Diagnostic Pathology

CASE REPORT

Open Access

# Multiple pulmonary mucinous cystadenoma with Ovarian-like stroma: a case report

Lei Wang[1], Xieraili Wumener[2] and Wenting Huang[3*]

## Abstract

**Background** Pulmonary mucinous cystadenoma with ovarian-like stroma has rarely been reported. To the best of our knowledge, only two prior cases have been reported to date.

**Case presentation** A 47-year-old female underwent an $^{18}$F-fluorodeoxyglucose(FDG) positron emission tomography/computed tomography(PET/CT) scan, revealig multiple solid and cystic nodules with mild FDG uptake in both lungs. The tumor exhibited an adenoid or papillary structure, covered by monolayer mucous columnar epithelium and pseudostratified ciliated columnar epithelium, with abundant mesenchymal cells. Nuclei were oval, fusiform, or polygonal, resembling ovarian-like stroma, and showed mild nuclear atypia without atypical mitoses. Immunohistochemical analysis indicated: CK (epithelial cell +), P63 (epithelial basal cells +), CK7 (epithelial cell +), CK20 (–), TTF-1 (epithelial cell +), napsin A (partial epithelial cell +), α-inhibin (–), S100 (–), SMA (–), EMA (epithelial cell +), CEA (–), WT-1 (mesenchymal cells +), ER (mesenchymal cells +), P16 (partial mesenchymal cells +), CD10 (mesenchymal cells +), and Ki-67 (2% +).

**Conclusion** Pulmonary mucinous cystadenoma with ovarian-like stroma is rare, and its pathological nature and classification are not yet fully understood.

**Keywords** Pulmonary, Cystadenoma, Case, Mesenchymal, Histology, Immunohistochemistry

## Background

Pulmonary mucinous cystadenoma (PMCA) is a rare, benign tumor. Mucinous cystadenomas with ovarian-like stroma typically occur in the ovaries and pancreas, but are seldom found in the lungs. The 2021 World Health Organization classification of thoracic tumor (5th edition) defines mucinous cystadenomas as a localized cystic mass filled with mucin and lined by columnar mucinous epithelium, lacking significant atypia or invasive growth [1]; however, it does not mention the presence of ovarian-like stroma. We present a case that histologically resembles lung mucinous cystadenoma, yet features ovarian-like stroma with noticeable pathological and clinical differences from PMCA. The ovarian-like stromal cells were oval, fusiform, or polygonal, exhibiting strong immunohistochemical expression of WT-1

*Correspondence:
Wenting Huang
huangwt@cicams.ac.cn
[1]Department of Pathology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen 518116, China
[2]Department of Nuclear Medicine, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen 518116, China
[3]Department of Pathology, Shenzhen Hospital, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen 518116, China

and ER. Clinically, multiple lung tumors were identified, with positron emission tomography (PET)/computed tomography (CT) showing radioactive uptake that could be misinterpreted as metastasis. This is a rare case of pulmonary disease, with only two prior instances reported worldwide, making this the third documented case in the literature.

## Case presentation

The patient was a 47-year-old female admitted to the hospital with a chief complaint of multiple lung masses detected during a health examination 5 days prior. The patient had previously undergone a total hysterectomy due to adenomyosis 10 years ago. Physical examination, vital signs and laboratory test were unremarkable. Thoracic CT revealed multiple bilateral subpleural lung nodules (3–25 mm), some with internal cavity shadows, but no lymphadenopathy, pleural thickening or effusion. The radiologic differential diagnoses included metastasis and granulomatous inflammation. Three months later, $^{18}$F-fluorodeoxyglucose (FDG) PET/CT demonstrated larger size and multiple solid or cystic nodules with mild FDG uptake in both lungs, with no primary tumors elsewhere. The largest lesion was located in the upper lobe of the right lung (Fig. 1 and a: maximum intensity projection, 1b: fusion, 1c and 1d: lung CT). Thoracoscopic wedge resection of the right lung was performed, removing three nodules, the largest of which measuring 2.5 cm.

The postoperative pathology specimen revealed grayish-yellow nodules with a mucus-rich cut surface and clear boundaries. Microscopically, the tumor presented an adenoid or papillary structure, covered by a monolayer of mucous and pseudostratified ciliated columnar epithelium, with abundant mesenchymal cells. The nuclei were oval, fusiform, or polygonal, resembling ovarian-like stroma, showing mild nuclear atypia without atypical mitoses. The formation of a mucus lake is visible. (Figure 2a - d). Immunohistochemical analysis indicated: CK (epithelial cell +), P63 (epithelial basal cells +), CK7 (epithelial cell +), CK20 (–), TTF-1 (epithelial cell +) (Fig. 2e), napsin A (partial epithelial cell +), α-inhibin (–), S100 (–), SMA (–), EMA (epithelial cell +), CEA (–), WT-1 (mesenchymal cells +) (Fig. 2f), ER (mesenchymal cells +) (Fig. 2g), P16 (partial mesenchymal cells +), CD10 (mesenchymal cells +), and Ki-67 (2%+) (Fig. 2h). The immunohistochemistry results and the clone numbers of the antibodies are summarized in Table 1.

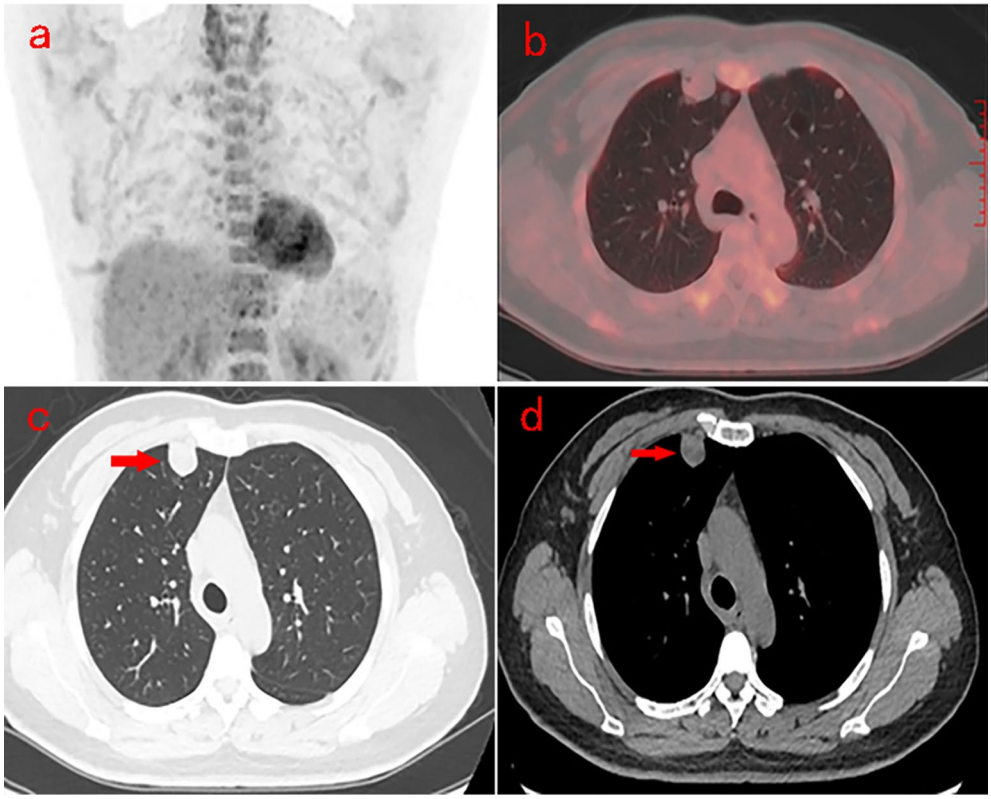


**Fig. 1** $^{18}$F-FDG PET/CT images of PMCA-OS. The patient underwent $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) (**a**: maximum intensity projection, **b**: fusion, **c** and **d**: lung CT). $^{18}$F-FDG PET/CT revealed a solid cystic nodule with mild FDG uptake. The largest nodule was located in the upper lobe of the right lung (**c**, **d** as indicated by the arrow), with a size of 2.5 × 1.7 cm, maximum standardized uptake value of 1.1 (**b**)

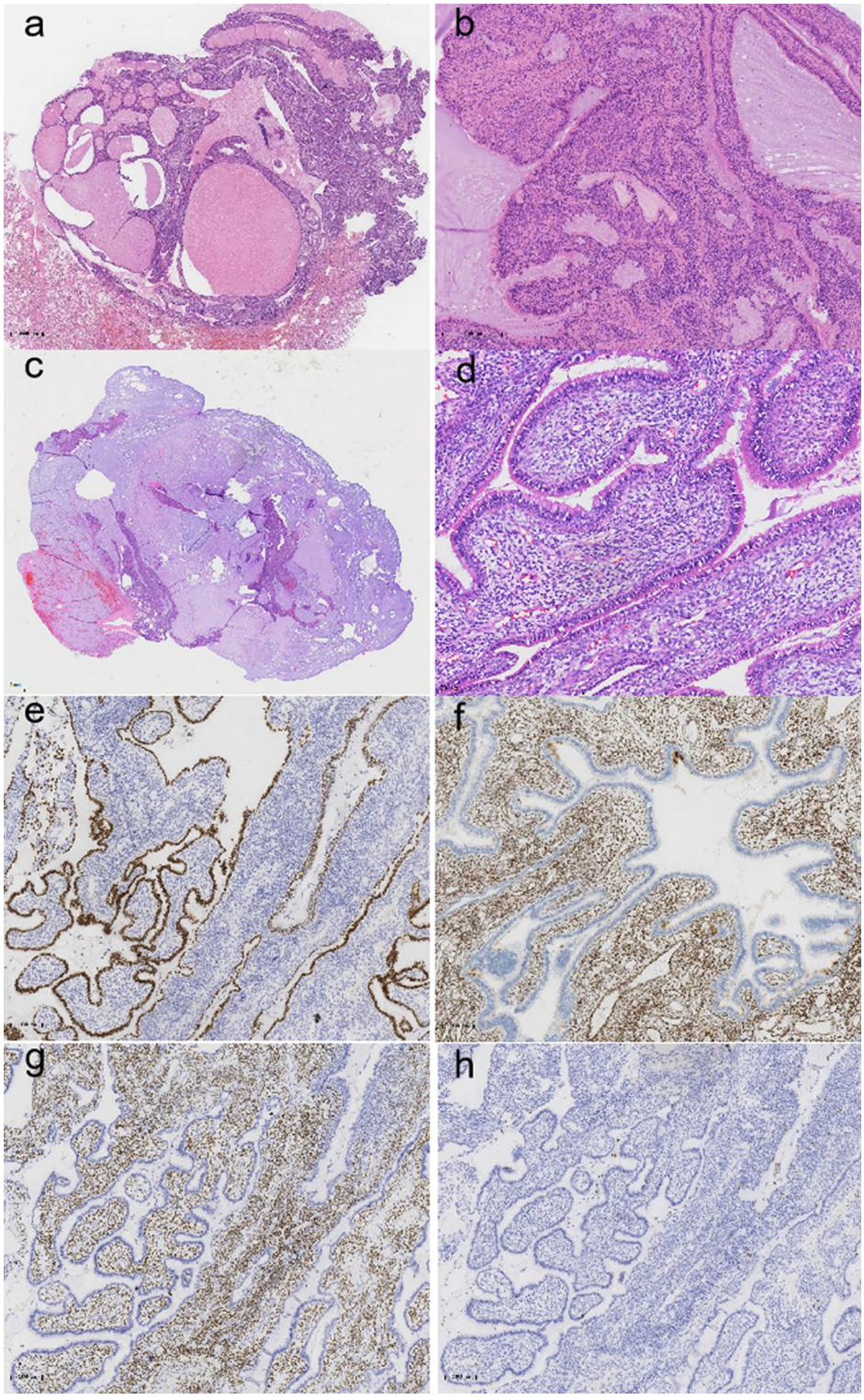


**Fig. 2** Pathological morphology and immunohistochemical results. **a** The tumor tissue was cystic-solid with clear boundaries (magnification ×20). **b** The tumor was covered by a monolayer mucous columnar epithelium and pseudostratified ciliated columnar epithelium. The mesenchymal cells were densely packed, and the nuclei were oval, fusiform, or polygonal, indicating similarity to ovarian-like stroma (magnification ×200). **c** The formation of mucus lake(magnification ×20). **d** The nuclei were oval, fusiform, or polygonal, resembling ovarian-like stroma, showing mild nuclear atypia without atypical mitoses(magnification ×300). **e** Epithelial cells were positive for TTF-1 (magnification ×100). **f-g** Epithelial cells were negative for WT-1 and ER (magnification ×100). Stromal cells were positive for WT-1 and ER (magnification ×100). **h** Ki-67 index was very low in both epithelial and stromal cells (magnification ×100)

**Table 1** Summary of immunohistochemistry and antibody clone numbers

| Antibody | Epithelial cells | Stromal cells | clone number |
|---|---|---|---|
| CK | + | - | MX005(Maixin) |
| P63 | basal cells + | - | MX013(Maixin) |
| CK7 | + | - | MX053(Maixin) |
| CK20 | - | - | MX059(Maixin) |
| TTF-1 | + | - | MX011(Maixin) |
| napsinA | + | - | MX015(Maixin) |
| α-inhibin | - | - | AMY82(Zhongshan Golden Bridge) |
| S100 | - | - | 4C4.9(Maixin) |
| SMA | - | - | MX097(Maixin) |
| EMA | + | - | E29(Maixin) |
| CEA | - | - | MX068(Maixin) |
| WT-1 | - | d+ | 6 F-H2(Roche) |
| ER | - | d+ | SP1(Maixin) |
| P16 | - | f+ | MX007(Maixin) |
| CD10 | - | d+ | MX002(Maixin) |
| PAX8 | - | - | EP298(Maixin) |
| Ki-67 | 2%+ | 2%+ | MX006(Maixin) |

+: positive, –: negative, f+: focally positive, d+: diffusely positive

**Table 2** Comparison between previously reported cases and the present case

| | Geramizadeh et al. | Shawash et al. | Present case |
|---|---|---|---|
| Sex | Female | Female | Female |
| Age | 47 y | 48 y | 47 y |
| Focality of the nodules | Multiple & bilateral | Multiple & bilateral | Multiple & bilateral |
| Maximum tumor size | 30 mm | 15 mm | 25 mm |
| Medical history | Simple hysterectomy secondary to abnormal uterine bleeding | Abdominal wall dermatofibrosarcoma protuberans with transformation into fibrosarcoma | Total hysterectomy due to adenomyosis |
| Immunohistochemistry | E: AE1/AE3 and CK7 +; CK20 and CK19 –<br>S: vimentin and ER + | E: AE1/AE3, EMA, and TTF-1 +<br>S: ER and CD10 d+; SMA f+; AE1/AE3, EMA, and TTF-1 –<br>Both E and S: S100, CD34, and inhibin – | E: CK, CK7, TTF-1, napsin A, and EMA +<br>S: ER, CD10, and WT-1 d+; AE1/AE3, CK7, EMA, TTF-1, and napsin A –<br>Both E and S: CK20, S100, SMA, PAX8, and inhibin – |
| Ovaries, pancreas, and liver | Normal | Normal | Normal |

E: epithelial cells, S: stromal cells, +: positive, –: negative, f+: focally positive, d+: diffusely positive

## Discussion

We present this case to emphasize the ovarian-like stroma in pulmonary mucinous cystadenoma with ovarian-like stroma(PMCA-OS), expand the histological spectrum of PMCA, and propose that it may represent a unique subtype of PMCA that could be missed in clinical diagnosis.

PMCA is already rare [2], and the occurrence of ovarian-like stroma is even rarer, first documented by Geramizadeh et al. in 2014 [3] and subsequently by Shawash et al. in 2019 [4]. We report the third known case of this unusual tumor, with all three patients were middle-aged women. Their clinical presentations were nonspecific.

The initial differential diagnoses to consider, given the seemingly benign biological features, are classic PMCA and Pulmonary adenofibroma (PAF). Imaging in reported cases typically shows multiple nodules in both lungs, with a maximum diameter of ≤ 30 mm, as summarized in Table 2. In contrast, classic PMCA usually appears as a well-defined single cystic mass, more commonly located in the right lobe [2, 5–7]. PAF generally presents as a solid mass on imaging.

Microscopically, the primary difference between classic PMCA and Pulmonary adenofibroma (PAF) lies in their stromal components. In PMCA-OS, mesenchymal cells are densely packed, with oval, fusiform, or polygonal nuclei, resembling ovarian-like stroma, and exhibit mild nuclear atypia without atypical mitoses. These mesenchymal characteristics have not been documented in classic PMCA by WHO [1]. Meanwhile, the stroma of PAF is fibrotic and collagen-rich, with spindle-shaped stromal cells. Although PAF stromal cells can also express ER and PR, the expression of WT-1 and CD10 indicates a potential origin related to the ovarian stroma, supporting our diagnosis of PMCA-OS.

Moreover, this histological characteristic is similar to mucinous cystic neoplasms of the ovary(MCN(O)) and mucinous cystic neoplasms of the pancreas(MCN(P)), all featuring mucin-producing tall columnar epithelium supported by ovarian-like stroma. Both MCN (P) and MCN (O) have malignant potential. To date, metastases of MCN (P) to the lungs are unreported, with only a few cases to the liver [8]. While rare, lung metastasis from MCN (O) has been documented [9]. However, the positive expression of CK7, TTF-1, and napsin A, alongside negative CK20 expression in the epithelial component in our case, indicates the origin from lung epithelial cells. Meanwhile, radiological results showed no neoplastic lesions in the liver, pancreas, or ovaries, allowing us to rule out the possibility of MCNs metastases.

Similar to MCNs, which exhibit a histological spectrum ranging from low-grade dysplasia to high-grade dysplasia and associated invasive carcinoma, Gao et al. [7] described the histological spectrum of pulmonary

mucinous cystic neoplasia (PMCN) based on the degree of cellular atypia in the tumor epithelium and the presence or absence of invasive growth. However, none of the PMCN cases have demonstrated ovarian-like stroma, making PMCA-OS a potentially unique subtype.

To better understand the distinct features of PMCA-OS, various theories regarding the origin and function of ovarian-type stroma in MCNs offer valuable insights, suggesting it may arise from ectopic ovaries [10] or primordial germ cells [11]. These findings of developmental abnormalities may explain the presence of multiple nodules in the patients. Zamboni et al. [10] proposed that the stroma can release hormones and growth factors, contributing to cystic tumor formation. Notably, unlike MCNs [12], the ovarian-like stromal in our PMCA-OS case is negative of α-inhibin, indicating it displays ovarian-like differentiation without actual functional ovarian hormone secretion. Additionally, the expression of ER and PR may partially explain the enlargement of PMCA-OS in female patients.

Unfortunately, neither our case nor previous cases underwent molecular testing to explore their molecular characteristics. Since the tumor's discovery, the patient has survived for two and a half years with no significant physical discomfort, indicating the benign biological behavior of this tumor.

## Conclusion

PMCA-OS exhibits distinct pathological and radiological features, and we recommend that pathologists pay close attention to the ovarian-like stromal components that may be present in PMCA, as these might represent a potential subtype of this entity. Given the very limited number of reported cases, the biology, malignant potential, and molecular characteristics of PMCA-OS remain unclear. Considering that adenocarcinoma arising from PMCA has been previously reported in the literature [13, 14], we recommend rigorous sampling and detailed microscopic evaluation, and thorough molecular investigations. Such approaches are crucial for assessing the malignancy risk in PMCA-OS and uncovering its genetic and molecular features. Long-term clinical follow-up is strongly advised, even when current histological findings suggest benign lesions.

### Abbreviations

| | |
|---|---|
| PMCA | Pulmonary mucinous cystadenoma |
| PET | Positron emission tomography |
| CT | Computed tomography |
| FDG | Fluorodeoxyglucose |
| PMCA-OS | Pulmonary mucinous cystadenoma with ovarian-like stroma |
| PAF | Pulmonary adenofibroma |
| MCN (O) | Mucinous cystic neoplasms of the ovary |
| MCN (P) | Mucinous cystic neoplasms of the pancreas |
| PMCN | Pulmonary mucinous cystic neoplasia |

### Acknowledgements

Not applicable.

### Author contributions

Each author made substantial contributions to the conception and design of this paper. The author(s) read and approved the final manuscript. LW was the major contributor in writing the manuscript. XW analyzed and interpreted the imaging manifestations. WH was responsible for pathological diagnosis, literature review and paper revision.

### Funding

Supported by Shenzhen High-level Hospital Construction Fund.

### Data availability

Not applicable. Our manuscript does not contain any numerical data.

## Declarations

### Ethics approval and consent to participate

Not applicable. Our manuscript does not report experiments involving animals, humans, or plants.

### Competing interests

The authors declare no competing interests.

Received: 10 May 2023 / Accepted: 1 April 2025
Published online: 16 April 2025

### References

1. WHO Classification of Tumours Editorial Board. Thoracic tumours. Lyon(France):International Agency for Research on Cancer. 2021, p.51.
2. Savu C, Melinte A, Gibu A et al. Pulmonary Mucinous Cystadenoma - A Rare Pathology[J]. In Vivo,2021,35(1):629–634.
3. Geramizadeh B, Ziyaian B, Khaleghi S. Multifocal pulmonary mucinous cystic neoplasm with ovarian type stroma, a new finding in an extremely rare case report[J]. Indian J Pathol Microbiol. 2014;57(1):92–3.
4. Shawash S, Abdeljalil R, Haddad H. Multifocal pulmonary mucinous cystic neoplasm with ovarian-like stroma: once in a blue moon-case report[J]. Respir Med Case Rep. 2019;26:276–80.
5. Roux FJ, Lantuejoul S, Brambilla E et al. Mucinous cystadenoma of the lung[J]. Cancer 1995,76(9):1540–4.
6. Guimaraes AR, Wain JC, Mark EJ, et al. Mucinous cystadenoma of the lung[J]. AJR Am J Roentgenol. 2004;183(2):282.
7. Gao ZH, Urbanski SJ. The spectrum of pulmonary mucinous cystic neoplasia: a clinicopathologic and immunohistochemical study of ten cases and review of literature[J]. Am J Clin Pathol. 2005;124(1):62–70.
8. Jang KT, Park SM, Basturk O, et al. Clinicopathologic characteristics of 29 invasive carcinomas arising in 178 pancreatic mucinous cystic neoplasms with ovarian-type stroma: implications for management and prognosis[J]. Am J Surg Pathol. 2015;39(2):179–87.
9. Mackay JB, Holloway LJ. Late onset pulmonary metastases from 'benign' mucinous ovarian cystadenomata[J]. Respir Med. 1991;85(2):147–50.
10. Zamboni G, Scarpa A, Bogina G, et al. Mucinous cystic tumors of the pancreas: clinicopathological features, prognosis, and relationship to other mucinous cystic tumors[J]. Am J Surg Pathol. 1999;23(4):410–22.
11. Elias KM, Tsantoulis P, Tille JC, et al. Primordial germ cells as a potential shared cell of origin for mucinous cystic neoplasms of the pancreas and mucinous ovarian tumors[J]. J Pathol. 2018;246(4):459–69.
12. Lam MM, Swanson PE, Upton MP, et al. Ovarian-type stroma in hepatobiliary cystadenomas and pancreatic mucinous cystic neoplasms: an immunohistochemical study[J]. Am J Clin Pathol. 2008;129(2):211–8.

13. Moneke I, Zeisel C, Elze M et al. Mucinous cystadenocarcinoma arising from mucinous cystadenoma of the lung: case report and review of the literature[J]. J Thorac Dis 2018,10(4):E243–9.
14. Davison AM, Lowe JW, Da CP. Adenocarcinoma arising in a mucinous cystadenoma of the lung[J]. Thorax 1992,47(2):129–30.

## Publisher's note