Received: 8 October 2018 | Revised: 5 November 2018 | Accepted: 14 November 2018

DOI: 10.1002/dc.24126

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BRIEF REPORT

Primary pulmonary meningioma: A rare case report of aspiration cytological features and immunohistochemical assessment

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Funding information
Ministry of Education, Culture, Sports, Science and Technology, Grant/Award Number: Grant-in-Aid for Scientific Research (C) (15K08373

Abstract

Ectopic meningioma is a generally rare type of benign tumor that very rarely occurs in the lung. Here, we report the cytological findings of a primary pulmonary meningioma with a particular focus on immunohistochemical (IHC) assessment. A healthy 60-year-old woman visited our hospital with an asymptomatic nodule in the right lower lung lobe. She had no particular past-history and no other tumors in the central nervous system or elsewhere according to an imaging examination. Transbronchial fine-needle aspiration cytology revealed clusters of spindle cells in a whorled formation and psammoma bodies. The tumor cells exhibited spindle-shaped cytoplasm, small fusiform or round nuclei and numerous intranuclear cytoplasmic inclusions. IHC staining of the cytological specimen revealed that the tumor cells were positive for epithelial membrane antigen, negative for thyroid transcription factor-1 and p40, and equivocal for claudin-1. Progesterone receptor immunoreactivity of cytology specimen resulted negative at first by manual method but retrieved positive by an autostainer. Following segmentectomy, the pathological diagnosis was a meningothelial meningioma. The patient has remained well without recurrence for 36 months postoperatively. Because the cytological preparation exhibited characteristic findings of meningioma, a correct diagnosis based on preoperative cytological findings with appropriate IHC would be possible. Here, we report the cytological and IHC features of this case and highlight the importance of IHC-quality assurance.

KEYWORDS

ectopic meningioma, fine needle aspiration cytology, immunohistochemistry, lung neoplasm, primary pulmonary meningioma, quality assurance

1 | INTRODUCTION

Meningioma is a benign or indolent mesodermal tumor with arachnoidal cell features. These tumors mainly arise in the central nervous system (CNS) and rarely occur at extra-cranial sites, particularly in the lung.[1] To date, fewer than 60 cases of primary pulmonary meningioma (PPM) have been reported since the first case report in 1982.[2] The observation of similar genetic abnormalities has led to a discussion of a possible relationship between minute pulmonary meningothelial-like nodules (MNs) and PPM,[3] and accordingly, the differential diagnosis of MN and PPM is determined using size as a criterion (MN: <3 mm).[4] To date, only a few reports have described both cytological features and an immunohistochemical (IHC) assessment of PPM.

2 | CASE REPORT

An otherwise healthy 60-year-old woman who had never smoked underwent routine medical screening. A 2-cm sized solid nodule in

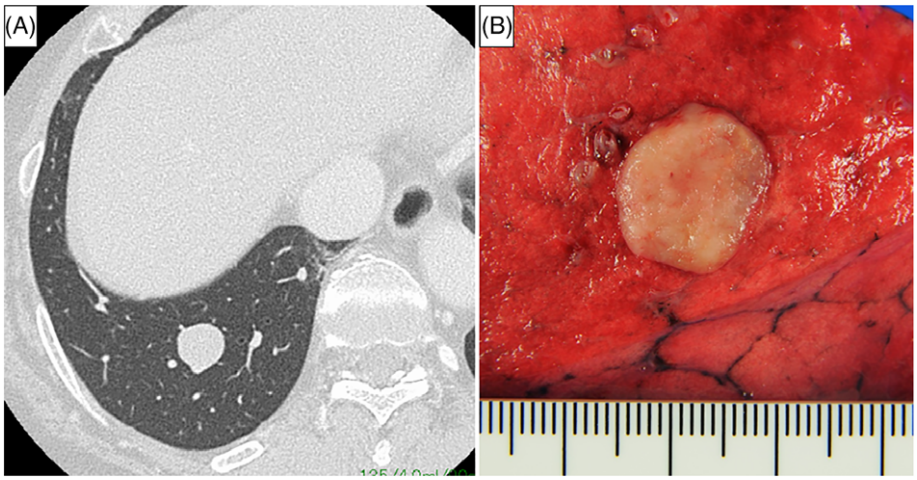

FIGURE 1 Computed tomography and macroscopic images of PPM. CT revealed a 2-cm-sized solid nodule in the right lung (A). The cut surface of the tumor showed a well-demarcated, yellowish-white, firm and solid nodule (B) [Color figure can be viewed at wileyonlinelibrary.com]

the right lung was incidentally identified on a chest radiograph (Figure 1A, computed tomography). She had a history of surgery for tongue leukoplakia 10 years earlier. Both her father and grandfather had developed bile duct cancers. The patient's laboratory test results were within normal limits, and a transbronchial biopsy led to a preoperative diagnosis of meningioma (Figure 2A).

The patient underwent segmentectomy of the right lower lung lobe, and thyroidectomy for a co-incidentally detected thyroid papillary carcinoma. The resected lung revealed a well- demarcated, yellowish-white, firm and solid nodule (Figure 1B). Computed tomography and magnetic resonance imaging did not detect any other tumors in the CNS or elsewhere. She has remained well without recurrence for 36 months after surgery.

3 | MATERIALS AND METHODS

The cytological specimen obtained from transbronchial aspiration and imprint from the resected lung were fixed in 95% ethanol for 3 hours and subjected to Papanicolaou staining. A 4-μm thick formalin-fixed paraffin-embedded (FFPE) histological specimen of the resected lung was submitted for hematoxylin and eosin staining. Transferred cells from the imprint cytology specimen were subjected to IHC both manually and using an autostainer according to the manufacturers' protocols. The FFPE specimen was immunostained using an autostainer. Antibodies against the following markers were used: epithelial membranous antigen (EMA; E29, Dako, Agilent Technology, Tokyo, Japan), progesterone receptor (PgR; 1E2, Ventana/Roche Diagnostics, Tokyo,

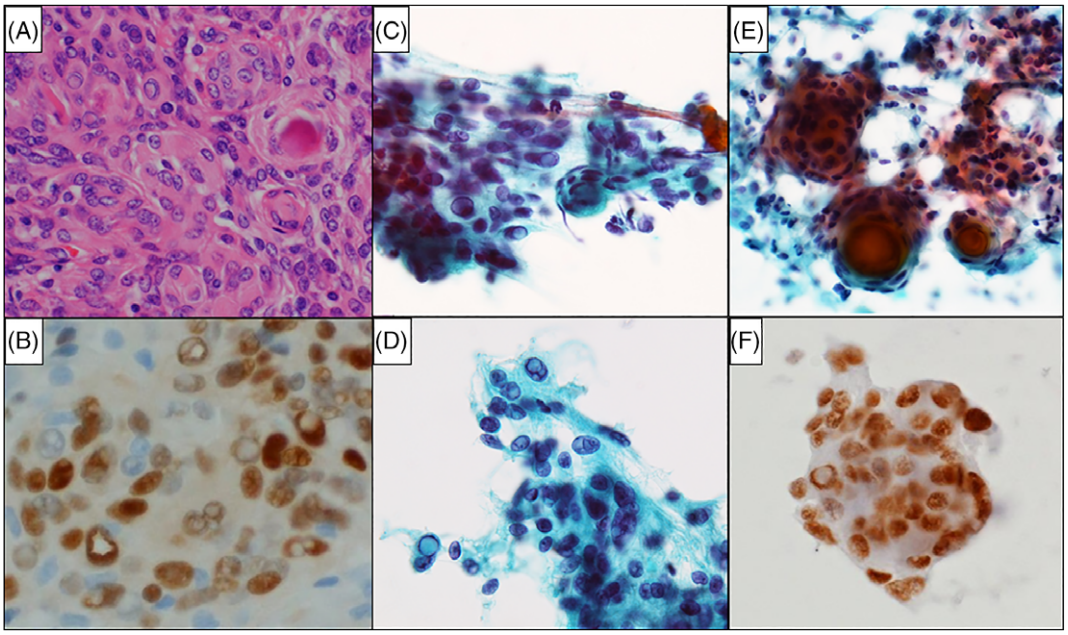

FIGURE 2 PPM shows proliferation of spindle to round cells with inconspicuous cell border and frequently with whorl formation on the biopsied FFPE specimen (A). In the aspiration (C, D) and imprint (E) cytology specimen, spindle to round tumor cells formed small- to medium-sized clusters with frequent whorl arrangements. Psammoma bodies are found in all specimens (A, C, E). Many intranuclear inclusions are noted on cytology (D, E). Through IHC staining, PgR-nuclear positivity of tumor cells are detected on both FFPE (B) and imprint cytology (F). (A, Hematoxylin and eosin stain; B and F, IHC stain against PgR with DAB visualization; C-E, Papanicolaou stain) [Color figure can be viewed at wileyonlinelibrary.com]

Japan), thyroid transcription factor-1 (TTF-1; 8G7G3/1, Dako, Agilent Technology) and p40 (BC28, Abcam, Cambridge, UK). The EnVision FLEX detection system/LINK48 autostainer (Dako, Agilent Technology) was used for EMA, TTF-1, and p40 staining, while the UltraView detection system/Benchmark XT autostainer (Ventana/Roche Diagnostics) was used to detect PgR.

4 | RESULTS

4.1 | Cytological findings and histological correlation

Aspiration cytology revealed sheet-like clusters composed of spindle cells in whorl formations and psammoma bodies on clear background (Figure 2C,D). The rapid on-site cytological evaluation revealed atypical cells that suggested a neoplasm, although we could not confirm whether it was benign or malignant. The tumor cells contained spindle-shaped cytoplasm, small fusiform or round nuclei with a fine chromatin pattern and numerous intranuclear cytoplasmic inclusions. No mitotic figures were observed. The findings of the imprint cytology evaluation were similar to those of aspiration cytology but included more tumor cells (Figure 2E). Examination of an intraoperative frozen section revealed meningioma. Histological findings of the biopsied (Figure 2A) and resected tumor were similar to that of cytology.

4.2 | IHC examination

Tumor cells in the resected lung specimens were positive for EMA and PgR (Figure 2B) and negative for TTF-1 and p40. Similar results were observed on the imprint cytology, except that manual staining indicated PgR negativity (data not shown). However, positive PgR reactivity was observed in the same cytology specimen using an autostainer (Figure 2F).

5 | DISCUSSION

A summary of the present case and 57 previously published cases (Table 1) suggests that PPM tends to occur in middle-aged women (median age: 56 years; male: female ratio = 25:33), as a solitary solid nodule in the periphery of the lung and at a size smaller than 30 mm,[1,5,6] Most PPMs are asymptomatic, although some patients may exhibit hemoptysis, sputum, cough, or chest pain. Generally, PPM is considered an indolent and mostly benign tumor, except for 2 cases reported with metastasis.[7,8] Here, we report a rare case of PPM together with the pre-operative aspiration cytological findings and an IHC evaluation of imprint cytology from the resected specimen.

In this case, the cytological specimen exhibited characteristic features of meningothelial meningioma, with spindle cells in a whorl formation and many psammoma bodies. According to reports, PPM shares cytological and histological findings with CNS-meningioma.[4,9–11] Accordingly, appropriate cytology sampling can enable a prediction of meningioma even during the pre-operative period. A tumor containing spindle-to-epithelioid cells should include the following elements in differential diagnosis: solitary fibrous tumors, nerve sheath tumors, mesothelioma, spindle cell carcinoid and non-small cell carcinoma. A tumor with intranuclear inclusions and psammoma bodies could include thyroid papillary carcinoma as differential diagnosis, especially in case with thyroid tumor. IHC can be helpful for excluding incorrect diagnoses.

Initially, in our case, imprint cytology failed to yield a positive PgR result via manual staining. However, positive PgR staining was achieved using an autostainer. As cytological samples can be suitable for IHC, it is important to guarantee stable IHC processing by using an autostainer for quality assurance. Previous reports indicate that PPM tends to express vimentin, EMA, and PgR but is generally negative for S100, CD34 and keratin (Table 1).[6] In our case, biopsy specimens exhibited equivocal immunoreactivity for claudin-1, a positive marker of CNS meningioma.[12] In contrast to vimentin and EMA, PgR is a relatively reliable and common positive marker for meningioma; therefore, the probability of a false-negative PgR result is low. The discrepancy in our PgR staining results indicates the importance of quality assurance of IHC evaluation of a cytological specimen. We hypothesize that some of the staining conditions (eg, temperature, time, technical handling) may have affected our results. However, we could not identify the cause of the IHC discrepancy because of sample limitations.

In conclusion, we report a rare case of PPM. To the best of our knowledge, this is the first report to describe PPM based on aspiration cytological findings and an IHC assessment. Although PPM is very rare, we should remain aware of this entity, especially when evaluating solitary peripheral lung nodules in middle-aged women. Additionally, cytological specimens should be subjected to an appropriate IHC analysis, as this is a useful differential diagnostic tool. Further studies

TABLE 1 Clinicopathological and IHC characteristics of PPM

Number of cases		58	
Age	Median (range)	56 y.o (18-108)	
Sex	Male: Female	25:33	
Size	Median (range)	24 mm (8-150)	
Location	Right/left	25:27	
	Upper/ middle/ lower	19:3:23	
WHO grade	I/II/III	55:1:1 (*1)	
Recurrence	Yes/no	2:46 (*2)	
Follow up duration		1 month to 39 years	
IHC		Positive rate (*n*)	Examined case (*n*)
	Vimentin	100% (38)	38
	EMA	88% (37)	42
	PgR	82% (9)	11
	NSE	50% (5)	10
	S100	27% (9)	33
	ER	25% (2)	8
	CD34	22% (2)	9
	Keratin	15% (4)	27
	GFAP	0% (0)	3

Abbreviations: WHO, World Health Organization; IHC, immunohistochemistry; EMA, epithelial membranous antigen; PgR, progesterone receptor; NSE, neuron specific enolase; ER, estrogen receptor; GFAP, glial fibrillary acidic protein; EMA, epithelial membrane antigen.
*1: Missing 1 case, *2: Missing 10 cases.

should be conducted to establish suitable IHC conditions for cytological assessments.

ACKNOWLEDGMENTS

This study was reviewed and approved by our institutional review board (No. 2015-289 and 2010-077). The authors wish to express their gratitude to Sachiko Miura, Toshiko Sakaguchi, and Chizu Kina for their excellent technical assistance, Sachiyo Hasegawa and Yuko Kashiwazaki for their secretarial assistance, and Editage for English language editing. The authors also thank Naoshi Sasaki, Dr Nobuyoshi Hiraoka and Dr Atsushi Ochiai for providing valuable support.

CONFLICT OF INTEREST

A case report part of this manuscript was presented at the 19th International Congress of Cytology, Yokohama, Japan, in 2016. Dr Motoi reports personal fee (for the lecture, advisory board) from Bristol-Myers Squibb, Miraca Life Sciences, AstraZeneca, Chugai Pharma, MSD, Agilent and Novartis; institutional research funding from Roche Diagnostics outside of this work.

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How to cite this article: Ohashi-Nakatani K, Shibuki Y, Fujima M, et al. Primary pulmonary meningioma: A rare case report of aspiration cytological features and immunohistochemical assessment. *Diagnostic Cytopathology*. 2019;47:330–333. https://doi.org/10.1002/dc.24126