



## Low grade intracranial meningioma presenting with pulmonary metastasis: Case report and literature review

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### ABSTRACT

Meningioma is a common neoplasm in the central nervous system. Even though most meningiomas tend to have a benign, indolent clinical course, metastasis can occur. We describe a case of a 59-year-old woman who presented with an incidental finding of multiple lung masses. The patient underwent a wedge lung excision, and a diagnosis of meningioma was rendered. Magnetic resonance imaging of the brain revealed an extra-axial mass with left transverse venous sinus involvement, supporting the diagnosis of metastatic meningioma to the lung. Metastatic meningioma can be a challenging diagnosis in a patient with no previous diagnosis of an intracranial lesion. Thus, it should be considered in the differential diagnosis when encountering a spindled cell proliferation with a whorled pattern and psammoma bodies. Positive immunohistochemical staining with epithelial membrane antigen (EMA) and vimentin may be helpful in achieving the diagnosis.

### 1. Introduction

Meningioma comprises a group of neoplasms that are derived from the meningeothelial cells of the arachnoid layer [38]. It is the most frequently reported brain tumor in the United States, accounting for 36% of all central nervous system neoplasms [11]. The median age at diagnosis is 65 years, with a female: male ratio of 2:1 [11]. The classification of meningioma is based on morphology, which portends a clinical course that can range from benign (grade I) to more aggressive with a higher recurrence rate (Grade II, atypical; Grade III, anaplastic). There are a total of 15 subtypes of meningioma in the current 2016 World Health Organization (WHO) classification [38]. The WHO grading system is also the most useful predictor of recurrence rate. Incomplete surgical resection is another factor associated with recurrence [4]. Extracranial metastasis to the lung is considered a rare event in meningioma, with a reported rate of 0.15% of all intracranial meningioma cases in a referral center [1].

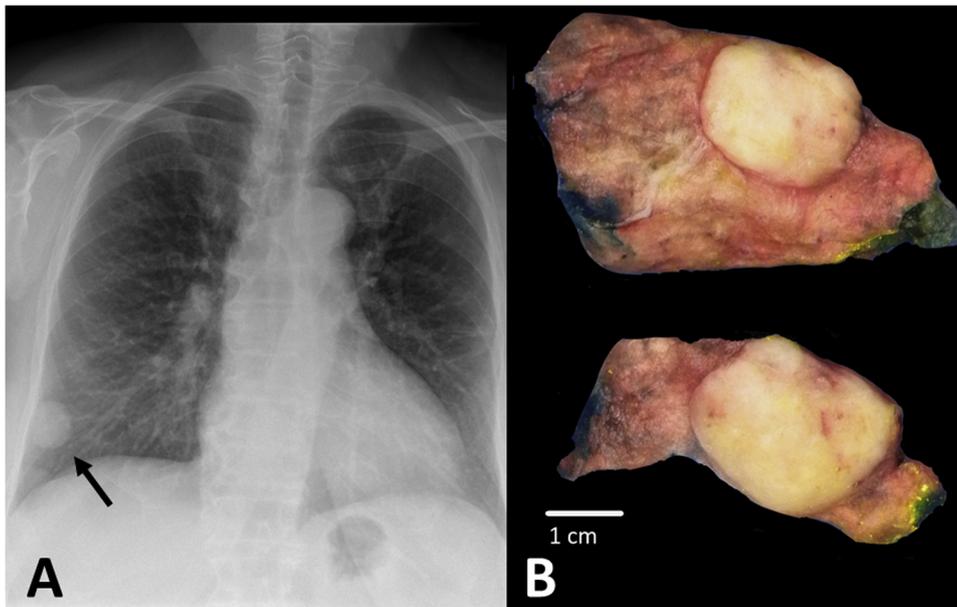
Here, we describe a case of a middle aged woman who presented with multiple lung masses and was later discovered to have an intracranial meningioma. Previous cases of metastatic pulmonary meningioma are reviewed and described.

### 2. Case report

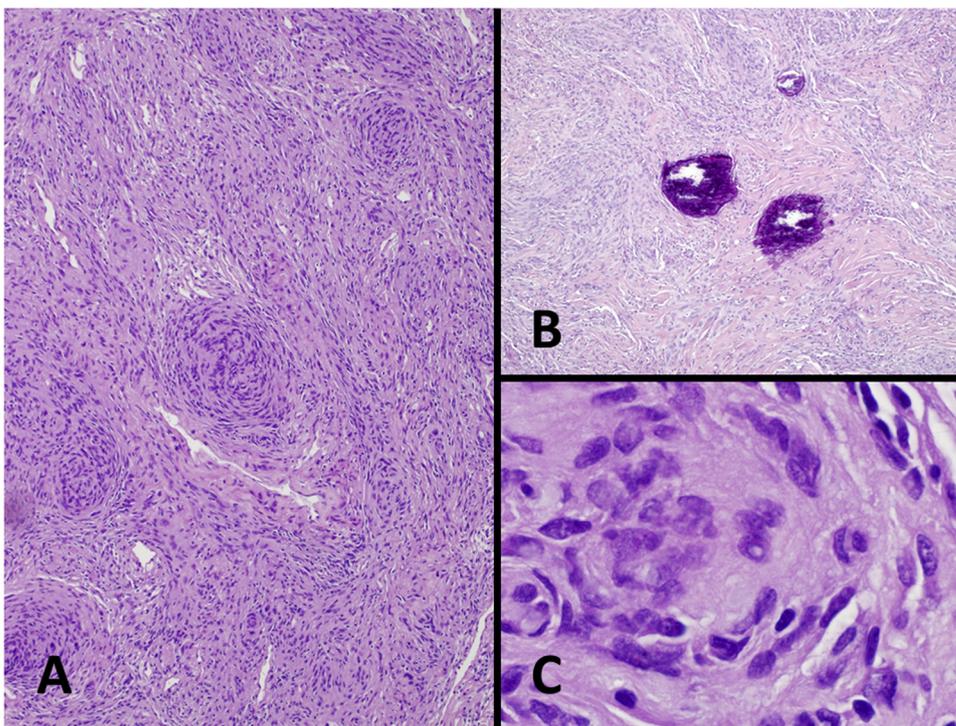
The patient was a 59-year-old woman, who presented to the emergency department with fever, chills, cough, and back pain. Complete blood count and urine exam supported the diagnosis of acute pyelonephritis. Since she had respiratory symptoms, a chest X-ray was performed, which showed a round 2.7 cm mass in the right lung (Fig. 1A). Computed tomography (CT) scan of the chest confirmed the well-circumscribed 2.7 cm nodule in the right lower lobe, as well as an additional 1.8 cm round well-circumscribed nodule in the same lobe. These findings were suspicious for metastases. CT scan of the abdomen was negative for any potential site of primary tumor. CT-guided core needle biopsy of the lung lesion was performed and a diagnosis of atypical spindle cell lesion was rendered.

The patient underwent a wedge resection of the lung nodules. On gross examination, the 2 lung nodules were characterized as tan-white, firm, lobulated masses, measuring 2.7 and 1.7 cm in greatest diameter (Fig. 1B). Microscopic examination showed well-circumscribed nodules composed of uniform spindled to ovoid cells with a whorled growth pattern and short fascicles (Fig. 2A). Multiple psammoma bodies were scattered throughout (Fig. 2B). On high power examination, the tumor cells contained abundant eosinophilic cytoplasm with focal areas of poorly-defined cell borders, imparting a syncytial appearance. The tumor cells exhibited uniform nuclei that were smooth in contour and

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**Fig. 1.** 1A, Initial chest X-ray image of the patient shows round 2.7 cm mass lesion in the right lower lung field (arrow). 1B, Cross sections of the wedge resection specimen show non-capsulated, well-circumscribed, white nodules, measuring  $2.7 \times 2.5 \times 2.0$  cm.



**Fig. 2.** 2A, Microphotograph of the tumor shows whorled growth pattern and short fascicles. 2B, Several psammomatous calcifications can be seen throughout the tumor. 2C, High power view shows proliferation of spindled cells with eosinophilic and abundant cytoplasm. The cell border was poorly-defined in some areas, showing the syncytial appearance. The tumor cell nuclei were uniform, contain delicate chromatin, and had smooth contour. Few pseudo-intranuclear inclusion is visible (hematoxylin-eosin, original magnification 100x [A], 100x [B], 1000x [C]).

containing delicate chromatin (Fig. 2C). There was no necrosis, increased mitotic activity, or marked nuclear pleomorphism. Immunohistochemical stains of the tumor cells were positive for epithelial membrane antigen (EMA) (Fig. 3A), vimentin (Fig. 3B), and progesterone receptor (Fig. 3C), while negative for desmin, S-100, and STAT6. Based on the morphology and the immunophenotypic profile, a diagnosis of meningioma with low grade features was rendered.

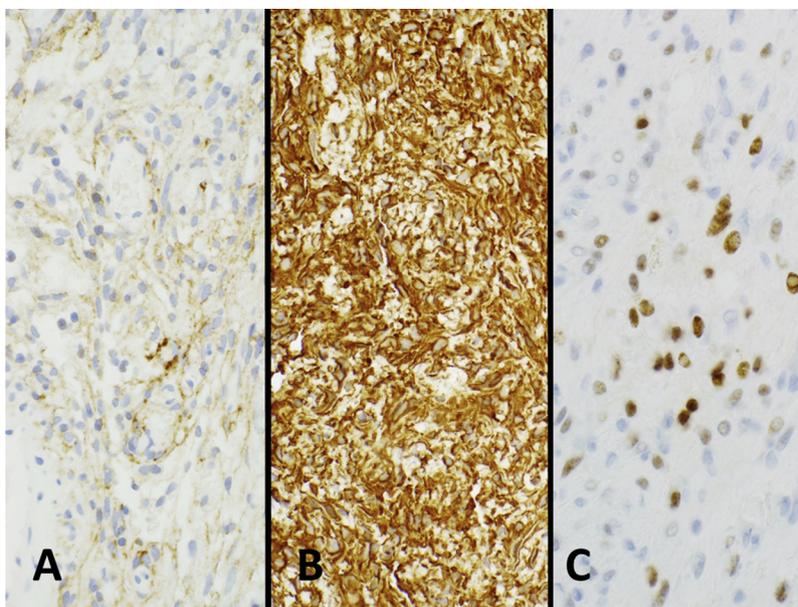
Magnetic resonance imaging (MRI) was performed to evaluate the brain for an intracranial lesion following the diagnosis of meningioma. The MRI revealed a homogeneously enhancing extra-axial mass along the left occipital convexity, measuring  $2.0 \times 1.7 \times 1.1$  cm, with invasion of the adjacent left transverse sinus (Fig. 4). Given the presence of

multiple pulmonary lesions, a presumed diagnosis of intracranial meningioma with metastases was attained.

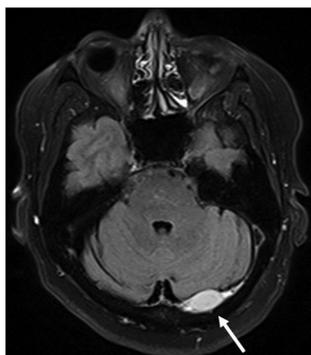
The intracranial meningioma was treated with radiosurgery gamma knife. 5 months after excision of the lung lesions, the patient has remained asymptomatic.

### 3. Discussion

Although rare, the lung was reported to be the most common site of extracranial metastasis in meningioma, consisting 35% of metastatic cases [50]. A review of the literature revealed 54 case reports of metastatic meningioma to the lungs in the PubMed database dating from



**Fig. 3.** Immunohistochemistry stains of the tumor. 3A, Epithelial membrane antigen shows membranous staining. 3B, Vimentin shows strong cytoplasmic staining. 3C, Progesterone receptor shows nuclear staining (original magnification 400x [A, B, C]).



**Fig. 4.** An MRI image of the brain showed hyperintense extra axial mass lesion on T2-FLAIR, measuring  $2.0 \times 1.7 \times 1.1$  cm (arrow), with dural tail sign along the left occipital convexity.

1985 to 2016 (Table 1). A total of 55 patients, including the current case, were analyzed. The median age at diagnosis of pulmonary metastasis was 54 years (range 13–76). There was no gender predilection (30 women, 25 men, F:M ratio 1.2). In more than half of the cases (31, 56.4%), the primary tumors were located in the fronto-parietal and parasagittal areas. Venous sinus involvement was identified in 10 cases (18.2%). The sizes of the primary tumors were available in 14 cases, ranging from 1 to 8 cm (median 5 cm). Thirty-one cases (56.4%) were considered to be grade I meningiomas. Grade II or atypical meningiomas accounted for 11 cases (20.0%). Grade III morphologies were found in 10 cases (18.2%). Data regarding the tumor grade was not available in 3 cases. Thirty-six cases (65.5%) had at least 1 recurrence of the intracranial lesion, ranging from 4 months to 18 years after diagnoses.

In most cases (42, 76.4%), the pulmonary metastases were multiple. Of those 42 cases, 29 (69.0%) presented with bilateral lungs metastasis and the remainder (31%) were unilateral; with only the right or left lung involved in 11 and 2 cases, respectively. The size of the largest metastases varied from 1 to 18 cm (median 3 cm). Approximately one-fourth of these patients (13, 23.6%) presented with a solitary lung nodule detected by imaging. The solitary nodules ranged in size from 1.3 to 5.5 cm (median 2.5 cm).

The time intervals from primary tumor diagnosis to pulmonary

metastasis were available in 51 cases. Most (41, 80.4%) were diagnosed with pulmonary metastases after the treatment of the intracranial lesion, with the interval ranging from 2 months to 26 years (median 7.5 years). Three cases (5.5%) were found to have a concurrent primary intracranial lesion. Two were diagnosed by preoperative chest X-ray [19,32], and one was discovered at autopsy [36]. In 7 cases (12.7%), the metastases were diagnosed prior to the primary intracranial lesions. These patients were found to have lung nodules incidentally by annual/routine chest x-ray in 4 cases [9,21,26,35], and 2 were diagnosed during evaluations for dyspepsia [1] and chronic cough [8]. The metastasis in the current case was also found incidentally, during evaluation for a urinary tract infection.

Even though higher grade tumors are known to be associated with increased risk of metastasis, grade I tumors comprise 56.4% of the previous reported cases. This may be due to the fact that metastatic diseases with low grade histology have a greater tendency to be reported in the literature. Several investigators hypothesized that venous sinus involvement and previous surgery were likely the mechanisms of extracranial metastasis [50]. However, venous sinus involvement is noted in only 18.2% of reported cases. Furthermore, 13.2% reported pulmonary metastases prior to intracranial surgery. Shaungshoti et al. also noted that 25% of their patients did not undergo surgery prior to the development of extracranial metastasis [47].

The differential diagnosis of metastatic meningioma is broad. The findings of whorled spindled cells may be seen in granulomas, or well-differentiated squamous cell carcinoma [37]. Both primary intrathoracic soft tissue neoplasms with spindled cell morphology e.g., solitary fibrous tumor, schwannoma, fibromatosis, and synovial sarcoma, along with metastatic sarcoma e.g., uterine leiomyosarcoma should be considered [37,52]. Malignant solitary fibrous tumor of the meninges (or meningeal hemangiopericytoma) should be included in the differential diagnosis of an intracranial anaplastic meningioma presenting with metastases [37]. Primary or metastatic adenocarcinoma should be the first diagnostic consideration when tumor cells have a predominantly epithelioid morphology [5]. The presence of intranuclear inclusions, nuclear grooves, and psammoma bodies also raises the possibility of a metastatic papillary thyroid carcinoma [37].

Primary extracranial meningioma is another consideration in the differential diagnosis of metastatic meningioma. They are rare and most commonly located in the head and neck region, involving the sinonasal

**Table 1**  
Prior case reports of metastatic pulmonary meningiomas.(1985–2016)

Author/year	Age	Gender	Primary intracranial meningioma			Pulmonary metastasis				
			Primary site	Venous sinus involvement	Size (cm)	Histologic type (WHO grade)	Recurrence interval (year)	Location/number of lesions	Size of the largest metastasis (cm)	Interval from primary tumor diagnosis (year)
Miller 1985 [32]	61	M	Left fronto-parietal	Superior sagittal sinus	3	Transitional (I)	-	Right lower lobe/1	2.5	Concurrent
Aumann 1986 [3]	45	F	Left frontal	N/A	N/A	Transitional (I)	5	Bilateral lungs/multiple	1	5
Stoller 1987 [50]	63	F	Left frontal	N/A	N/A	Transitional (I)	8, 18	Left lower lobe/1	1.3	18
Som 1987 [49]	50	M	Parasagittal	N/A	N/A	Meningothelial (I)	3, 4	Right lung/3	N/A	5
	53	F	Right sphenoid wing	N/A	N/A	Meningothelial (I)	4.5, 5	Bilateral lungs/multiple	N/A	5
LeMay 1989 [31]	56	F	Right temporal	N/A	5	Meningothelial (I)	2, 8, 10	Right lung/multiple	N/A	10
Fukushima 1989 [18]	40	M	Left cerebellar convexity	N/A	6	Papillary (III)	-	Bilateral lungs/9	N/A	8
Ng 1990 [36]	66	M	Left parasagittal	N/A	2.5	Transitional (I)	-	Bilateral lungs/multiple	1.5	Concurrent
Kodama 1991 [27]	61	F	Cerebellar	N/A	N/A	Fibrous (I)	-	Bilateral lungs/4	4.1	19
Tao 1991 [52]	32	F	Right frontal	N/A	N/A	Benign (I)	5, 14, 18	Bilateral lung/2	N/A	18
Hishima 1995 [21]	25	F	Right parietal	Superior sagittal sinus	5 cm	Meningothelial (I)	3	Right lung/3	4	Prior to primary
Shin 1996 [46]	53	F	Left frontal	N/A	N/A	Transitional (I)	5, 8, 9	Bilateral lungs/9	4.5	9
Murrah 1996 [33]	53	F	Left frontal	N/A	N/A	N/A	4, 7, 8	Bilateral lungs/9	4.5	8
Tworek 1997 [55]	50	F	Left temporal	N/A	N/A	Fibrous (I)	6	Bilateral lungs/multiple	N/A	6
Sironi 1997 [48]	46	M	Left parietal	Superior sagittal sinus	N/A	Meningothelial (I)	12	Right lower lobe/1	1.5	12
Adlakha 1999 [1]	17	F	Left parietal-occipital	N/A	N/A	Papillary (III)	4	Left lower lobe/1	5	6
	70	F	Left frontal parasagittal	Superior sagittal sinus	1.5	Psammomatous (I)	-	Right middle and lower lobe/2	N/A	Prior to primary
	30	M	Left parasagittal	N/A	N/A	Rhabdoid (III)	4.5, 6	Bilateral lungs/multiple	N/A	6
Baisden 1999 [5]	71	F	Right middle cranial fossa	N/A	N/A	Atypical (II)	13	Bilateral lungs/multiple	2.5	13
Kros 2000 [29]	13	M	Left posterior cranial fossa	N/A	N/A	Papillary (III)	-	Right pleura/1	N/A	1
Drummond 2000 [12]	76	M	Right fronto-parietal	N/A	N/A	Atypical (II)	8, 10	Right upper lobe/1	4	10
Kaminski 2001 [24]	68	M	Right anterior cranial fossa	N/A	N/A	Anaplastic (III)	2	Left lung/multiple	N/A	3
Kovoor 2002 [28]	40	F	Left parietal parasagittal	N/A	N/A	Meningothelial (I)	1	Left upper lobe/1	N/A	2
Pramesh 2003 [40]	29	F	Right occipital	N/A	N/A	Psammomatous (I)	-	Bilateral lungs/2	18	8, 9
Cerda-Nicolas 2003 [7]	75	M	Left frontal parasagittal	N/A	N/A	Fibrous (I)	4/12	Bilateral lungs/multiple	1.5	4/12
Knoop 2004 [26]	53	M	Right fronto-parietal	N/A	8.2	Meningothelial (I)	-	Right lower lobe/1	4.7	Prior to primary
D'Aiuto 2005 [10]	71	M	Right temporo-occipital	N/A	N/A	Psammomatous (I)	13	Bilateral lungs/multiple	5	7
Erman 2005 [13]	34	F	Left frontal parasagittal	N/A	N/A	Meningothelial (I)	4, 6, 8	Bilateral lungs/multiple	N/A	8
Teague 2005 [53]	64	M	Biparietal	N/A	N/A	Atypical (II)	3	Bilateral lungs/3	3	8
Yekeler 2005 [59]	43	M	Right convexity	N/A	N/A	N/A	-	Bilateral lungs/multiple	4.5	2/12
Fabi 2006 [16]	57	F	Right frontal	N/A	N/A	Anaplastic (III)	1	Bilateral lungs/multiple	3.5	1

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Table 1 (continued)

Author/year	Age	Gender	Primary intracranial meningioma			Pulmonary metastasis				
			Primary site	Venous sinus involvement	Size (cm)	Histologic type (WHO grade)	Recurrence interval (year)	Location/number of lesions	Size of the largest metastasis (cm)	Interval from primary tumor diagnosis (year)
Asioli 2007 [2]	58	F	N/A	N/A	N/A	Meningothelial (I)	-	Bilateral lungs/multiple	2.6	12
Gladin 2007 [20]	58	M	Petrous dural sinus	N/A	N/A	Fibrous (I)	13	Bilateral lungs/multiple	N/A	13
Fulkerson 2008 [19]	47	M	Right frontal	N/A	N/A	Transitional (I)	3, 9	Right lung/3	N/A	9
Ishibashi 2008 [23]	54	M	Right lateral ventricle	N/A	N/A	Fibrous (I)	-	Right lower lobe/1	2	Concurrent
Pearas 2009 [41]	68	M	N/A	N/A	N/A	N/A	-	Bilateral lungs/3	6	26
	49	F	Left parietal	Superior sagittal sinus	6 cm	Meningothelial (I)	-	Bilateral lungs/multiple	N/A	15
Estaniislau 2009 [14]	75	M	Right temporo-parietal	N/A	N/A	Atypical (II)	2, 6	Right lower lobe/1	N/A	6
Brennan 2010 [6]	74	F	Parasagittal	N/A	N/A	Atypical (II)	3, 7	Bilateral lungs/2	3.8	22
Etienne-Mastroianni 2010 [15]	58	M	N/A	N/A	N/A	Anaplastic (III)	-	Right lung/4	4.3	6
Cheng 2011 [8]	46	M	Right parietal	Superior sagittal sinus	N/A	Meningothelial (I)	-	Left and Right lower lobe/2	N/A	Prior to primary
Kanzaki 2011 [25]	67	F	N/A	N/A	N/A	Atypical (II)	4	Right lung/2	2.2	15
Sabet 2011 [44]	62	F	Left temporal	N/A	N/A	Anaplastic (III)	Multiple	Left upper lobe/multiple	N/A	N/A
Lambertz 2011 [30]	65	F	Right frontal	N/A	N/A	Atypical (II)	1, 1, 2/12	Bilateral lungs/multiple	N/A	1, 2/12
Nakano 2012 [34]	34	M	Bilateral parasagittal	Superior sagittal sinus	8 cm	Transitional (I)	1, 5	Bilateral lungs/multiple	2	4
Ocque 2014 [37]	47	M	N/A	N/A	N/A	Atypical (II)	N/A	Bilateral lungs/multiple	N/A	N/A
	44	F	N/A	N/A	N/A	Anaplastic (III)	N/A	Bilateral lungs/multiple	N/A	N/A
Nakayama 2014 [35]	25	F	Right parietal lobe	Superior sagittal sinus	5 cm	Meningothelial (I)	4, 10	Right lung/4	3	Prior to primary
Tao 2014 [51]	51	F	Right lateral ventricle	N/A	7 cm	Anaplastic (III)	1, 1, 6/12	Left lung/1	N/A	1
Chiarelli 2015 [9]	68	M	Planum sphenoidale	N/A	1 cm	Meningothelial (I)	-	Right middle lobe/1	5.5	Prior to primary
Frydrychowicz 2015 [17]	72	F	Left parieto-occipital	Occipital sinus	N/A	Atypical (II)	5, 7, 13	Middle and lower lobe/1	1.85	11
	45	F	Left frontal	N/A	N/A	Atypical (II)	3	Bilateral lungs/multiple	N/A	5
Wang 2015 [56]	54	F	Left middle cranial fossa	N/A	6	Transitional (I)	2, 6/12	Right upper lobe/multiple	N/A	2, 6/12
Wang 2016 [57]	59	M	Left occipital	N/A	5	Atypical (II)	2	Right lung/multiple	2.6	2
Current case	59	F	Left occipital	Left transverse sinus	2	Transitional (I)	-	Right lower lobe/2	2.7	Prior to primary

tract, ear, temporal bone, and scalp [43]. Primary pulmonary meningioma is a rare form of extracranial meningioma. A literature review by Incabone et al. in 2008 revealed 37 case reports of primary pulmonary meningioma [22]. All except one presented as a solitary pulmonary nodule and showed grade I morphology [22]. A case of primary pulmonary meningioma with liver metastasis has been reported [58]. Overall, there were no differences in the microscopic features of primary pulmonary meningioma and metastatic meningioma [37].

Immunohistochemistry may be a helpful ancillary tool in diagnosing metastatic meningiomas. Both primary and metastatic meningiomas typically stain with epithelial membrane antigen (EMA) and vimentin [45,54]. S-100 may be focally or weakly positive [37,45]. Cytokeratins may also be positive in meningiomas, but do not usually show strong or diffuse staining like carcinomas [37,54]. Ki-67 may be used as a prognostic marker in meningiomas. Ki-67 proliferation index of greater than 4% had an increased risk of recurrence similar to that of atypical meningioma, while an index of greater than 20% was associated with the same mortality rate as anaplastic meningioma [39]. Progesterone receptor (PR) status has been mentioned as another prognostic marker, as its absence suggested a worse outcome [42].

#### 4. Conclusion

Though rare, metastatic pulmonary meningioma should be considered when encountering a bland spindle cell proliferation with whorls and psammoma bodies. A clinical history of intracranial meningioma can corroborate the diagnosis. Expression of EMA and vimentin by immunohistochemical studies may provide further support.

#### Conflict of interest statement

The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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