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Is Primary Pulmonary Meningioma a Giant Form of a Meningothelial-Like Nodule? A Case Report and Review of the Literature

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Key Words
CD56 · Primary pulmonary meningioma · Pulmonary meningothelial-like nodule

Abstract
Minute pulmonary meningothelial-like nodules (PMNs) are asymptomatic, small nodules that are occasionally detected in surgical or autopsy specimens. Recent improvements in tumor imaging and the increased use of computed tomography (CT) scans of the chest have led to the early detection of these pulmonary nodules in various clinical settings, often before surgery or health examinations. However, large PMNs have rarely been observed. In this study, we report a patient with a large PMN, which was almost identical to so-called 'primary pulmonary meningioma'. A CT scan of his chest revealed a small, well-circumscribed nodule. Immunohistochemical analysis of the tumor revealed that the tumor cells were positive for CD56, epithelial membrane antigen, and progesterone receptor. Given the similarity of these results to the staining pattern of minute PMNs in previous reports, we suggest that the primary pulmonary meningiomas reported to date are, in fact, a giant form of PMN.

Introduction

Minute pulmonary meningothelial-like nodules (PMNs) are asymptomatic, small nodules often representing incidental microscopic findings in surgical or autopsy specimens of the lung. In recent years, minute PMNs have been detected with the

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increased use of high-resolution computed tomography (CT) scans. The clinicopathological and histological characteristics of minute PMNs have also been analyzed in several reports [1, 2]. However, large PMNs have rarely been observed.

The present case is of a 76-year-old man diagnosed with a rare, large PMN. The tumor was detected during a 3-year follow-up period after surgical resection of a primary gastric cancer. The patient was diagnosed with pulmonary metastasis from the primary gastric malignancy. Subsequently, the patient underwent a partial resection of the pulmonary nodule.

Case Presentation

The patient was a 76-year-old Japanese man with an asymptomatic left upper lung nodule. The pulmonary nodule was incidentally discovered on a CT scan of his chest, which was performed during the staging of his gastric cancer (**fig. 1**a). The patient underwent a segmental gastrectomy with lymph node dissection. Histopathological examination of the explanted stomach revealed a poorly differentiated adenocarcinoma with submucosal invasion, and no lymph node metastasis (type 2, 30 × 25 mm in size, pT1N0M0). Preoperative measurements of carcinoembryonic antigen (CEA, <0.05 ng/ml; normal value: <0.5 ng/ml) and CA19–1 (2.5 U/ml; normal value: ≤37 U/ml) levels were within normal limits.

During an annual follow-up CT scan, the pulmonary nodule was found to have increased in size from 6 to 8 mm (fig. 1b, c). Subsequently, a partial pulmonary resection of the nodule was performed. Based on the surgical specimen, the nodule was well circumscribed, 10 mm in diameter, and tan-white in color (**fig. 2**a). The specimen was fixed in neutral, buffered formalin and routinely processed by embedding tissue sections in paraffin. The sections were cut 4 μm thick and stained with H&E. Immunohistochemical stains were performed with the antibodies listed in **table 1**.

Upon further examination, the nodule was found to contain cytologically bland, rounded, and spindled cells with abundant pale eosinophilic cytoplasm, lying in dense collagenous stroma (fig. 2b, c). Scattered psammoma bodies were noted within the tumor, and no mitotic activity, cytological atypia, or necrosis was identified (fig. 2d).

The tumor cells were diffusely positive for CD56, epithelial membrane antigen (EMA), and progesterone receptor (PR, **fig. 3**a–c). The Ki-67 labeling index was 4% (fig. 3d). The cells were negative for cytokeratin, microphthalmia-associated transcription factor (MITF), human melanin black 45 (HMB45), estrogen receptor (ER), S-100, actin, thyroid transcription factor (TTF-1), anaplastic lymphoma kinase (ALK), CD34, chromogranin, and synaptophysin.

Discussion

PMNs are interstitial cellular proliferations that were first identified in 1960 [3]. To date, the exact origin and pathogenesis of these curious lesions is still unknown. Currently, PMNs are considered to be reactive and to have histological, immunohistochemical, and ultrastructural features similar to meningiomas [4]. PMNs are asymptomatic, small (100 μm to 3 mm) nodules often representing incidental microscopic findings in lung specimens [5]. Large PMNs such as the one reported in our case are rare.

Most PMNs are incidental findings of no clinical significance. The reported incidence of these nodules varies in the literature from 0.3 to 9.5% of cases at autopsy or surgical resection [5–8]. The recent development of high-resolution CT scans has provided the

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means of detecting these minute lesions. The increased use of high-resolution CT scanning has also led to the occasional detection of PMNs before surgery.

Because PMNs are microscopic lesions, it is generally rare for PMNs to be found prior to surgery. However, such tumors may be interpreted as ground-glass opacity on high-resolution CT scans [9, 10] in cases where PMNs constitute multiple lesions. Such findings often draw clinical attention. In contrast, a solitary giant nodule such as the one found in our case is quite rare. However, it is critically important to determine the appropriate clinical management of patients with these nodules before surgery of the primary malignancy [11, 12]. If the pulmonary nodules in these cases had been deemed as metastatic disease with no further pathologic correlations, options for curative surgical therapy for the primary malignancy may have been erroneously delayed or denied.

Unlike pulmonary metastases from intracranial or intraspinal meningiomas, primary pulmonary meningiomas have rarely been observed [13]. It may be difficult to distinguish PMNs from primary pulmonary meningiomas because of their morphologic similarity, with exception of their size. In a recent report, a wide range of immunohistochemical stains was performed to clarify the histogenesis of minute PMNs. The nodules were found to be positive for PR and CD56 [1, 14], in addition to the classical immunohistochemical markers, such as vimentin and EMA. The detection of PR and CD56 has potential implications for the histogenesis of minute PMNs. We suggest that primary pulmonary meningiomas reported to date are a giant form of PMN. In previous reports on solitary primary pulmonary meningiomas [13, 15–35], newer markers such as PR and CD56 had not been evaluated (**table 2**). Given the similarity of the immunohistochemical results of our case to reported minute PMNs, including the positive PR and CD56 staining [1, 14], these previously reported primary pulmonary meningiomas may include a similar disease entity. Interestingly, Ionescu et al. [5] reported that meningiomas had their own lineage-specific genetic pathways involving molecular genetic events on chromosomes 22q, 14q, and 1p, which were not shared by minute PMNs. This finding may support our hypothesis based on our findings in this study.

Conclusion

In this study, we report a rare case of a giant PMN that was almost identical to so-called primary pulmonary meningioma. In a recent report, PMNs were examined using newly developed markers, and the resulting immunophenotype was identical to that seen in this tumor. Based on the results of our study, we suggest that primary pulmonary meningioma is a giant form of PMN.

Disclosure Statement

The authors declare no competing interests.

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Table 1. Antibodies used

Antibody	Clone	Source	Dilution
CD56	123C3	Dako	Predilute
PR	SP2	Neomarkers	1/100
EMA	E29	Dako	1/50
S-100	S100	Dako	1/600
Cytokeratin	OSCAR	Signet	1/40
MITF	D51	Dako	1/50
HMB45	HMB45	Dako	1/50
ER	SP1	Dako	Predilute
TTF-1	8G7G3/1	Neomarkers	1/100
Chromogranin A	SP12	Nichirei	1/200
Actin	1A4	Santa Cruz	Predilute
ALK	5A4	Dako	1/1000
CD34	QBEND10	Dako	1/1000
Synaptophysin	SP11	Neomarkers	1/100
Ki-67	SP6	Neomarkers	1/100

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Table 2. Immunohistochemical study

References first author	Patients' age years (gender)	Tumor size, cm	Vimentin	EMA	CD56	PR	Other positive findings
Kemnitz [27]	59 (F)	4.0	NR	NR	NR	NR	NR
Chumas [16]	58 (M)	4.0	NR	NR	NR	NR	NR
Zhang [35]	58 (F)	2.5	NR	NR	NR	NR	NR
Kodama [28]	53 (M)	2.6	NR	NR	NR	NR	NR
Drlicek [20]	41 (M)	2.5	P	P	NR	NR	NR
Flynn [22]	63 (F)	3.0	P	P	NR	NR	NR
	74 (F)	1.7	P	P	NR	NR	NR
Maiorana [30]	68 (M)	1.8	P	P	NR	NR	Cytokeratins (focal)
Lockett [29]	65 (M)	0.8	NR	P	NR	NR	CEA
Kaleem [25]	45 (F)	1.2	P	P	NR	NR	NR
de Perrot [19]	57 (F)	0.9	P	P	NR	NR	NR
Spinelli [13]	71 (F)	1.5	NR	P	NR	NR	NR
Falleni [21]	59 (M)	2.5	P	N	NR	NR	S-100 (focal)
Cesario [15]	56 (M)	2.0	P	P	NR	NR	NR
Cura [18]	58 (F)	2.0	NR	NR	NR	NR	NR
Comin [17]	33 (M)	2.0	P	P	NR	P (focal)	NSE; ER (focal) S-100 (focal)
Rowsell [33]	51 (M)	4.0	P	P	NR	NR	NR
Picquet [32]	54 (F)	1.4	NR	P	NR	NR	NR
Kaneda [26]	49 (F)	1.4	P	P	NR	NR	S-100 (focal)
Meirelles [31]	48 (M)	1.5	P	P (focal)	NR	NR	NR
Incarbone [23]	24 (M)	2.4	P	P	NR	NR	NR
Izumi [24]	18 (F)	3.3	P	NR	NR	NR	S-100; CD68
Satoh [34]	74 (F)	3.0	P	P	NR	P (focal)	CD68 (focal)
Present report	76 (M)	1.0	NR	P (focal)	P	P	none

NSE = Neuron-specific enolase; P = positive; N = negative; NR = not reported.

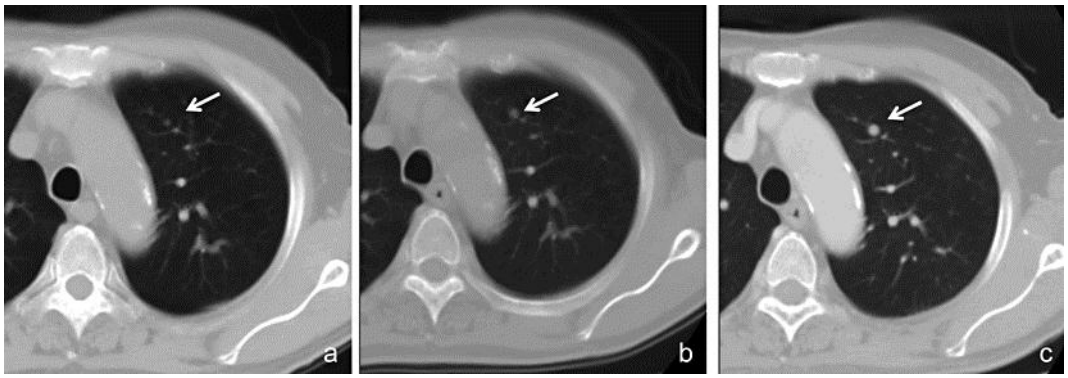

Fig. 1. Chest CT revealing a pulmonary nodule (white arrows) before surgery (**a**). In subsequent CT scans taken after 1 year (**b**) and 2 years (**c**), the nodule slightly increased in size.

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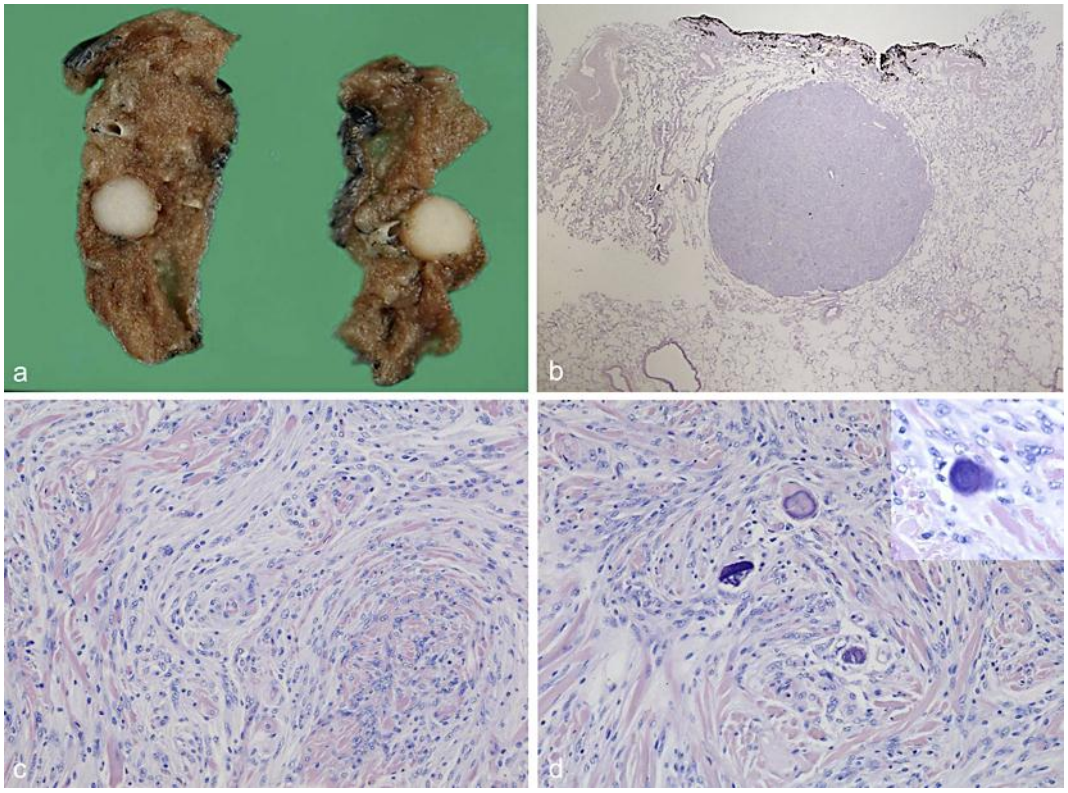

Fig. 2. Surgical specimen showing a well-circumscribed, tan-white nodule (**a**). H&E staining showing that the nodule is well circumscribed (**b**), and contains cytologically bland, rounded, and spindled cells when examined under high-power magnification (**c**). Scattered psammoma bodies are noted (**d**).

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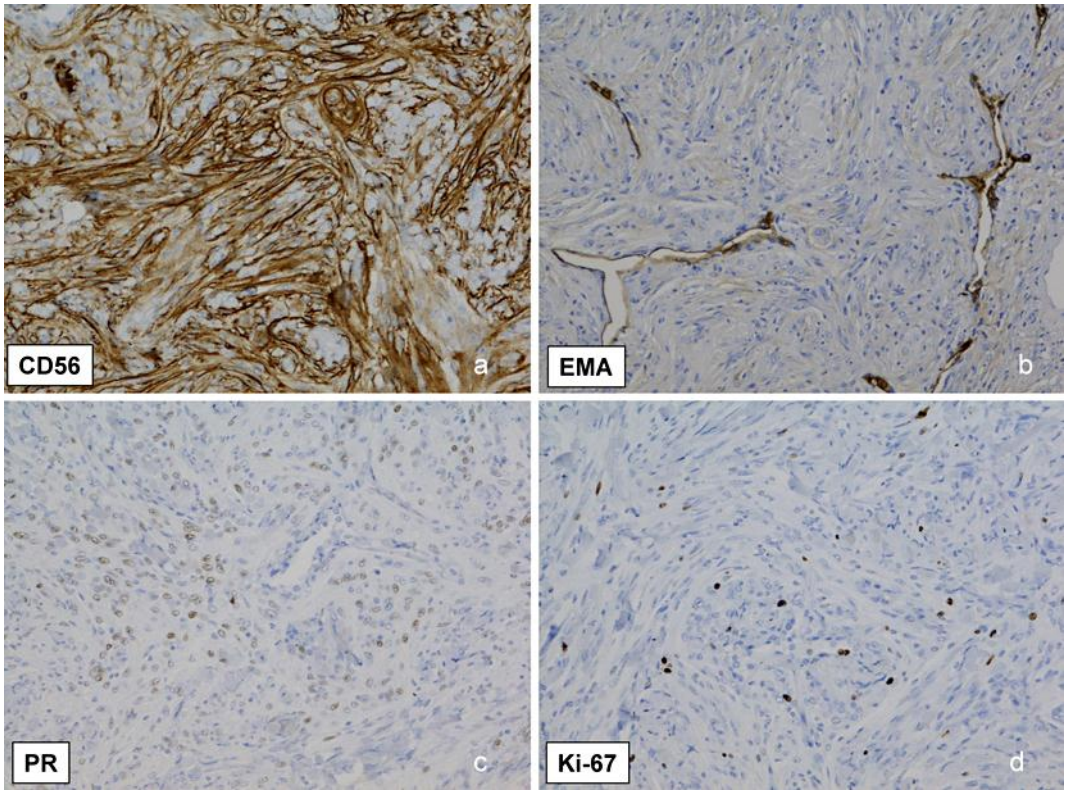

Fig. 3. High-power magnification of immunohistochemical analysis of a tumor specimen of the left lung nodule. The tumor was positive for CD56 (**a**), weakly positive for EMA (**b**), positive for PR (**c**), and the Ki-67 labeling index was 4% (**d**).

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