Metastasis of pulmonary adenocarcinoma to right occipital parafalcine meningioma
A case report and literature review

Tianhao Hu, MDa, Run Wang, MDa, Yifu Song, MDa, Juanhan Yu, MDb, Zongze Guo, MDa, Sheng Han, MD, PhDa, *

Abstract
Rationale: Tumor-to-tumor metastasis is a rare clinical phenomenon. Although meningioma is the most common intracranial recipient of cancer metastasis, only a few cases have been reported. We present a case of metastasis of lung adenocarcinoma into intracranial meningioma and review the published literature.

Patient concerns: A 70-year-old woman was admitted to our hospital for a 1-month history of headache and pain in her lower extremities.

Diagnosis: Brain and lumbar vertebral magnetic resonance imaging showed an intracranial space-occupying lesion in the right occipital region and spinal canal stenosis. Pulmonary computed tomography showed an irregular mass in the right upper lobe of the lung. The postoperative histological examination demonstrated adenocarcinoma metastasis to meningioma.

Intervention: The patient underwent right occipital craniotomy for tumor removal and lumbar spinal canal decompression.

Outcomes: There were no initial abnormal conditions after the operation. However, the patient died suddenly 7 days after surgery.

Lessons: Tumor-to-meningioma metastasis is a rare but important phenomenon. According to previous reports, it is associated with rapid onset of symptoms and a poor prognosis. Histological examination is of great importance in diagnosis. The history and process of malignant carcinoma should be closely monitored.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, TMM = tumor-to-meningioma metastasis, TTM = tumor-to-tumor metastasis.

Keywords: lung carcinoma, meningioma, tumor-to-tumor metastasis

1. Introduction
Metastasis from one tumor to another is known as tumor-to-tumor metastasis (TTM), which is a rare phenomenon.[1] Meningioma, which constitutes 20% of intracranial tumors, is the most common intracranial recipient of systemic metastases.[2] Breast and lung carcinomas are the most common origins of TTM.[2,3] Because there have been few reported cases of metastasis to meningioma, the clinical characteristics of such patients are still unclear. According to previous reports, patients suffering from TTM have an extremely poor prognosis. Therefore, the accumulation of such cases is clinically relevant. Here, we report a case of lung adenocarcinoma metastasizing to meningioma.

2. Case report
This study was approved by the institutional review board at The First Hospital of China Medical University. Written consent was obtained from the patient’s relatives for publication of this report.

A 70-year-old woman was admitted to our institution with headache and pain in her lower extremities for 1 month, with the left side being more severe. Brain and lumbar vertebral magnetic resonance imaging (MRI) at the local hospital suggested an intracranial space-occupying lesion and spinal canal stenosis. Recently, she had suffered from pain in her waist and both hips and experienced laborious defecation. The patient had no history of smoking or drinking. She had grade 1 hypertension but no diabetes. We performed brain contrast-enhanced MRI and lumbar vertebral (L1–S1) 3-dimensional computed tomography (3D-CT). Brain MRI showed a well-circumscribed mass (4.5 ×
3.6 × 4.7 cm) that had isointense signals on T1-weighted images and isointense signals with heterogeneity on T2-weighted image in the right occipital parafalcine region (Fig. 1A). Lumbar vertebral 3D-CT showed L3–S1 intervertebral disc bulge, ligamentum flavum thickening, and spinal canal stenosis. Lumbar CT showed an irregular mass in the upper lobe of the right lung (3.6 × 3.3 cm), bone destruction in the bilateral ribs, inflammation in the lower field of both lungs, and pleural effusion, which suggested a malignant lesion derived from the lung (Fig. 1B). Comprehensive analysis of pulmonary function showed mixed ventilation dysfunction, small airway dysfunction, and a ventilation reserve of 89%. Following the advice of a respiratory physician, the patient underwent atomization inhalation treatment with ipratropium bromide aerosol, budesonide suspension, and ambarroxol hydrochloride for inhalation during the perioperative period. According to the imaging examination, the preoperative diagnosis of the patient was lung cancer, lumbar spinal stenosis, and right occipital meningioma or metastatic tumor. Although lung biopsy was recommended, the patient refused.

Subsequently, the patient underwent right occipital craniotomy for tumor removal (Simpson grade II resection) and lumbar spinal canal decompression. Postoperative brain CT revealed normal postoperative changes, and the tumor was totally removed (Fig. 2A). There were no initial abnormal conditions after the operation. However, the patient died suddenly of a cardiopulmonary accident 7 days after surgery. Due to the rapid deterioration of the patient, treatment for the lung lesion was not performed.

Immunohistochemically, the brain tumor stained positive for epithelial membrane antigen (EMA), progesterone receptor (PR), vimentin, and E-cadherin (Fig. 2B) and negative for glial fibrillary acidic protein (GFAP), S-100, p53, and oligodendrocyte transcription factor 2 (Olig2), which was consistent with WHO grade I meningioma. The focus within the meningioma stained positive for cytokeratin 7 (CK7) and thyroid transcription factor 1 (TTF-1; Fig. 2B) and negative for CK5/6, p63, CD56, and synaptophysin. TTF-1 and CK7 are markers expressed in adenocarcinoma of lung. Histologically, the brain tumor was psammomatous meningioma characterized by numerous psammoma bodies (Fig. 2C, yellow arrow). Furthermore, there were hyperchromatic nuclei and prominent nucleoli cancer cells (Fig. 2C, red arrow) among meningioma cells (Fig. 2C, white arrow), which was consistent with metastatic carcinoma. The adenocarcinoma cells showed dense papillary hyperplasia with nuclear atypia (Fig. 2C, red arrow). Therefore, histopathological examination demonstrated adenocarcinoma metastasis to meningioma (Fig. 2C). Immunohistochemical and histopathological examinations were performed and reported by the Department of Pathology at China Medical University.

3. Discussion

TTM is a rare and well-recognized phenomenon.[4,5] The most common malignant recipient tumor is renal cell carcinoma.[1,2] Meningiomas are the most common benign tumors to harbor systemic metastases,[6] but tumor-to-meningioma metastasis (TMM) has rarely been reported since the first case reported by Fried in 1930.[7–9] To the best of our knowledge, there are fewer than 30 reports of lung carcinoma metastasis to meningioma.[3–5,7,10–34] The epidemiology of TMM is still unknown. From January 2011 to January 2019, there were 2922 consecutive patients diagnosed with meningioma and 540 consecutive patients diagnosed with intracranial metastatic tumor at the Department of Neurosurgery at The First Hospital of China Medical University. There was only 1 TMM patient, accounting for 0.03% of meningioma and 0.19% of intracranial metastasis cases.

For diagnosis of TTM, Campbell et al proposed the following criteria: at least 2 primary tumors must exist, the metastatic focus must show established growth inside the host tumor and not be of contiguous growth, and the host tumor must be a true neoplasm and cannot be a lymph node involved in leukemia or lymphoma.[1,33] Our case fulfilled the inclusion criteria for TTM established by Campbell et al. Previous studies presented different hypotheses related to the reasons why meningioma is the
most common intracranial host in TTM. Meningiomas can provide an accessible and favorable environment for growth to receive metastases\(^ {19} \) because they are highly vascular tumors\(^ {36} \) and exhibit slow growth and an indolent nature.\(^ {19,37} \) Furthermore, their high collagen and lipid content may provide a “fertile soil” for the seeding of malignant cells.\(^ {6,19,20,38} \) Some researchers have suggested that cell–cell adhesion molecules, such as E-cadherin,\(^ {39,40} \) may play a role in TMM.\(^ {2,26,38,39} \) E-cadherin expression is downregulated when carcinoma cells escape from the primary tumor.\(^ {41} \) Metastatic cells resume E-cadherin expression upon seeding their destination.\(^ {14} \) It has been demonstrated that meningiomas highly express E-cadherin.\(^ {40,42} \) Moreover, meningiomas harboring metastases are more likely to express E-cadherin than meningiomas in general.\(^ {6} \) Therefore, the above evidence reveals that E-cadherin may play a role in TMM. Consistent with previous reports, in the present case, the tumor also exhibited high expression of E-cadherin, as demonstrated by immunohistochemistry (Fig. 2B). However, the relationship and underlying mechanism between E-cadherin and TMM requires further research. Psammoma bodies are concentric whorl calcification structures that exist in 45% of meningiomas.\(^ {43} \) The possible protective role of psammoma bodies in the spread of TMM has been discussed in previous reports,\(^ {11,22} \) and the meningioma in our case was rich in psammoma bodies.

We summarize the published lung carcinoma TMM cases in Table 1 and immunohistochemical results in Table 2. The mean age of patients was 65.03 years (range, 39–91 years), and there were 15 women and 14 men among the published cases (female: male = 1.07:1). According to the available immunohistochemical results of published cases, the meningioma components were often positive for EMA, PR, and vimentin (except for 1 case of secretory meningioma), and the pulmonary carcinoma components were frequently positive for TTF-1 and CK7. All the cases were supratentorial lesions. Except for 1 case of atypical meningioma, the others were benign meningiomas. The most common type of lung carcinoma was adenocarcinoma (69.0%). Most of them were discovered by chance at surgery or autopsy and had the feature of a previously existing malignant tumor. However, cases of TMM of occult lung malignant tumors have
## Table 1

### Summary of cases of lung carcinoma metastasis to intracranial meningioma.

| References          | Age  | Sex | Symptom                                                   | Size of meningioma (cm) | Psammoma bodies | Type of meningioma | Location of meningioma | Type of lung carcinoma | Two tumors discovered concurrently | Surgery                                                                 | Postoperative therapy | Survival time |
|---------------------|------|-----|-----------------------------------------------------------|-------------------------|-----------------|--------------------|-----------------------|-------------------------|-----------------------------------|-------------------------------------------------------------------------|----------------------|--------------|
| Fried et al., 1960  | 57   | F   | Pain in the lumbar region and left leg, inability to walk | 2                      | +               | Meningothelial     | Right frontal lobe   | Adenocarcinoma          | No                                 | No                                                                      | None                 | 2 mo         |
| Osterberg et al., 1967 | 71   | M   | Generalized weakness and loss of appetite, loss of weight  | 5 × 3 × 2.5             | +               | NA                 | Left frontoparietal   | Paranglioma             | Yes                              | None                                                                      | None                 | 4 mo         |
| Best et al., 1963   | 48   | M   | Headache, nausea, loss of appetite                        | 3 × 2 × 2               | +               | Meningothelial     | Right temporal lobe  | Squamous cell carcinoma | Yes                              | Cranectomy for meningioma with metastatic carcinoma | Radiotherapy         | 70 d         |
| Wilson et al., 1966 | 39   | M   | A single generalized seizure 1 mo earlier                 | 6 × 6 × 5               | +               | Meningothelial     | Bilateral surrounding | Adenocarcinoma          | Yes                              | Cranectomy for meningioma with metastatic carcinoma | None                 | NA           |
| Wolintz and Matri, 1970 | 64   | M   | NA                                                        | NA                      | +               | Psammomatous       | Sphenoid ridge       | Adenocarcinoma          | NA                               | NA                                                                      | NA                   | NA           |
| Gyor et al., 1976   | 69   | F   | Fainting and dizziness                                    | 5 × 3 × 2               | +               | Transitional       | Parasagittal         | Carcinoma              | No                               | No                                                                      | None                 | 6 d          |
| Weems and Gardner, 1977 | 68   | F   | Hemiparesis                                               | 2 × 2 × 1               | +               | Meningothelial     | Sphenoid wing        | Adenocarcinoma          | No                               | No                                                                      | None                 | 40 d         |
| Hope and Symon, 1979 | 61   | F   | Tiredness and lethargy for 3 weeks, diplopia for 10 d     | NA                      | +               | Meningothelial     | Sphenoid ridge       | Adenocarcinoma          | Yes                              | Cranectomy for meningioma with metastatic carcinoma | None                 | 30 h         |
| Chambers et al., 1980 | 72   | M   | Shortness of breath and hemoptysis                          | 2.5                    | 5               | Meningothelial     | Left frontoparietal   | Small cell carcinoma    | No                               | Died                                                                     | None                 | NA           |
| Lodris and Savianto, 1981 | 59   | M   | Headache and right subarachnoidic pain on inspiration for 3 weeks | NA                      | +               | Fibrous            | Right parietal        | Adenocarcinoma          | No                               | No                                                                      | None                 | 2 mo         |
| Smith et al., 1981  | 65   | F   | Increasing shortness of breath, hemiparesis, dyspnea, and fatigue of 4 weeks | 2 × 2 × 1.5             | 5               | Fibrous            | Right frontal lobe   | Malignant carcinoid     | No                               | None                                                                     | None                 | 16 d         |
| Schmidt, 1984       | 60   | M   | Episodic headache and occasional grand-mal seizures       | NA                      | 5               | Angiomatous        | Left frontoparietal   | Paranglioma             | Yes                              | None                                                                      | None                 | 2 mo         |
| Pamphlett, 1984     | 79   | M   | Increasing cough and shortness of breath for 1 mo, confusion for 1 week | 3 × 2.5 × 2.5           | 5               | Angiomatous        | Left fronto temporal  | Adenocarcinoma          | Yes                              | None                                                                      | None                 | 2 weeks      |
| Conran et al., 1986 | 69   | M   | Progressive right hemiparesis                              | 2.7 × 2.3 × 1.3         | 5               | Mixed              | Left frontoparietal   | Paranglioma             | No                               | Pneumonectomy for lung carcinoma (6 mo before), cranectomy for meningioma with metastatic carcinoma | None                 | NA           |
| Arnold et al., 1995 | 71   | F   | Progressive visual loss                                    | 2.3                    | +               | Meningothelial     | Optic nerve sheath   | Adenocarcinoma          | No                               | Pneumonectomy for lung carcinoma (1 yr before)                          | None                 | 9 mo         |
| Gardiman et al., 1996 | 62   | M   | NA                                                        | NA                      | 6               | Transitional       | None                  | None                    | NA                               | None                                                                      | None                 | NA           |
| Bhargava et al., 1999 | 52   | M   | Recurrent left-sided seizures accompanied by progressive weakness in the left extremities | 5 × 3.5                | 5               | Transitional       | Right paranglioma     | Adenocarcinoma          | Yes                              | Cranectomy for meningioma with metastatic carcinoma | Radiotherapy         | 3 mo         |
| Cserni et al., 2002 | 48   | F   | Severe headache with 2 weeks onset                        | 2                      | 5               | Transitional       | Right temporal lobe   | Adenocarcinoma          | No                               | Labectomy for lung carcinoma (4 mo ago), cranectomy for meningioma with metastatic carcinoma | Radiotherapy         | NA           |
| Takei and Powell, 2009 | 69   | F   | Headache and altered mental status                         | 3.7                    | 5               | Microcystic        | Left temporal lobe    | Adenocarcinoma          | No                               | Chemotherapy, radiotherapy | NA                   |
| Kim et al., 2013    | 71   | F   | Left arm weakness for 3 weeks                              | NA                      | +               | Fibrous            | Right frontal lobe    | Adenocarcinoma          | No                               | Chemotherapy               | NA                   |

(continued)
| References                  | Age | Sex | Symptom                                           | Size of meningioma (cm) | Psammoma bodies | Type of meningioma | Location of meningioma | Type of lung carcinoma | Two tumors discovered concurrently | Surgery                                      | Postoperative therapy | Survival time |
|-----------------------------|-----|-----|--------------------------------------------------|-------------------------|------------------|--------------------|----------------------|------------------------|-------------------------------|---------------------------------------------|-----------------------|---------------|
| Glass et al. [36] 2013      | 57  | M   | Mental status change, ataxia and 20 pound weight loss | 5.1                     | --               | Meningothelial     | --                   | Adenosquamous carcinoma   | Yes                           | Craniotomy for meningioma with metastatic carcinoma | Radiotherapy           | NA            |
| Chatani et al. [27] 2014    | 74  | F   | Amnesia and abnormal gait                        | 3                       | --               | Meningothelial     | Falcotentorial        | Adenocarcinoma           | No                            | Craniotomy for meningioma with metastatic carcinoma, lobectomy for lung carcinoma | None                  | NA            |
| Talukdar et al. [28] 2014   | 65  | M   | Focal seizure involving right side of body for 3 h | 2.9 × 1.8 × 1.7         | + NA             | NA                 | Left parietal parasagittal | Adenosquamous carcinoma   | Yes                           | Craniotomy for meningioma with metastatic carcinoma | None                  | NA            |
| Hampel et al. [29] 2015     | 69  | F   | Loss of weight and fatigue                       | NA                      | + Meningothelial  | Sphenoid wing      | Adenosquamous carcinoma | Yes                    | Craniotomy for meningioma with metastatic carcinoma | Chemotherapy, radiotherapy | NA            |
| Ranik et al. [28] 2015      | 77  | F   | Rigid deterioration of left-sided hemiparesis, headache and nausea | 3                       | --               | Angiomatous         | Right parietal parasagittal | Adenosquamous carcinoma   | No                            | Craniotomy for meningioma with metastatic carcinoma | None                  | NA            |
| Nadeem et al. [31] 2016     | 68  | F   | Progressively worsening right-sided hemiparesis and multiple episodes of adult onset epilepsy | NA                      | --               | NA                 | Left frontal lobe      | Adenosquamous carcinoma   | No                            | Craniotomy for meningioma with metastatic carcinoma | Chemotherapy, radiotherapy | 6 mo          |
| Schall et al. [32] 2018     | 61  | M   | Worsening dysmetria, unintentional weight loss and poor exercise tolerance | NA                      | --               | Meningothelial     | Right parietal parasagittal | Adenosquamous carcinoma   | Craniotomy for meningioma with metastatic carcinoma | Chemotherapy, radiotherapy | NA            |
| Nakaya et al. [33] 2019     | 91  | F   | Right limbs weakness and gait disturbance         | 3                       | --               | Meningothelial     | Left frontal lobe      | Adenosquamous carcinoma   | No                            | Hysterectomy for metastatic lung carcinoma (2 mo before), craniotomy for meningioma with metastatic carcinoma | None                  | NA            |
| Danisman Specialist et al. [34] 2019 | 70  | M   | Oligemia                                         | 2.5                     | --               | Atypical            | Left frontal lobe      | Small cell carcinoma      | NA                            | Craniotomy for meningioma with metastatic carcinoma | None                  | NA            |
| Our case                    | 70  | F   | Headache and lower extremities pain              | 4.5 × 3.6 × 4.7          | + Psammomatous   | Right occipital parafalcine | Adenosquamous carcinoma   | Yes                           | Craniotomy for meningioma with metastatic carcinoma | None                  | 7 d           |

F = female, M = male, NA = nonassessed.
Table 2

| No. | Reference | Histopathology | Lung carcinoma | Immunohistochemistry | Meningioma | Immunohistochemistry |
|-----|-----------|----------------|---------------|----------------------|------------|---------------------|
| 1   | Cserni et al, [24] 2002 | Adenocarcinoma | CK20, Vimentin, ER | EMA, CEA, CK7, CK, PR | NA | NA |
| 2   | Takei and Powell, [25] 2009 | Adenocarcinoma | NA | EMA, Ki-67:1% | Inhibin-alpha, CK | NA |
| 3   | Kim et al, [26] 2013 | Adenocarcinoma | NA | EMA, Vimentin | NA | NA |
| 4   | Glass et al, [3] 2013 | Adenosquamous carcinoma | NA | CK, GFAP, S-100 | Adenocarcinoma | CK7, TTF-1 |
| 5   | Chatani et al, [27] 2014 | Adenocarcinoma | NA | EMA, Vimentin, Ki-67:3.9% | E-cadherin | NA |
| 6   | Talukdar et al, [29] 2014 | Adenocarcinoma | NA | NA | P63 | NA |
| 7   | Hamperl et al, [28] 2015 | Adenocarcinoma | NA | Vimentin | NA | NA |
| 8   | Ravnik et al, [30] 2015 | Angiomatous | NA | NA | NA | NA |
| 9   | Nadeem et al, [31] 2016 | Adenocarcinoma | EMA, Vimentin | NA | CK | NA |
| 10  | Sohail et al, [34] 2018 | Adenocarcinoma | NA | NA | TTF-1 | NA |
| 11  | Nakaya et al, [32] 2019 | Adenocarcinoma | E-cadherin | NA | CK7, Surfactant protein A, TTF-1, E-cadherin | NA |
| 12  | Our case | Psammomatous | GFAP, S-100, Vimentin | EMA, PR, Vimentin, E-cadherin | NA | NA |

CEA = carcinoembryonic antigen, CK = cytokeratin, EMA = epithelial membrane antigen, ER = estrogen receptor, GFAP = glial fibrillary acidic protein, NA = nonassessed, Olig2 = oligodendrocyte transcription factor 2, PR = progesterone receptor, TTF-1 = thyroid transcription factor 1.
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