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Metastasis of pulmonary adenocarcinoma to right occipital parafalcine meningioma

A case report and literature review

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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 family of the patient for publication of this case report and any accompanying images.

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 ×

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Informed consent was obtained from the patient's relatives for publication of this report.

The authors report no conflicts of interest.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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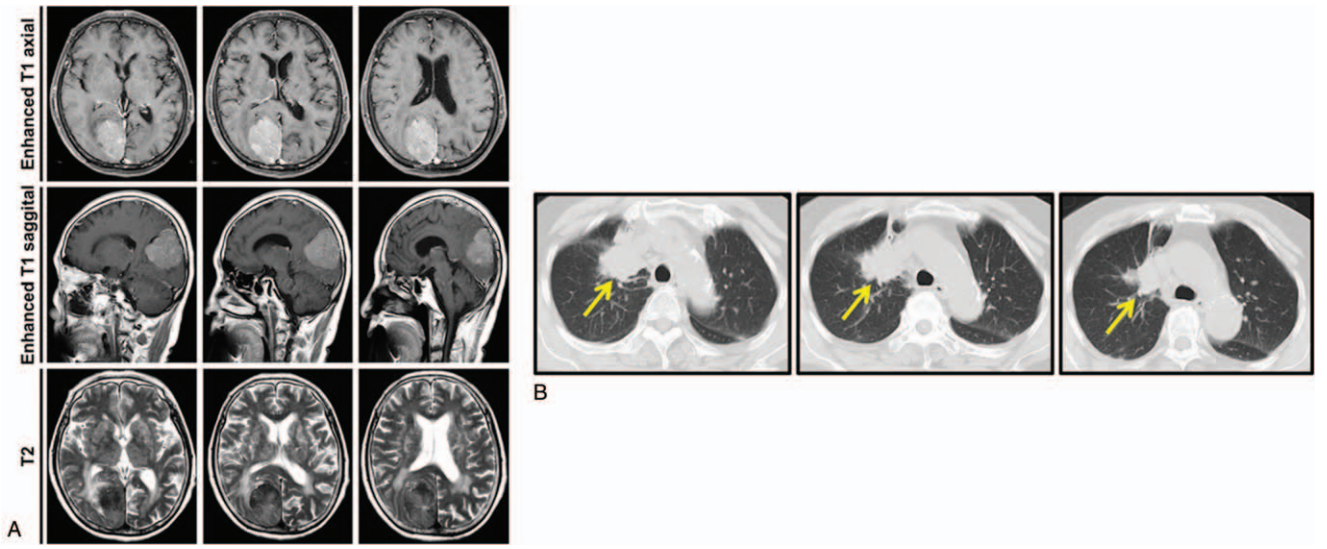

Figure 1. Imaging examinations of the brain and lungs before surgery. A, Preoperative contrast-enhanced MRI examination of the brain reveals a well-circumscribed mass (4.5 × 3.6 × 4.7 cm) in the right occipital parafalcine region. B, CT scan of the chest shows a 3.6 × 3.3 cm mass in the right upper lobe.

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. Lung 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 ambroxol 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 including 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.[1,35] 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

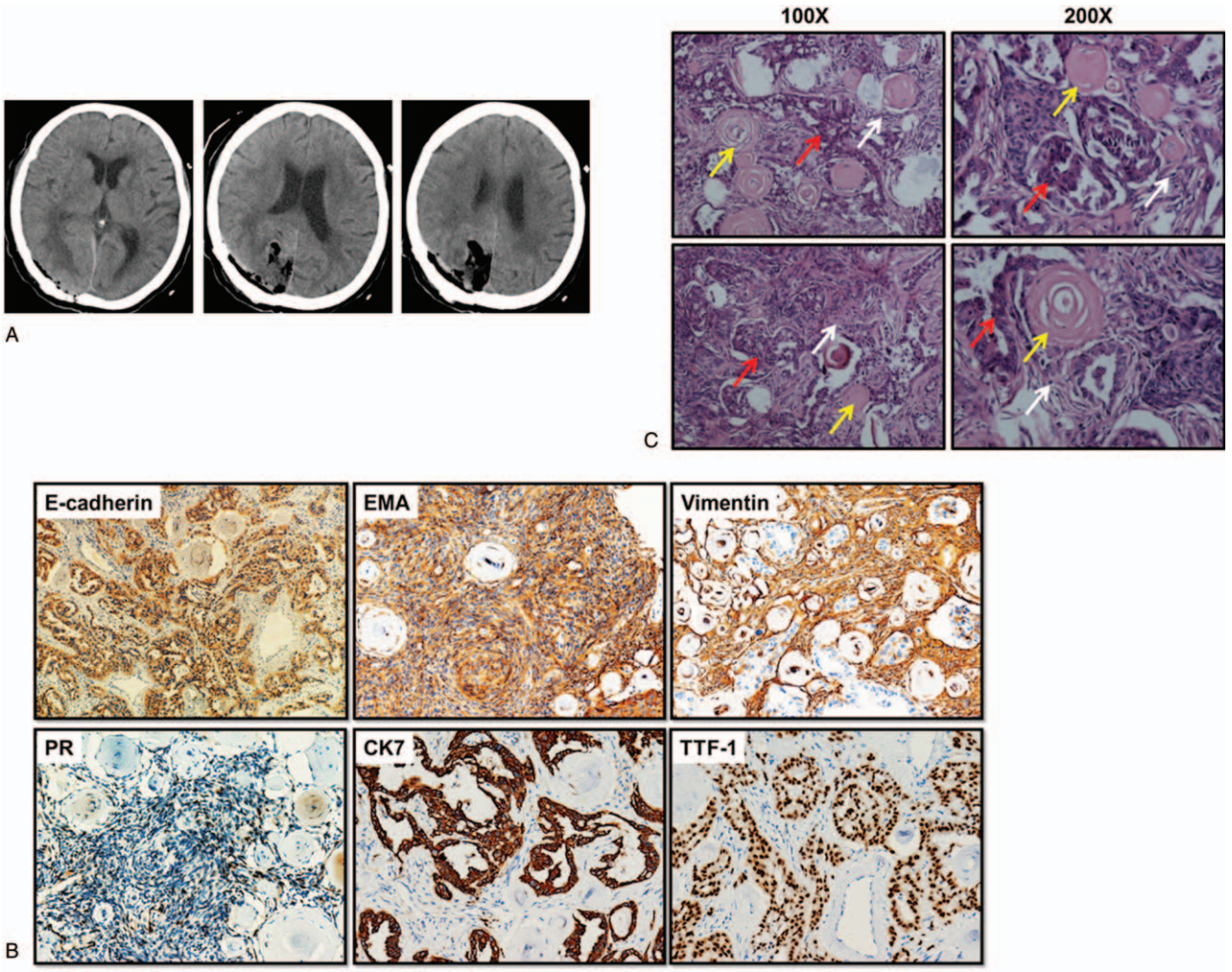

Figure 2. Postoperative CT reexamination and histopathological examination. A, Postoperative CT scan of brain shows that the tumor was totally removed. B, Immunohistochemistry showing the expression of E-cadherin, EMA, vimentin, PR, CK7, and TTF-1. C, Histopathological examination of the right occipital space occupied by the brain lesion was proved to be adenocarcinoma metastasizing to meningioma along with the presence of meningioma cells (white arrow), psammoma bodies (yellow arrow), and adenocarcinoma cells (red arrow) by hematoxylin and eosin (H&E) staining.

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,[7] 1930	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,[10] 1957	71	M	Generalized weakness and shortness of breath	5 × 3 × 2.5	+	NA	Left frontoparietal parasagittal	Carcinoma	No	No	None	4 mo
Best,[11] 1963	48	M	Headache, nausea, loss of appetite, loss of weight	3 × 2 × 2	+	Meningothelial	Right temporal lobe	Squamous cell carcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	Radiotherapy	70 d
Wilson et al,[12] 1967	39	M	A single generalized seizure 1 mo earlier	6 × 6 × 5	+	Meningothelial	Bifrontal surrounding falx	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	None	NA
Wolintz and Matri,[13] 1970	64	M	NA	NA	+	Psammomatous	Sphenoid ridge	Adenocarcinoma	NA	NA	NA	NA
Gyori,[14] 1976	69	F	Ataxia and dizziness	5 × 3 × 2	+	Transitional	Parasagittal	Carcinoma	No	No	None	6 d
Weems and Garcia,[15] 1977	68	F	Hemoptysis and right subscapular pain on inspiration for 3 weeks	2 × 2 × 1	+	Meningothelial	Sphenoid wing	Adenocarcinoma	No	Thoracotomy with lobectomy for lung carcinoma	None	40 d
Hope and Symon,[16] 1978	61	F	Tiredness and lethargy for 3 weeks, diplopia for 10 d	NA	+	Meningothelial	Sphenoid ridge	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	None	30 h
Chambers et al,[17] 1980	72	M	Shortness of breath and sputum tinged with blood	2.5	–	Meningothelial	Left frontoparietal	Small cell carcinoma	No	No	None	Died
Lodrini and Savoiardo,[18] 1981	59	M	Left hemiparesis	5	–	Fibrous	Right parietal parasagittal	Adenocarcinoma	No	Craniotomy for meningioma with metastatic carcinoma	None	2 mo
Smith et al,[19] 1981	65	F	Increasing shortness of breath, exertional dyspnea, and fatigue of 4 weeks	2 × 2 × 1.5	–	Fibrous	Right frontal lobe	Malignant carcinoid	No	No	None	16 d
Schmitt,[20] 1984	60	M	Episodic headache and occasional grand-mal seizures	NA	–	Angiomatous	Left frontoparietal parasagittal	Carcinoma	No	Craniotomy for meningioma with metastatic carcinoma	None	2 mo
Pamphlett,[4] 1984	79	M	increasing cough and shortness of breath for 1 mo, confusion for 1 week	3 × 2.5 × 2.5	–	Angiomatous	Left frontal lobe	Adenocarcinoma	Yes	No	None	2 weeks
Conzen et al,[21] 1986	69	M	Progressive right hemiparesis	2.7 × 2.3 × 1.3	–	Mixed	Left frontoparietal parasagittal	Adenocarcinoma	No	Pneumonectomy for lung carcinoma (6 mo before), craniotomy for meningioma with metastatic carcinoma	None	NA
Arnold et al,[22] 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,[23] 1996	62	F	NA	NA	–	Transitional	NA	NA	NA	NA	None	NA
Bhargava et al,[5] 1999	52	M	Recurrent left-sided seizures accompanied by progressive weakness in the left extremities	5 × 3.5	+	Transitional	Right parasagittal	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	Radiotherapy	3 mo
Cserni et al,[24] 2002	48	F	Severe headache with 2 weeks onset	2	–	Secretory	Right temporal lobe	Adenocarcinoma	No	Lobectomy for lung carcinoma (4 mo ago), craniotomy for meningioma with metastatic carcinoma	Radiotherapy	NA
Takei and Powell,[25] 2009	69	F	Headache and altered mental status	3.7	–	Microcystic	Left temporal lobe	Adenocarcinoma	No	Lobectomy for lung carcinoma (past history), craniotomy for meningioma with metastatic carcinoma	Chemotherapy, radiotherapy	NA
Kim et al,[26] 2013	71	F	Left arm weakness for 3 weeks	NA	+	Fibrous	Right frontal lobe	Adenocarcinoma	No	Lobectomy for lung carcinoma (2 yr ago), craniotomy for meningioma with metastatic carcinoma	Chemotherapy	NA

(*continued*)

Table 1

(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,[3] 2013	57	M	Mental status changer, 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,[29] 2014	65	M	Focal seizure involving right side of body for 3 h	$2.9 \times 1.8 \times 1.7$	+	NA	Left parietal parasagittal	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	None	NA
Hamperl et al,[28] 2015	69	F	Loss of weight and fatigue	NA	+	Meningothelial	Sphenoid wing	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	Chemotherapy, radiotherapy	NA
Ravnik et al,[30] 2015	77	F	Rapid deterioration of left-sided hemiparesis, headache and nausea	3	–	Angiomatous	Right parietal parasagittal	Adenocarcinoma	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	Adenocarcinoma	No	Craniotomy for meningioma with metastatic carcinoma	Chemotherapy, radiotherapy	6 mo
Sohail et al,[34] 2018	61	M	Worsening dysmetria, unintentional weight loss and poor exercise tolerance	NA	–	Meningothelial	Right parietal parasagittal	Adenocarcinoma		Craniotomy for meningioma with metastatic carcinoma	Chemotherapy, radiotherapy	NA
Nakaya et al,[32] 2019	91	F	Right limbs weakness and gait disturbance	3	–	Meningothelial	Left frontal lobe	Adenocarcinoma	No	Hysterectomy for metastatic lung carcinoma (2 mo before), craniotomy for meningioma with metastatic carcinoma	None	NA
Danisman Specialist et al,[33] 2019	70	M	Dizziness	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	$4.5 \times 3.6 \times 4.7$	+	Psammomatous	Right occipital parafalcine	Adenocarcinoma	Yes	Craniotomy for meningioma with metastatic carcinoma	None	7 d

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

Table 2

Immunohistochemical results of published lung carcinoma metastasis to meningioma.

No.	Reference	Meningioma			Lung carcinoma		
		Histopathology	Immunohistochemistry		Histopathology	Immunohistochemistry	
			Positive	Negative		Positive	Negative
1	Cserni et al,[24] 2002	Secretory	EMA, CEA, CK7, CK, PR	CK20, Vimentin, ER	Adenocarcinoma	EMA, CEA, CK7, CK	CK20, Vimentin, ER, PR
2	Takei and Powell,[25] 2009	Microcystic	EMA, Ki-67:1%	Inhibin-alpha, CK	Adenocarcinoma	CK, CK7, EMA, TTF-1	CK20
3	Kim et al,[26] 2013	Fibrous	EMA, Vimentin	NA	Adenocarcinoma	CK7, TTF-1	NA
4	Glass et al,[3] 2013	Meningothelial	EMA, Vimentin, PR, Ki-67:2%	CK, GFAP, S-100	Adenosquamous carcinoma	CK7, TTF-1	CK5/6, CK20, P63
5	Chatani et al,[27] 2014	Meningothelial	EMA, Ki-67:3.9%, E-cadherin	NA	Adenocarcinoma	CK7, TTF-1, Napsin, Alcian blue, E-cadherin	S-100, Thyroglobulin
6	Talukdar et al,[29] 2014	NA	EMA, Vimentin	NA	Adenocarcinoma	CK, TTF-1	P63
7	Hamperl et al,[28] 2015	Meningothelial	Vimentin	CK, TTF-1	Adenocarcinoma	CK, TTF-1	Vimentin
8	Ravnik et al,[30] 2015	Angiomatous	NA	NA	Adenocarcinoma	TTF-1	NA
9	Nadeem et al,[31] 2016	NA	EMA, Vimentin	CK	Adenocarcinoma	EMA, CK	Vimentin
10	Sohail et al,[34] 2018	Meningothelial	NA	NA	Adenocarcinoma	TTF-1	NA
11	Nakaya et al,[32] 2019	Meningothelial	E-cadherin	NA	Adenocarcinoma	CK7, Surfactant protein A, TTF-1, E-cadherin	CK20
12	Our case	Psammomatous	EMA, PR, Vimentin, E-cadherin	GFAP, S-100, P53, Olig2	Adenocarcinoma	CK7, TTF-1	Vimentin, CK5/6, P63, CD56, synaptophysin

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.

rarely been reported.[5,23,27,31] In our case, there were no preoperative symptoms of lung carcinoma except for an irregular mass on imaging examinations. Many authors have considered it difficult for clinicians to provide a specific preoperative diagnosis of TMM by imaging examination.[2,27,28] There are no conclusive MRI features.[25,27,28] Danisman Specialist et al suggested that perfusion MRI is an advantageous preoperative proposal for differential diagnosis of meningioma.[33]

Lung carcinoma is known to commonly metastasize to the brain, with 10% to 36% of all lung carcinomas developing brain metastasis.[44] The average survival of patients with brain metastasis is less than 6 months.[45,46] Whole-brain radiotherapy is the main treatment for brain metastases, but it is limited by long-term side effects.[47] A combination of stereotactic and whole-brain radiotherapy for brain metastases can significantly improve local control.[48] In the previous reports, 7 patients (24.1%) underwent lung lobectomy. Nineteen patients (65.5%) underwent craniotomy. In patients without early positive intervention for malignant carcinoma, the course of the disease often deteriorated quickly, and they had poor prognosis. For intracranial lesions of TMM, surgical indications are usually space-occupying effects and central nervous system symptoms. In the present case, the intracranial tumor had a maximum diameter of 4.7 cm. Based on the preoperative imaging examination, it was considered to be meningioma, although metastatic tumor could not be excluded because of the irregular mass in the lung. Therefore, surgical resection was performed. Owing to incomplete follow-up information in previous case reports and the rarity of the disease, we are unable to summarize the specific survival period. According to the data available to us, the shortest postoperative survival time is 30 hours, and the longest is 9 months. The patient in our case suddenly developed dyspnea and cardiac arrest at 7 days postoperatively. Although rescue was performed, her condition continued to deteriorate. Our patient died shortly after surgery, and since autopsy was not performed, we were unable to determine the exact cause of death. However, we should carefully assess the systemic status of patients and surgical indications, because coexistent malignancy and TMM might significantly affect patients' physical function. Therefore, aggressive surgical treatment should be carefully considered and advised. Due to the poor prognosis, it is necessary to develop an optimal management method for these superimposed malignancies.

4. Conclusion

TMM is a rare but important phenomenon. The precise mechanisms of this unique event remain undefined, and most patients have an extremely poor prognosis. Histological examination is the only diagnostic approach. The history and clinical process of TMM should be closely monitored.

Author contributions

Conceptualization: Tianhao Hu.
Funding acquisition: Sheng Han.
Investigation: Juanhan Yu.
Methodology: Sheng Han.
Resources: Run Wang, Yifu Song, Zongze Guo.
Writing – original draft: Tianhao Hu.
Writing – review & editing: Sheng Han.

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