tumor resection. After surgery, the patient gradually regained consciousness and improved motor weakness without any new neurological impairment.

From the histological findings, tumor cells formed lobules where they appeared to form a syncytium with oval nuclei, occasionally showing central clearing (Figure 1B). A diagnosis of WHO grade I meningothelial meningioma was made.

Two years after the second surgery, the patient suffered from progressive right hemiparesis again. Magnetic resonance imaging of the brain showed a recurrent homogeneously enhanced mass protruding through the craniectomy site, 6.2x7.0x5.5 centimeters in size (Figure 1C). The patient underwent a re-explored wound with subtotal tumor resection. Microscopic examination of this surgical specimen showed hypercellularity, small cells with a high nuclear to cytoplasmic ratio, and a sheeting pattern with mitosis 4/10 high-power field (Figure 1D), and tumor cells were immunoreactive for the Epithelial Membrane Antigen (EMA) (Figure 1E). In addition, brain invasion was observed from this specimen (Figure 1F). Therefore, the diagnosis was WHO grade II atypical meningioma, and postoperative radiotherapy was performed.

One month after the third operation, she developed a cough during follow-up and her chest x-ray showed multiple lung masses (Figure 2A). Therefore, she underwent a CT-guided biopsy of the right lung mass (Figure 2B). Histopathology of the biopsy specimens showed a sheeting pattern, hypercellularity with small cells, and a high nuclear to cytoplasmic ratio (Figure 2C). Moreover, a tumor showed immunoreaction for EMA that was in concordance with an intracranial tumor (Figure 2D). Finally, pulmonary metastatic meningioma was diagnosed, and the patient refused further treatment. However, she has since received a follow-up and was still able to manage daily activities from the time of the previous follow-up.

3. Discussion

Extracranial metastasis of meningioma is an uncommon presentation. The incidence of meningioma metastasis was reported to be 0.18-0.67% [1, 2]. Common metastatic sites include the lungs and intra-abdominal organs. According to Stoller et al. [3], the proportion of extracranial metastasis to lung/pleura, musculoskeletal system, liver, lymph node, and kidney was reported at 35%, 17%, 13%, 11%, and 8%, respectively. Moreover, EMA is one of the biomarkers used for the diagnosis

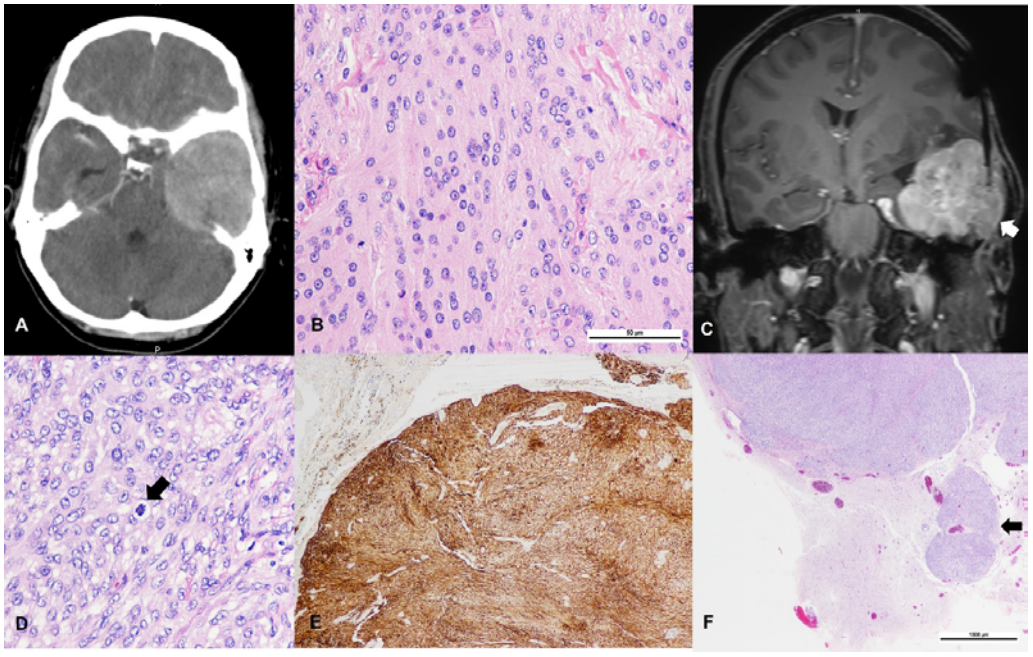

Figure 1. Imaging and histological findings of the case report

(A) a cranial CT scan of an enhanced mass in the left temporal lobe, (B) Syncytia of tumor cells with oval centrally located nuclei, (C) T1-weighted coronal images with gadolinium administration showing a large lobulated tumor extended to both the extracranial regions (arrow), (D) a histological examination of hypercellularity, small cells with a high nuclear to cytoplasmic ratio, and a sheeting pattern with mitosis (arrow), (E) a tumor showing immunoreaction for epithelial membrane antigen, and (F) a tumor invading the brain parenchyma (arrow).

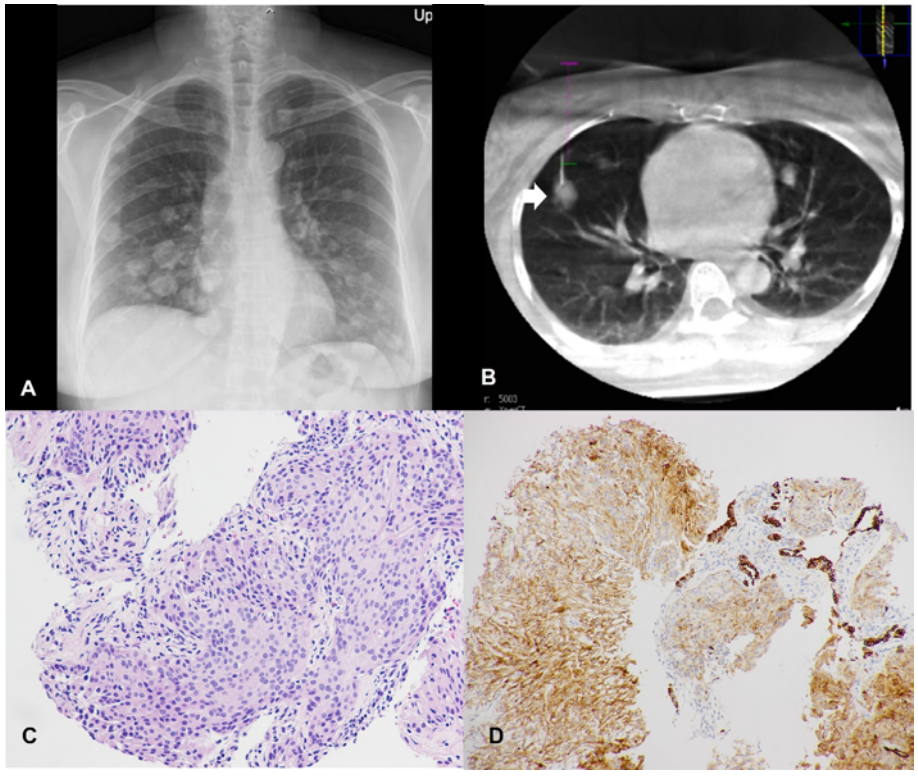

Figure 2. Pulmonary metastatic meningioma

(A) an upright chest x-ray of multiple lung masses on both sides, (B) a CT-guided biopsy done on the right lung mass (arrow), and (C) histological examination of the syncytia of tumor cells with hypercellularity, and (D) a tumor showing immunoreactive for epithelial membrane antigen.

Table 1. Summary of intracranial meningioma cases with multiple pulmonary metastases from the literature review

Author and Year	Age	Gender	Grading of Intracranial Meningioma	Recurrence/Malignant Transformation of Intracranial Tumor	Metastatic Findings
Hishima et al., 1995 [5]	25	Female	Meningothelial meningioma, WHO grade I at the right parietal lobe	Recurrence at the same site	Multiple metastases
Murrah et al., 1996 [6]	53	Female	NA	Recurrence at the same site	Multiple bilateral pulmonary metastases
Adlakha et al., 1999 [7]	17	Female	Anaplastic papillary meningioma, WHO grade I at left parieto-occipital mass	Recurrence at the same site	Solitary mass in the left lung
Adlakha et al., 1999 [7]	70	Female	Psammomatous meningioma, WHO grade I in the left parasagittal area	NA	Multiple metastases
Adlakha et al., 1999 [7]	30	Male	Atypical meningioma, WHO grade II in the left parasagittal area	Recurrence	Multiple small bilateral pulmonary nodules
Figueroa et al., 1999 [8]	50	Female	Transitional meningioma, WHO grade I at the left temporal fossa	Recurrence	Multiple bilateral pulmonary nodules
Teague et al., 2005 [9]	64	Male	Atypical meningioma, WHO grade II at the biparietal lobe	Recurrence	Multiple bilateral lung masses
D'Aiuto et al., 2005 [10]	71	Male	Meningioma, WHO grade I at right temporo-occipital lobe	Recurrence with malignant transformation (Atypical meningioma, WHO grade II)	Multiple bilateral pulmonary nodules
Erman et al., 2005 [11]	34	Female	Meningotheliomatous meningioma, WHO grade I in the left parasagittal area	Recurrence and malignant transformation (Atypical meningioma, grade II)	Multiple metastases
Fabi et al., 2006 [12]	57	Female	NA	Intracranial recurrence at the same site but no report of grading of meningioma	Multiple bilateral pulmonary nodules with rib metastasis
Psaras et al., 2009 [13]	65	Female	Meningothelial meningioma, WHO grade I at falx cerebri and superior sagittal sinus	Residual tumor but no recurrence.	Multiple metastases
Frydrychowicz et al., 2015 [14]	72	Female	Atypical meningioma, WHO grade II at the bi-occipital lobe	Recurrence (Atypical meningioma, WHO grade II)	Solitary mass in the right lung
Frydrychowicz et al., 2015 [14]	45	Female	Atypical meningioma, WHO grade II at the biparietal lobe	Recurrence (Atypical meningioma, WHO grade II)	Multiple small tumor nodules
Mutnuru et al., 2015 [15]	30	Male	Fibroblastic meningioma, WHO grade I at the right frontal lobe	Intracranial recurrence with malignant transformation (Anaplastic meningioma, WHO grade III)	Multiple bilateral pulmonary lesions
Wang et al., 2016 [16]	56	Male	Atypical meningioma, WHO grade II at the left occipital lobe	Recurrence at the same site	Multiple lesions at the right pulmonary lobe
Honda et al., 2017 [17]	3	Male	Anaplastic meningioma, WHO grade III.	Recurrence at the same site	Solitary mass with pleural effusion in the right lung
Enomoto et al., 2019 [18]	65	Male	Fibrous meningioma, WHO grade I at the occipital lobe with sinus invasion	Recurrence at the same site	Solitary pulmonary metastasis
Utsumi et al., 2022 [19]	75	Male	Atypical meningioma, WHO grade II at the left parietal lobe	Recurrence at the same site	Solitary pulmonary metastasis

NA: Not Applicable; WHO: World Health Organization.

of meningioma and 80% of this biomarker is positive in meningioma [4]. In the present case, EMA was expressed in both intracranial and lung lesions that confirmed metastasis of meningioma.

We reviewed cases of intracranial meningioma with pulmonary metastasis from the literature. The characteristics of the patients, intracranial meningioma, and pulmonary metastases are summarized in Table 1 [5-19]. This rare scenario is more frequently observed in the fifth-to-seventh decades of life, and tumors are usually located in the parasagittal region. Histological diagnosis of intracranial meningioma was equally observed for both benign and malignant tumors after the first surgery. The disease relapses in most cases; however, malignant transformation is an uncommon presentation. The present case had recurrent disease with malignant transformation and distant metastasis, which is in concordance with other prior reports [10, 11, 15]. Additionally, the majority of pulmonary metastasis cases involve multiple bilateral metastases.

The pathogenesis for distant metastasis of meningioma has been inconclusive. Frydrychowicz et al. reported two patients with atypical meningioma and pulmonary metastasis with a deletion of chromosomes 1p and 22 by cytogenetic analysis [14]. In the era of translational medicine, various biomarkers have been studied in genetic alteration for an explanation [20, 21]. The C-X-C chemokine receptor type 4/C-X-C motif chemokine ligand 12 (CXCR4/CXCL12) axis has been discussed for the metastasis ability of malignant tumor cells [20, 22]. Zagzag et al. [22] studied the CXCR4/CXCL12 axis that involved migration and metastasis of glial cell tumors. In addition, no association is reported among *NF2*, *CDKN2A*, *BAP1*, *ARID1A*, and *TP53* mutations between disseminated and non-disseminated meningiomas [23].

Higher grade, more frequent metastasis has been found in the literature review. The incidence of extracranial metastatic meningioma grade I ranged from 3.6-29.3%, grade II ranged from 6.8-57.1%, and grade III ranged from 39.3-63.9% according to prior studies [1, 2]. The present case was initially diagnosed with meningothelial meningioma, WHO grade I with malignant transformation to atypical meningioma. Finally, extracranial metastasis developed into multiple pulmonary metastases.

Nakasu et al. [24] conducted a systematic review and meta-analysis of malignant transformation in benign meningioma and found that the incidence rate of malignant transformation of meningioma was 2.98/1000 patient-years (95% confidence interval 1.9–4.3) and non-skull-based meningioma had a higher proportion of this event than skull-based meningioma. However, the molecular mechanism of malignant transformation has remained under investigation.

Shao et al. [25] reviewed the pathogenesis for malignancy development of meningioma, which is closely related to the chromosomal variations and abnormal molecular signals involved, as follows: chromosomal loss of 1p, 6q, 10, 14q, and 18q and gains at 1q, 9q, 12q, 15q, 17q, and 20q. Meanwhile, Tunthanathip et al. investigated the whole-genome sequencing of five patients with low-grade glioma who developed malignant transformation and proposed the hypothesis that alterations of various genes, such as *IDH 1*, *KMT2C*, and *GGT1* may be involved in the processes of malignant transformation of glioma [20, 26, 27].

Because distant metastasis of this tumor is rare, there is no standard treatment for metastatic meningioma; chemotherapy is the only alternative treatment. The prognosis for patients with metastasis is poor; a previous study reported that patients with metastatic meningioma were significantly associated with a poor prognosis compared to patients without metastasis [2]. Moreover, the median survival time for patients with metastasis was 35 months (Interquartile Range [IQR] 8–69), while patients without metastasis had a median survival time of 50 months (IQR, 25–84) [2].

4. Conclusion

In summary, we presented a case of pulmonary metastatic meningioma that developed malignant transformation before distant metastasis. Further study of the genetic alteration should be conducted in the future for the pathogenesis of both malignant transformation and extracranial metastasis.

Ethical Considerations

Compliance with ethical guidelines

Informed consent was obtained from the patient for publication.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization and design: Kanisorn Sungkaro, Sakchai Sae-heng; Data collection: Kanisorn Sungkaro; Data analysis and interpretation: Kanisorn Sungkaro, Sakchai Sae-heng; Drafting the article: Kanisorn Sungkaro; Critically revising the article: Kanisorn Sungkaro, Sakchai Sae-heng; Reviewing submitted version of manuscript: Kanisorn Sungkaro, Sakchai Sae-heng; Approving the final version of the manuscript: Kanisorn Sungkaro, Sakchai Sae-heng.

Conflict of interest

The authors declared no conflict of interest.

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