



## Case report

# Multifocal pulmonary mucinous cystic neoplasm with ovarian-like stroma: Once in a blue moon-case report

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## ABSTRACT

Mucinous cystic neoplasm of the lung is a rare well known entity in the WHO classification of lung tumors. It is defined as “a localized cystic mass filled with mucin and surrounded by a fibrous wall lined by well-differentiated columnar mucinous epithelium.” The presence of ovarian-like stroma is not mentioned in this definition. Reviewing the literature, we have found only one reported case mentioning this finding, described by Geramizadeh et al., in 2014. Here we present a similar case of a patient who was initially thought to have lung metastases. Hence, our case is the second one to be reported in the literature.

After gross dissection of the received specimens, microscopic examination was performed. The H&E slides revealed that the lesions are composed of non-infiltrative biphasic proliferation of benign mucinous epithelial cells forming cysts and gland-like structures with intervening cellular ovarian-like stroma. Differential diagnosis included hamartoma and sclerosing pneumocytoma. Additionally, ancillary studies were performed including cytokeratin AE1/AE3, EMA, TTF-1, MUC5AC, ER, CD10, SMA, CD34, S100, Inhibin, PAS, PAS/D and Mucicarmine.

Immunohistochemistry showed Cytokeratin AE1/AE3, EMA and TTF-1 are positive in the epithelial cells and negative in the stromal cells. MUC5AC is weakly positive at the surface of the epithelial cells. The cells of the ovarian-like stroma are positive for ER and CD10 and focally positive for SMA. PAS, PAS/D and Mucicarmine highlighted mucin in the cystic spaces and the surface of epithelial cells. CD34, S100 and Inhibin are negative.

Mucinous cystic neoplasm with ovarian-like stroma is a well-known entity in the pancreas and liver. Its occurrence in the lung has been reported in a single case in the English-written literature. We believe that it should be considered in the differential diagnosis of benign biphasic pulmonary lesions. To our knowledge, our case is the second one to be ever reported.

## 1. Introduction

Mucinous cystic neoplasm of the lung is a rare well known entity in the WHO classification of lung tumors. It is defined as “a localized cystic mass filled with mucin and surrounded by a fibrous wall lined by well-differentiated columnar mucinous epithelium.” [1] The presence of ovarian-like stroma is not mentioned in this definition. Reviewing the literature, we have found only one reported case describing this finding, reported by Geramizadeh et al., in 2014 [2]. Here, we present a similar case of a patient who was initially thought to have lung metastases. Hence, our case is the second one to be reported in the literature.

## 2. Case report

Our patient is a 48 year old female known to have abdominal wall dermatofibrosarcoma protuberans with transformation into fibrosarcoma since one and a half years. On examination, she was conscious, alert and oriented. Her vital signs were stable. She had a scar on the left anterolateral abdominal wall. Her chest was clear with good bilateral air entry. CT scans were done for staging the tumor. The initial scan revealed multiple small bilateral pulmonary nodules which were reported as benign of uncertain nature. CT scans of the abdomen and pelvis were normal. No PET scan was done.

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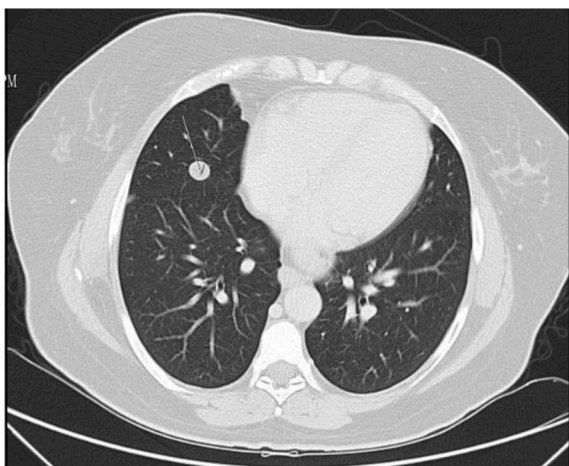


Fig. 1. Multiple bilateral lung nodules in CT scan.

On follow-up over a period of eighteen months, the patient was healthy with no complaints. Physical examination was normal as well. Serial CT scans revealed that two of the aforementioned pulmonary nodules had slightly increased in size (Fig. 1). One was located in the right middle lobe and increased from 0.9 cm to 1.2 cm. The other was located in the right lower lobe and increased in size from 1 cm to 1.5 cm. This progression raised the possibility that these lesions could represent metastasis from the patient's known primary fibrosarcoma rather than being benign. Consequently, the patient underwent right thoracotomy for multiple pulmonary metastasectomies.

Two right lung wedge resections were submitted to our pathology department; the first was from the middle lobe ( $8.5 \times 6 \times 1.5$  cm) and revealed a small cystic lesion measuring  $1.2 \times 1 \times 0.7$  cm. The second was from the lower lobe ( $5 \times 2 \times 1.5$  cm) and showed a cystic nodule measuring  $1.3 \times 1.3 \times 1$  cm. Both of these lesions were thin-walled and multiloculated and contained mucoid material. (Fig. 2).

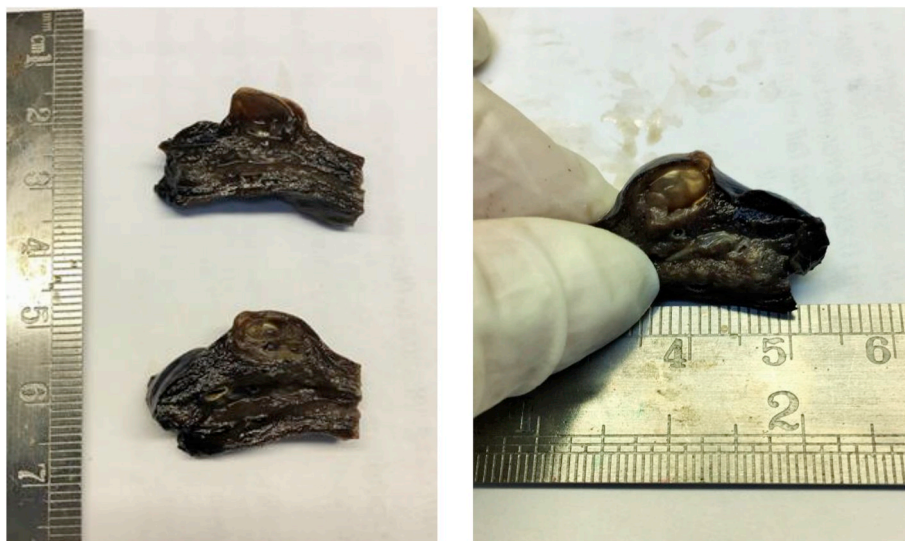


Fig. 2. Gross appearance of one of the cysts. Note the thin wall of the cyst and the multiloculation.

Microscopic examination revealed that both lesions are well demarcated and composed of biphasic proliferation of benign mucinous epithelial cells forming cysts and gland-like structures with intervening cellular ovarian-like stroma. (Fig. 3).

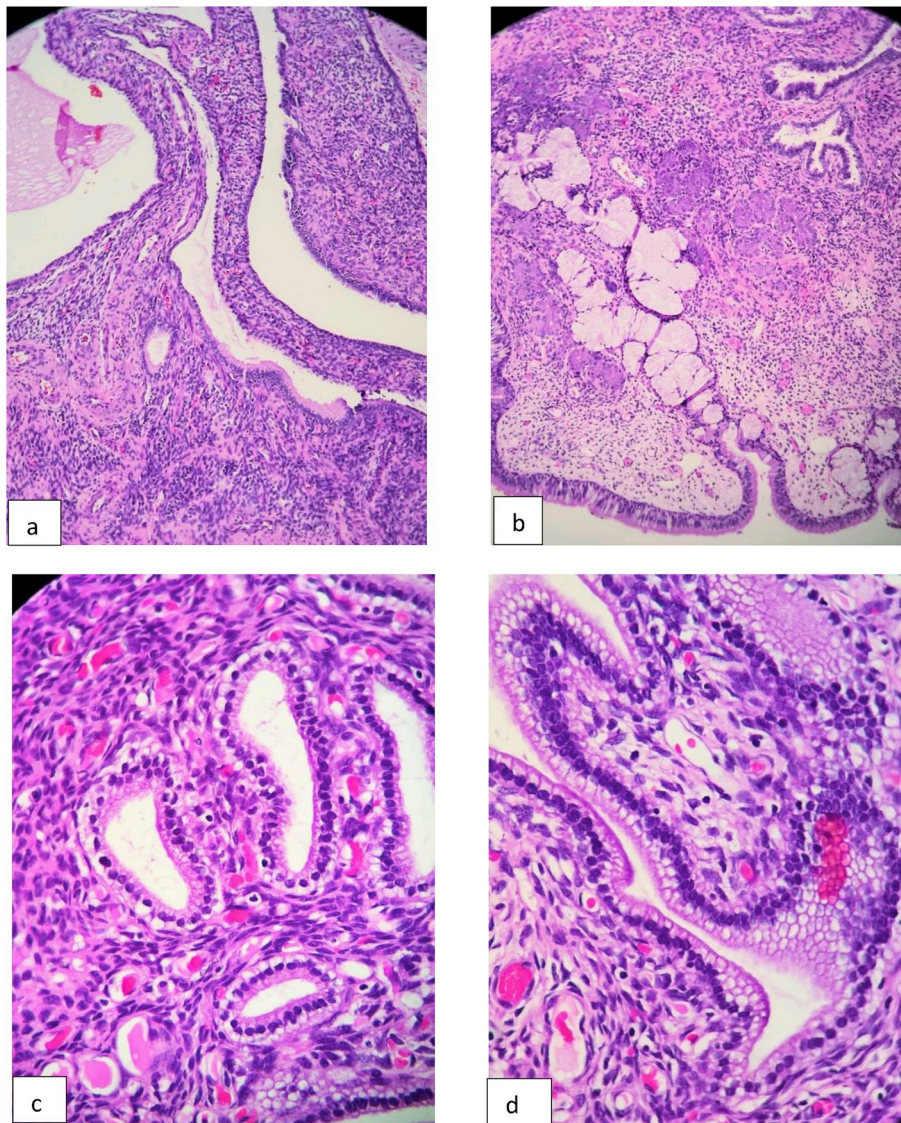
Immunohistochemistry showed that Cytokeratin AE1/AE3, EMA and TTF-1 are positive in the epithelial cells and negative in the stromal cells (Fig. 4a–c). MUC5AC is weakly positive at the surface of the epithelial cells. (Fig. 4d). The cells of the ovarian-like stroma are positive for estrogen receptors and CD10 and focally positive for SMA. (Fig. 4e and g). PAS, PAS/D and Mucicarmin special stains highlighted mucin in the cystic spaces and at the surface of the epithelial cells. (Fig. 4k–m). CD34, S100 and Inhibin are negative (Fig. 4h–j).

### 3. Discussion and literature review

Mucinous cystic neoplasm with ovarian-like stroma has been described in the pancreas and liver [3]. Only one case has been previously described as a primary lung lesion by Geramizadeh et al. [2].

Based on the morphology, our differential diagnosis included hamartoma and sclerosing hemangioma (sclerosing pneumocytoma). Hamartomas, however, are usually solitary and are composed of a mixture of more than one type of mesenchymal tissue, chondroid tissue being an almost constant constituent [4]. They are typically associated with entrapped respiratory epithelium. Our case does not show these features. On the other hand, sclerosing hemangioma usually presents as a solitary well circumscribed nodule, which may connect with bronchioles. It has variable histologic morphologies; solid, cystic and papillary. Basically, it has two types of cells: epithelial cells and oval stromal cells with relatively abundant eosinophilic cytoplasm. Both stromal and epithelial cells are positive for TTF1 and EMA [5]. However, pancytokeratin is positive only in the epithelial cells. At low power, it may resemble our case, but actually neither the morphology nor the immunohistochemistry are consistent with our case (Table 1).

In order to support our diagnosis with evidence, we applied a comprehensive panel of immune-histochemical and special stains including cytokeratin AE1/AE3, EMA, TTF-1, MUC5AC, estrogen



**Fig. 3.** H&E stain showing a benign biphasic lesion composed of mucinous glandular epithelium, and ovarian-like stroma. Original magnification (a,b) x 200, (c,d) x 400.

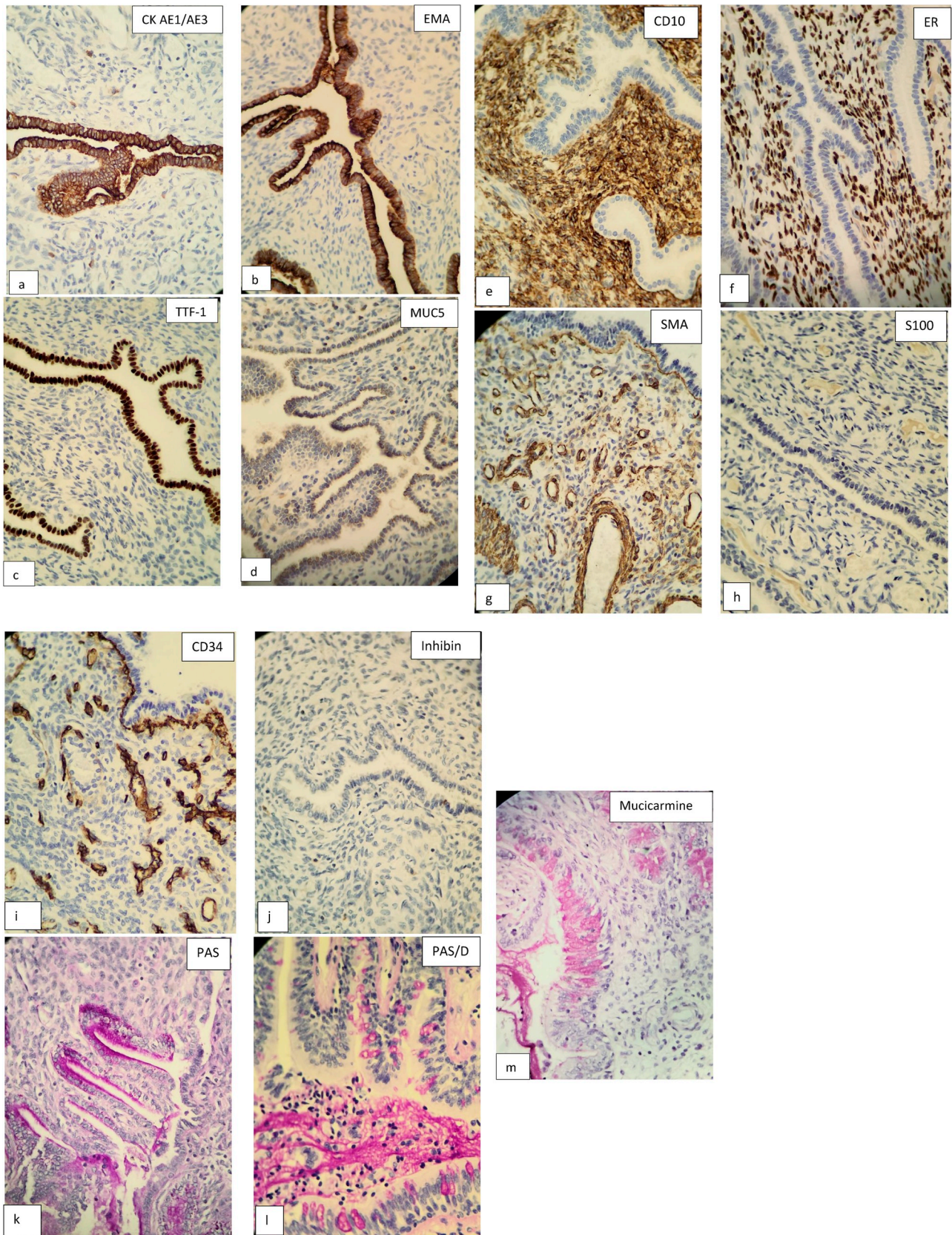
receptors, CD10, SMA, CD34, S100, Inhibin PAS, PAS/D and Mucicarmine. This is in contrast to the previously reported case by Geramizadeh et al. which only included cytokeratin AE1/AE3, cytokeratin 7, cytokeratin 20, cytokeratin 19, vimentin and estrogen receptor (Table 2).

The pancreaticobiliary mucinous cystic neoplasm with ovarian-like stroma was suggested to originate from the epithelial lining of the early fetal embryonic gonads [3]. Similarly, the presence of immunophenotypically proven ovarian-like stroma in the primary pulmonary neoplasm may suggest its genesis from misplaced Mullerian tissue during embryonic development. Inhibin and estrogen receptor immunostains in the pancreaticobiliary counterpart show variable patterns and intensities; these being weaker and focal in the pancreatic

counterpart compared to the hepatobiliary one [6]. In comparison, our case showed strong and diffuse Estrogen receptor positivity. However, Inhibin was negative, being closer to the staining pattern of the pancreatic counterpart.

#### 4. Conclusion

Primary pulmonary mucinous cystic neoplasm with ovarian-like stroma is an extremely rare entity with a single case previously reported in the literature. To our knowledge, our case is the second one to be reported.



**Fig. 4.** The epithelial cells are positive for CK AE1/AE3 (a), EMA (b), MUC5AC (c) and TTF-1 (d). PAS/Diastase (k,l) highlighted diastase indigestible mucin. The stromal cells are focally positive for SMA (g), while diffusely positive for ER (f) and CD10 (e). Both cell types were negative for S100 (h), CD34 (i) and Inhibin (j).

**Table 1**

Our differential diagnoses for a biphasic benign lung nodule, as well as the justification for the final diagnosis are explained in Table 1.

	Hamartoma	SP	PMCN
Focality	Solitary	Solitary	Multiple
Histology	Variable mesenchymal components with constant chondroid constituent	Biphasic epithelial & oval stromal cells with eosinophilic cytoplasm	Biphasic; mucinous epithelium & ovarian-like stroma
AE1/AE3		+ in E only	+ in E only
EMA		+ in S & E	+ in E only
TTF-1		+ in S & E	+ in E only
SMA		Neg.	<i>f</i> + in S
ER		<i>f</i> + in E & S	<i>d</i> + in S only
CD10		Neg.	<i>d</i> + in S only

SP: sclerosing pneumocytoma. PMCN: pulmonary mucinous cystic neoplasm. E: epithelial cells. S: stromal cells. +: positive. Neg.: negative. *f*+: focally positive. *d*+: diffusely positive.

**Table 2**

A comparison between the first reported case in the English-written literature by Geramizadeh et al. and the second one (our case).

	Geramizadeh et al.	Shawash et al.
Gender	Female	Female
Age	47 year	48 year
Focality of the nodules	Multiple & bilateral	Multiple & bilateral
Nature of the nodules	Thin-walled cysts with mucoid content	Thin-walled cysts with mucoid content
Histology	Biphasic; mucinous epithelium & ovarian-like stroma	Biphasic; mucinous epithelium & ovarian-like stroma
Ancillary studies	E: + AE1/AE3& CK7. Neg. CK20 & CK19 S: + ER & vimentin	E: + AE1/AE3, EMA, TTF-1 & PAS/D. S: <i>d</i> + ER, CD10 & <i>f</i> + SMA. Both S & E Neg. for S100, CD34& inhibin.

E: epithelial cells. S: stromal cells. +: positive. Neg.: negative. *f*+: focally positive. *d*+: diffusely positive.

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