

Case Report

Histopathology and Cytology of Pulmonary Myoepithelial Neoplasms: 2 Cases

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Keywords

Myoepithelioma · Myoepithelial carcinoma · Myoepithelial neoplasm · Histopathology · Cytology

Abstract

Myoepithelial neoplasms (MNs) of the lung are extremely rare tumors. Approximately 40 cases of pulmonary MNs have been reported to date. Herein, we report extremely rare cases of different types of pulmonary MN, including cytological features. Case 1 is an 18-year-old female, and case 2 is a 73-year-old female patient. They presented to our hospital with nodules of the lung. Histological examination revealed tumor cells with round to oval nuclei and acidophilic cytoplasm that formed nests or fascicles with mild hyalinized stroma in case 1 and tumors containing the bi-phasic components of a nest-like and fascicle pattern with pleomorphism in case 2. Immunohistochemically, these tumors were positive for cytokeratin (CK) AE1/AE3, CK5/6, vimentin, calponin, and EMA, and focal positive for S-100a protein and alpha smooth muscle actin. The pathological diagnoses in cases 1 and 2 were myoepithelioma and myoepithelial carcinoma, respectively. In conclusion, we encountered two cases of extremely rare MNs that occurred in the lung. This disease can be diagnosed by collecting appropriate cytological and histological findings and should be listed as a differential diagnosis.

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Introduction

Myoepithelial neoplasms (MNs) of the lung are extremely rare tumors. They are categorized as a kind of salivary-type tumor according to the World Health Organization classification and defined as tumors with similar morphological, immunophenotypic, and genetic features to their counterparts in soft tissue, salivary glands, bone, and skin [1]. MNs can be divided into myoepitheliomas and myoepithelial carcinomas, which are benign and malignant tumors, respectively. To our knowledge, around 40 cases of pulmonary MNs have been reported in the literature to date [2, 3]. Due to their rarity, the precise criteria for MNs remain unknown. Herein, we report extremely rare cases of different types of pulmonary MNs, especially as this is the first report on the cytological features of pulmonary MN to our knowledge.

Case Report/Case Presentation

Case 1

An 18-year-old female patient presented to our hospital with a 20 mm nodule in the upper lobe of right lung. The patient had no relevant medical or family history and no significant physical examination findings. Routine laboratory test results were unremarkable. Chest computed tomography (CT) was performed, revealing a homogeneous 24 mm mass in the right lung (shown in Fig. 1a). Positron emission tomography-CT showed a peak standard

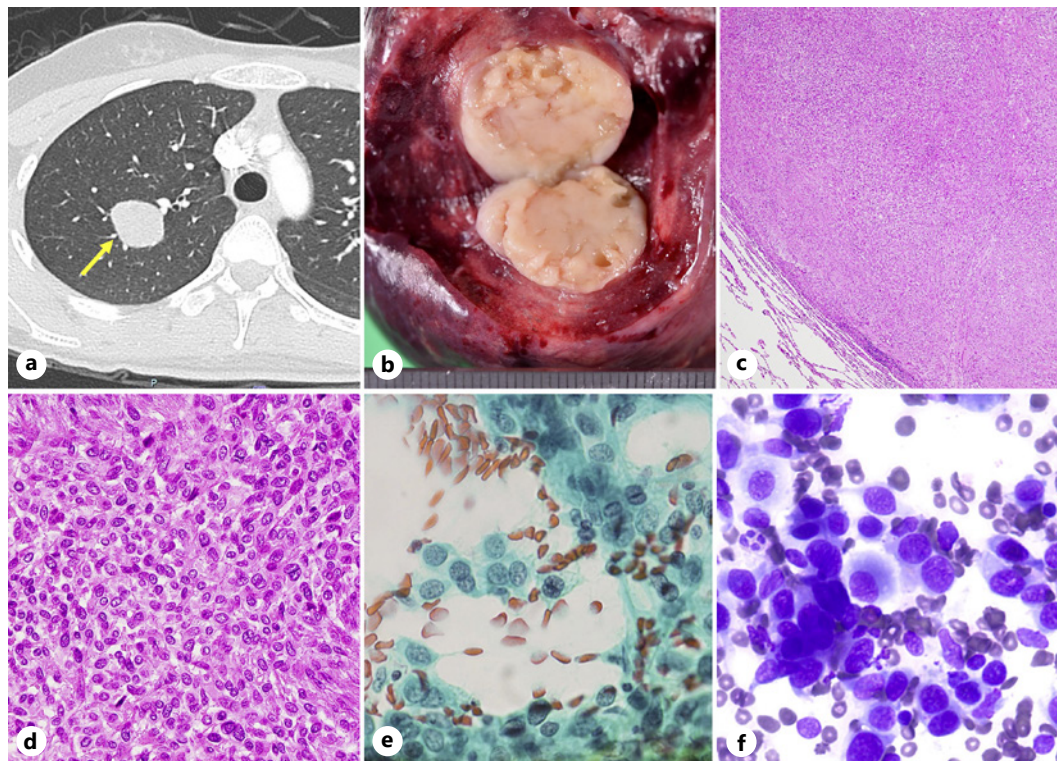


Fig. 1. Clinical, histopathological, and cytological features of case 1. **a** CT: pulmonary window. **b** Gross findings. **c, d** Histological findings. Magnification: **(c)** $\times 40$ and **(d)** $\times 400$. **e, f** Cytological findings. Magnification, $\times 400$.

uptake value of 5.53 for 18-fluoro-deoxyglucose in the mass, and no other lesions were detected. A right upper lung lobectomy was performed.

Grossly, the tumor was yellowish-grayish white with a clear border, and it was 21 mm in size (shown in Fig. 1b). Histological examination showed that the tumor cells had round to oval nuclei and acidophilic cytoplasm that formed nests or fascicles with mild hyalinized stroma (shown in Fig. 1c, d). The border of the tumor was well circumscribed. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) AE1/AE3, CK5/6, vimentin, calponin, and EMA, focal positive for S-100a protein and alpha smooth muscle actin (SMA), and negative for desmin, CD34, and p63. The Ki-67-positivity rate was 10.74% (114/1,061).

Cytologically, stamp preparation revealed clusters and isolated plasmacytoid cells. Binucleation, mild pleomorphism, cytoplasmic vacuoles, and granules were observed frequently. The individual tumor cells had low nucleus-to-cytoplasm ratios, oval to round nuclei, bright chromatin, scant cytoplasm, and no nucleoli (shown in Fig. 1e). No material indicating metaphase was observed on Giemsa staining (shown in Fig. 1f). The pathological diagnosis was myoepithelioma. After resection, the patient was followed up and showed no recurrence or metastasis in 5 years.

Case 2

A 73-year-old female patient presented to our hospital with a 12 mm nodule in the lower lobe of right lung. The patient had no relevant medical family history or significant physical examination results. Routine laboratory test results were also unremarkable. Chest CT was performed, revealing a homogeneous 12-mm mass in the right lung (shown in Fig. 2a). Positron emission tomography-CT showed a peak standard uptake value of 3.1 for 18-fluoro-deoxyglucose in the mass, and no other lesions were detected. A right lower lung wedge resection was performed.

Gross findings revealed that the tumor was well circumscribed and grayish in color. The tumor was 1.6 cm in size (shown in Fig. 2b). Histological examination showed that tumor contained a bi-phasic component, namely, nest-like and fascicle patterns with hyalinized stroma (shown in Fig. 2c). The hyalinized stroma was seen mainly in the central area, with irregular tumor cells at the margins. Tumor cells comprising both components had marked nuclear atypia, such as pleomorphism and prominent nucleoli (shown in Fig. 2d). Immunohistochemically, the tumor cells were positive for CK AE1/AE3, CK5/6, vimentin, calponin, and EMA, focal positive for S-100a protein and alpha SMA, and negative for desmin, CD34, and p63. The Ki-67-positivity rate was 6.21% (138/2,221).

Cytologically, stamp preparation revealed clustered cells with binucleation and marked pleomorphism, and cytoplasmic vacuoles and granules were found. The individual tumor cells had high nucleus-to-cytoplasm ratios (shown in Fig. 2e). No materials indicating metaphase were observed on Giemsa staining (shown in Fig. 2f). The pathological diagnosis was myoepithelial carcinoma (pT1b: TNM/UICC scoring). After resection, the patient was followed up and showed no recurrence or metastasis in 1 year.

Discussion/Conclusion

In the current report, we drew histopathologic or cytologic findings in 2 cases of pulmonary MN. MN itself can occur throughout the body [4–7], and 10 of 101 MN cases occurring in soft tissues observed in a previous report occurred in the trunk [8]. Pulmonary MN is a very rare tumor and is often reported collectively as both benign and malignant [2, 3]. Nevertheless, the number of reported cases remains approximately 40. Half of the

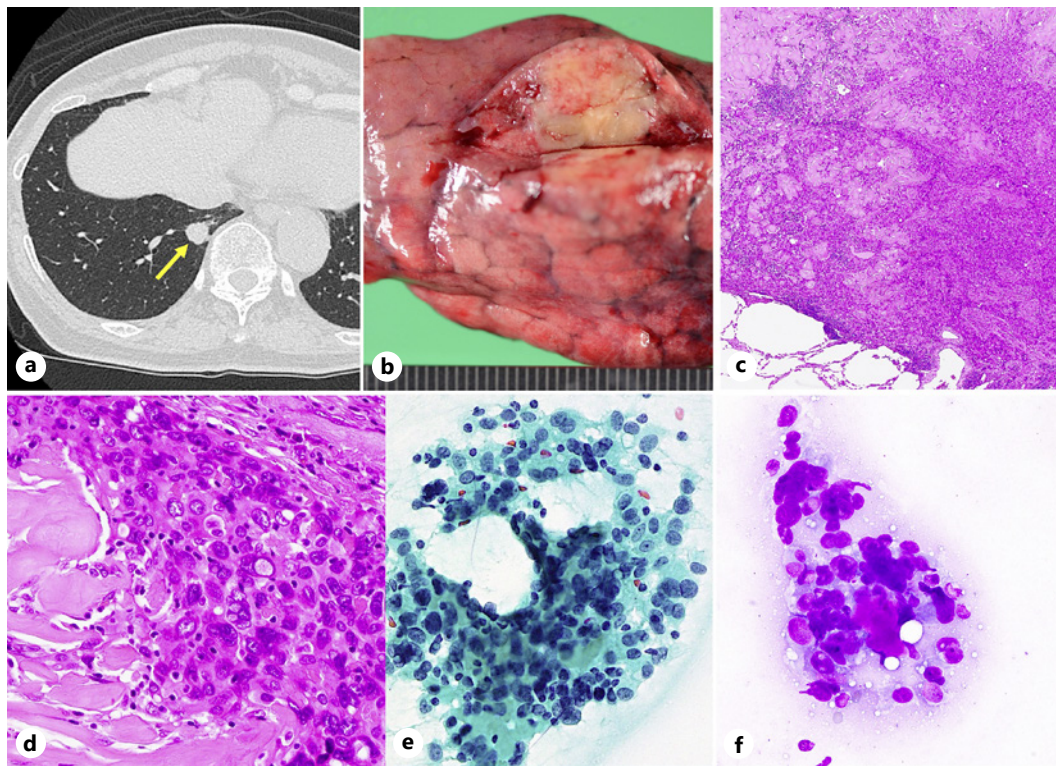


Fig. 2. Clinical, histopathological, and cytological features of case 2. **a** CT: pulmonary window. **b** Gross findings. **c, d** Histological findings. Magnification: **(c)** $\times 40$ and **(d)** $\times 400$. **e, f** Cytological findings. Magnification, $\times 400$.

neoplasms occurred in the airways and the rest in the peripheral lungs [2]. Imaging of pulmonary MNs demonstrates that central endobronchial neoplasms are well circumscribed and homogeneous, whereas intraparenchymal ones are well-defined nodules or irregular masses with calcifications. MNs arising in the intraparenchymal area are asymptomatic, whereas those arising in the central bronchus can cause symptoms of airway obstruction, such as coughing [1]. In our cases, both cases were well circumscribed, and both were typical cases in terms of imaging and clinical presentation.

The histopathological findings of pulmonary MN can be diverse. Tumor cells can be epithelioid, round, clear, plasmacytoid, or spindled. MN may have a reticular or trabecular pattern with myxoid, myxochondroid, or hyalinized stroma. It may also have duct-like epithelium or may appear thus due to preexisting alveolar epithelium being incorporated [3]. MNs with clear cells have also been reported in salivary glands [9]. Myoepithelial carcinomas can exhibit significant cytologic pleomorphism, necrosis, infiltrative growth, and increased mitotic activity [2, 6, 8, 10]. However, no clear criteria have been established for morphologically benign or malignant neoplasms. Regarding immunohistochemical findings, tumor cells of MN variably express keratins, EMA, S-100, p63, p40, alpha SMA, and GFAP [2]. MNs have myoepithelial properties by definition, but these are not clearly defined. Therefore, the pathologist plays a large role in determining the diagnosis based on these immunostaining and morphological findings. The morphological features of our 2 cases are summarized in Table 1, and the immunohistochemical features in Table 2. We found a marked polymorphism in case 2 and therefore diagnosed it as myoepithelial carcinoma.

Table 1. Summary of morphologic features in 2 cases

	Case 1 benign	Case 2 malignant
Borders	Well circumscribed	Well circumscribed
Architecture	Nests, sheets	Nests, fascicles
Matrix	Hyalinized	Hyalinized
Cytomorphology	Epithelioid, plasmacytoid	Epithelioid, pleomorphic
Atypia	Moderate	Marked
Mitosis/2 mm ²	1	1
Necrosis	None	None

Table 2. Summary of immunohistochemical studies in 2 cases

	Case 1 benign	Case 2 malignant
CK AE1/AE3	Positive	Positive
CK 5/6	Positive	Positive
Vimentin	Positive	Positive
Calponin	Positive	Positive
EMA	Positive	Positive
S-100a protein	Focal positive	Focal positive
alpha SMA	Focal positive	Focal positive
Desmin	Negative	Negative
CD34	Negative	Negative
p63	Negative	Negative
Ki-67 positivity	10.74% (114/1,061)	6.21% (138/2,221)

Interestingly, this report contains cytological findings of each MN case. In MNs, which occur in salivary glands [11], soft tissues [12], and thyroid gland [13], cytological findings revealed the presence of round to oval, spindle, epithelioid, and plasmacytoid cells in the myxoid background, and uniform or round to ovoid nuclei with distributed chromatin and eosinophilic or pale cytoplasm. Differential diagnosis was challenging in all of these reports. Polymorphous adenoma in the salivary glands; metastatic tumor, such as lobular carcinoma derived from breast in the soft tissues; and medullary carcinoma in the thyroid gland were the most common differential diagnoses. In terms of lung tumors, the differential diagnosis may include a wide range of diseases, such as synovial sarcoma and adenocarcinoma [14, 15]. In our cases, case 1 exhibited typical myoepithelial cells but case 2 had a more pleomorphic morphology. Therefore, pleomorphic carcinoma was mentioned as a differential diagnosis in case 2. Diagnosis would have been difficult in both cases without prior knowledge of MNs.

We observed extremely rare MNs of the lung. Due to the rarity of this disease, sufficient prognostic data do not yet exist, but the ability to diagnose the disease using biopsy and cytology would lead to the delivery of more appropriate treatment.

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Statement of Ethics

The research in this case report was conducted ethically and in accordance with the World Medical Association Declaration of Helsinki. Written informed consents were obtained from the patients for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with national guidelines. This retrospective review of patient data did not require ethical approval in accordance with national guidelines.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Akira Ishikawa, Hiroki Fujisawa, Naoko Yasumura, and Kuraoka Kazuya: diagnosis and preparation of the manuscript. Junichi Zaitso, Akihisa Saito, Naohide Oue, Arisa Kan, Kazue Iwahiro, Fumika Kimura, and Kiyomi Taniyama: diagnosis and correction of the manuscript. Kazuki Tadokoro, Norifumi Tsubokawa, Takeshi Mimura, and Yoshinori Yamashita: management of the case.

Data Availability Statement

All data generated or analyzed during this study are included in this article.

References

- 1 Moch H, editor. [Thoracic tumours](#). [World Health Organ Classification of Tumours](#). 5th ed. Lyon, France: International Agency for Research on Cancer; 2021.
- 2 Leduc C, Zhang L, Öz B, Luo J, Fukuoka J, Antonescu CR, et al. Thoracic myoepithelial tumors a pathologic and molecular study of 8 cases with review of the literature. [Am J Surg Pathol](#). 2016 Feb;40(2):212–23.
- 3 Yuan L, Katabi N, Antonescu CR, Golden A, Travis WD, Rektman N. Pulmonary myoepithelial tumors with exuberant reactive pneumocytes: proposed reclassification of so-called pneumocytic adenomyoepithelioma. [Am J Surg Pathol](#). 2020 Jan;44(1):140–7.
- 4 Arch V, Moritani S, Ichihara S, Yatabe Y, Hasegawa M. Immunohistochemical expression of myoepithelial markers in adenomyoepithelioma of the breast: a unique paradoxical staining pattern of high-molecular weight cytokeratins. [Virchows Arch](#). 2015 Feb;466(2):191–8.
- 5 Falk N, Weissferdt A, Kalhor N, Moran CA. Primary pulmonary salivary gland-type tumors: a review and update. [Adv Anat Pathol](#). 2016 Jan;23(1):13–23.
- 6 Hysi I, Watted H, Benhamed L, Porte H. Primary pulmonary myoepithelial carcinoma. [Interact Cardiovasc Thorac Surg](#). 2011 Aug;13(2):226–8.
- 7 Gaio E, Perasole A, Bagatella F. Bilateral myoepithelioma of the nasopharynx: a case report. [Auris Nasus Larynx](#). 2009 Aug;36(4):496–500.
- 8 Hornick JL, Fletcher CD. Myoepithelial tumors of soft tissue: a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. [Am J Surg Pathol](#). 2003 Sep;27(9):1183–96.

- 9 Skálová A, Weinreb I, Hyrcza M, Simpson RHW, Laco J, Agaimy A, et al. Clear cell myoepithelial carcinoma of salivary glands showing EWSR1 rearrangement: molecular analysis of 94 salivary gland carcinomas with prominent clear cell component. *Am J Surg Pathol*. 2015 Mar;39(3):338–48.
- 10 Higashiyama M, Kodama K, Yokouchi H, Takami K, Kabuto T, Tsuji N, et al. Myoepithelioma of the lung: report of two cases and review of the literature. *Lung Cancer*. 1998 Apr;20(1):47–56.
- 11 Kumar PV, Sobhani SA, Monabati A, Hashemi SB, Eghtadari F, Hamidi SA. Myoepithelioma of the salivary glands: fine needle aspiration biopsy findings. *Acta Cytol*. 2004 May–Jun;48(3):302–8.
- 12 Wang G, Tucker T, Ng TL, Villamil CF, Hayes MM. Fine-needle aspiration of soft tissue myoepithelioma. *Diagn Cytopathol*. 2016 Feb;44(2):152–5.
- 13 Narick C, Velosa C, Pollice P, Silverman J. Fine needle aspiration cytology of a myoepithelioma presenting as a thyroid nodule. *Diagn Cytopathol*. 2015 Feb;43(2):153–7.
- 14 Furuya K, Yasumori K, Takeo S, Sakino I, Uesugi N, Momosaki S, et al. Part 1, Mimickers of lung cancer – spectrum of CT findings with pathologic correlation. *AJR Am J Roentgenol*. 2012 Oct;199(4):W454–63.
- 15 Salahudeen HM, Hoey ET, Robertson RJ, Darby MJ. CT appearances of pleural tumours. *Clin Radiol*. 2009 Sep;64(9):918–30.