

Case Report

Primary myoepithelial carcinoma of the lung: a case report and review of literature

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Abstract: Primary myoepithelial carcinoma of the lung is a very rare tumor arising from the salivary glands of the respiratory epithelium. Since it was first described by Higashiyama et al. in 1998, to the best of our knowledge, only eight actual cases reported in the English-language literature so far. The diagnosis is based entirely on histological and immunohistochemical evaluations. We report a primary myoepithelial carcinoma in a smoker 47-year-old Chinese man, who was referred to our institution for hemoptysis. Computed tomography revealed a 65 mm×78 mm solid mass in the left lower lobe of lung. The patient underwent the left lower lobe resection. The final histopathological diagnosis was primary myoepithelial carcinoma of the lung. Given the rare occurrences of this tumor, appropriate recommendations for treatment are difficult to formulate. Although classified as low-grade tumor, it has a significant rate of distant metastasis. Herein we report a case of a primary myoepithelial carcinoma of the lung and present a brief review of the literature.

Keywords: Lung, myoepithelial carcinoma, myoepithelial tumor, salivary gland type tumor

Introduction

Primary salivary gland type tumors of lung are very rare, accounting for 0.1-0.2% of all lung tumors [1]. These tumors usually arise from the epithelium of tracheobronchial submucosal glands. These tumors can display the same spectrum of histological variability as their salivary gland counterparts and are accordingly classified by the World Health Organization (WHO) criteria for salivary gland tumors, including mucoepidermoid carcinoma, adenoid cystic carcinoma, epithelial-myoepithelial carcinoma, acinic cell carcinoma, oncocytoma, benign myoepithelioma, and mixed tumors of both benign and malignant nature. Various benign and malignant tumors of these structures have been described in the lung. Primary myoepithelial carcinoma of the lung is an extremely rare, with only eight known prior cases reported in the literature to date [2-8]. Herein, we report a case of primary myoepithelial carcinoma of the lung, including clinical and histopathological features, clinical prognosis, and diagnostic and therapeutic approaches, and a review of the literature.

Case report

A 47-year-old Chinese man was admitted to our hospital because he presented with no apparent cause of hemoptysis for 1 month. He denied other concurrent symptoms including cough, expectoration, fever, nausea, vomiting or appetite loss. The patient was a smoker (20 cigarettes/day for 27 years) and had no history of salivary gland tumor. Routine laboratory investigations were normal, including complete blood count and serum urea and electrolyte levels. Tumor markers, including carcinoembryonic antigen, α -fetoprotein, and carbohydrate antigen 19-9, were all within normal limits. A chest computed tomography (CT) demonstrated a solid mass with calcification measuring 65 mm×78 mm in the left lower lobe (**Figure 1A, 1B**). We performed a new staging workup including an abdominal and a brain CT-scan, both of which were normal, and bone scintigraphy were negative. Although sputum cytology and a transbronchial lung biopsy were negative, imaging investigation was indicative of malignancy, and resection of the left lower lobe was

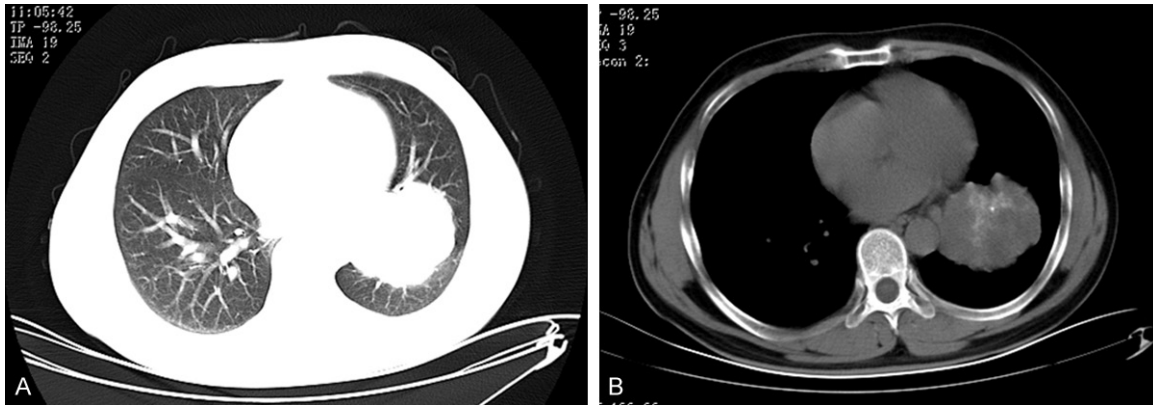


Figure 1. CT findings revealed a solid mass with calcification measuring 65 mm×78 mm in the left lower lobe (A and B).

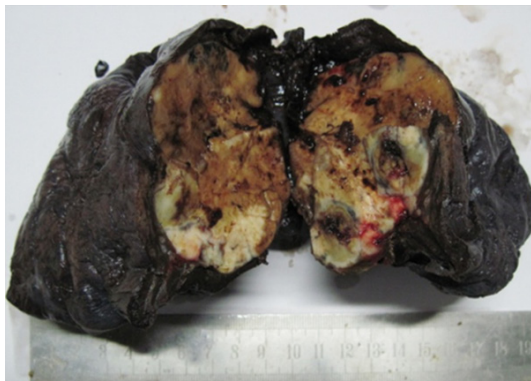


Figure 2. Gross pathologic findings that cross-sections of the tumor revealed a firm, grayish white and yellow mass involving the visceral pleura.

performed. Our patient was not given any treatment after operation. With a follow-up period of 4 months, no clinical and radiological evidence of recurrence and metastasis was found.

Pathological examination

On gross examination, the surgical specimen consisting of a left lower lobectomy which measuring 12 cm×10 cm×10 cm, 6 separate resected mediastinal lymph nodes and 7 hilar lymph nodes. The mass measured 6.5 cm transversely, cross-sections of the tumor revealed a firm, grayish white and yellow mass involving the visceral pleura (**Figure 2**), the margin of the bronchus was within 2.3 cm of the tumor. Microscopically, the tumor was located at the bronchial submucosa and cartilage (**Figure 3A**), and invaded surrounding pulmonary tissue. The tumor mainly consisted spindle and clear cells,

the spindle cells arranged in fascicles (**Figure 3B**), resembling spindle cell sarcoma; the clear cells had oval nuclei with mild or moderate atypia, forming solid or lamellar structure (**Figure 3C**), or were divided into small nests or trabecular-like structure by fibrous stromal (**Figure 3D, 3E**). In part region with squamous differentiation and calcification (**Figure 3F**). One mitoses were present per 10 High Power Fields (HPFs), 10% areas of necrosis were found. No ductal or acinic structures were found throughout the tumor. The hilar and mediastinal lymph nodes were negative. Immunohistochemically, neoplastic cells were strongly reactive for CK, CK5/6, vimentin, P63 (**Figure 4A**), S-100 (**Figure 4B**), calponin, GFAP, SMA, but were negative for cytokeratin 7 (CK7), CD117, CD68, HMB45, CD34, EMA and CD10. Ki-67 nuclear proliferation index was positive about 5%. The final histological diagnosis was primary myoepithelial carcinoma of the lung.

Discussion

Myoepithelial carcinoma is a relatively rare tumor showing only myoepithelial differentiation without any ductal formation and primarily arise from the salivary glands, the parotid, or the breast [9]. Primary myoepithelial carcinoma of the lung is an extremely rare malignant tumor, probably originating from the bronchial minor salivary gland, with only 8 patients reported in the English literature [2-8]; the previously reported cases are summarized in **Table 1**. Very limited information was available for only one patient [7]. Interestingly 6 patients are Japanese and one patient is Caucasian. The

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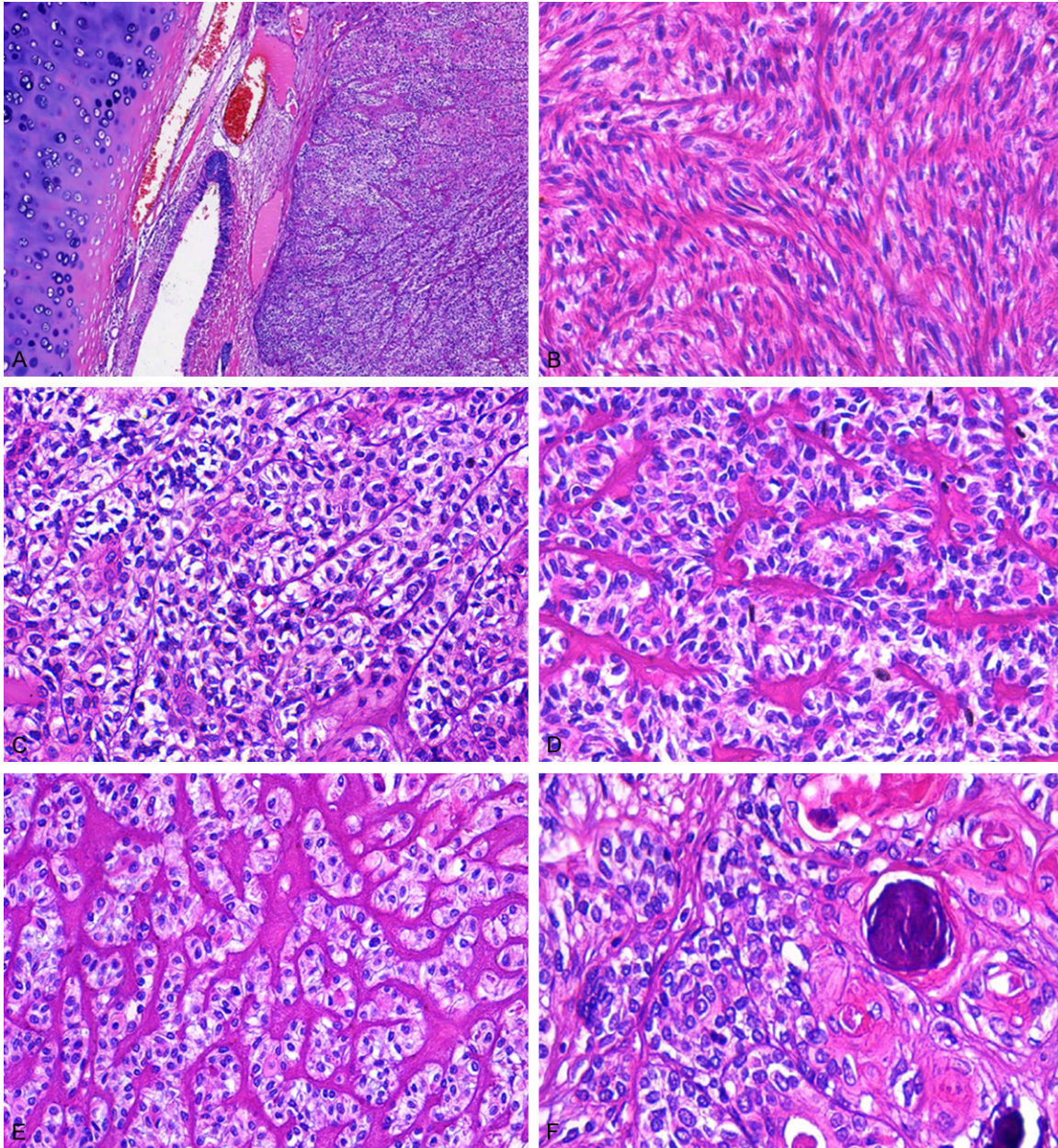


Figure 3. Microscopically, the tumor was located at the bronchial submucosa and cartilage (A: H&E, 25 \times), mainly consisted spindle and clear cells; the spindle cells arranged in fascicles (B: H&E, 100 \times); the clear cells have oval nuclei with mild or moderate atypia, forming solid or lamellar structure (C: H&E, 100 \times); or is divided into small nests or trabecular-like structure by fibrous stromal (D and E: H&E, 100 \times); in part region with squamous differentiation and calcification (F: H&E, 100 \times).

age of patients range from 46 to 76 years (average, 58.4 years), indicating that the tumor has been principally found in elderly adults. In contrast to salivary myoepithelial carcinoma which is greater prevalence in women, primary myoepithelial carcinoma of the lung appears to show significant sex predominance (5 men and 2 women). 4 patients smoked tobacco, therefore, we hypothesized that this tumor has

closed relationship with smoking. 3 tumors were located in an endobronchial position as polypoid, and presented with early clinical symptoms induced by obstruction of the lumen, such as cough, fever, chest discomfort and dyspnea. The excised lesions range in size from 1.5 to 13 cm (average, 5.1 cm). The mitotic rate of the tumor range from 5 to 32/10 HPFs (mean 14.7/10 HPFs).

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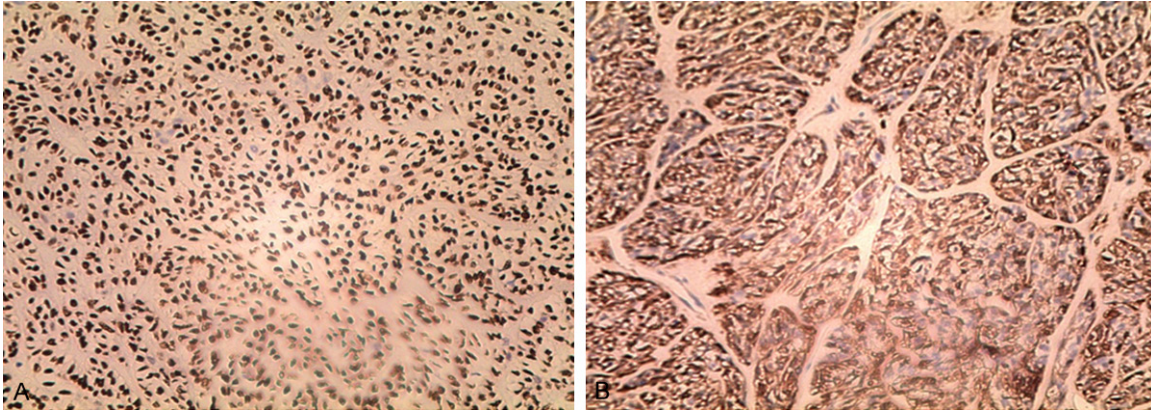


Figure 4. Immunohistochemically, neoplastic cells were strongly reactive for p63 (A; EnVision, 50 \times) and S-100 (B; EnVision, 50 \times).

There are no tumor markers or imaging characteristics that allow a preoperative diagnosis, and all cases have been diagnosed after surgical resection. The diagnosis is based entirely on histopathological and immunohistochemical evaluations. The morphology of neoplastic myoepithelial cells varies within the tumor, and mainly includes four morphologic types: the spindle, plasmacytoid, clear, and epithelioid types. In the limited reported cases, spindle and plasmacytoid cells were common; our case was mainly composed of clear and spindle cells. Although myoepithelial carcinoma are often positive to antibodies for both epithelial cells and smooth muscle cells, but immunohistochemical reactivity also varies among the different cell types [4]. According to review of the literature, we found that spindle myoepithelial cells are persistently positive for SMA but show variable immunostaining for CK, whereas plasmacytoid, clear and epithelioid myoepithelial cells are positive for CK and show variable immunostaining for SMA. S-100 is considered to be the best diagnostic markers. Myoepithelial carcinoma is consistently positive for vimentin, S-100, p63 and GFAP. The present tumor cells were positive for CK, P63, S-100, Calponin, GFAP, SMA, and vimentin. Therefore, the final diagnosis was primary myoepithelial carcinoma of the lung.

The differential diagnosis of primary myoepithelial carcinoma of the lung will mainly depend upon the morphology of predominance neoplastic myoepithelial cells in the tumor, but is likely to be a problem in small endobronchial biopsy and cytology specimens. Metastatic

lesions from the salivary gland first should always be ruled out. The differential diagnosis in the present case included myoepithelioma, leiomyoma/leiomyosarcoma, mucoepidermoid carcinoma and clear cell tumor of the lung. Separation of myoepithelial carcinoma from myoepithelioma is primarily based on cellular abnormalities, infiltrative growth, mitotic figures and necrosis. Regarding the immunoreactivity of the tumor for CK and p63, which is the most useful marker to help discriminate myoepithelial tumors from other mesenchymal tumors, like leiomyoma/leiomyosarcoma or clear cell tumor of the lung. But mucoepidermoid carcinoma is usually composed of epidermoid cells, mucous cells and intermediate cells.

According to review of the literature, although all the patients were treated by adequate surgery, and no local recurrences, but seven patients (87.5%) developed metastasis, either synchronous at time of resection, or presenting as metachronous recurrence, including metastasis to the contralateral lung [2, 6], the forearm and the hip [8], the liver [3, 8] and the brain [4]. The follow-up period ranged from 4 months to 5 years. One patient died of brain metastases 11 months after surgery [4]. One patient died at 14 months from synchronous metastatic adenocarcinoma [8]. One other patient developed liver metastases and died 5 years postoperatively [8]. Two patients were alive with disease [3, 6], and others were free of disease at relatively short follow-up intervals. Based on these data, we think that primary myoepithelial carcinoma of the lung is a highly malignant

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Table 1. Clinicopathologic characteristics of previously reported cases of Myoepithelial Carcinoma of the Lung

Author/References	Age (years)	Gender	Smoking	Location	Size (cm)	Metastasis	Treatment	Survival (months)
Jianguo et al (current case)	47	M	Yes	LLL	6.5 cm	None	LLL resection	6 (Alive without disease)
Hysi et al ²	60	F	NO	LLL	NA	metastasis to RLL	LLL and RLL resection	10 (Alive without second metastasis and recurrence)
Sarkaria et al ³	63	F	NO	RLL	13.0 cm	metastasis to liver	Wedge/local excision	36 (Alive with disease)
Tanahashi et al ⁴	76	M	Yes	LLL	2.2 cm	metastasis to brain	Partial resection of LLL	11 (Died of brain metastases)
Masuya et al ⁵	48	M	Yes	LLL	1.5 cm	None	LLL resection	15 (Alive without disease)
Miura et al ⁶	46	M	NA	Right lung	6.5 cm	metastasis to LLL	Right pneumonectomy	7 (Alive with disease)
Sekine ⁷	NA	NA	NA	NA	NA	have metastasis but NA	NA	NA
Higashiyama et al ⁸ (case 1)	58	M	Yes	RUL	3.8 cm	left forearm and the hip	RUL and RML resection	14 (Died of other causes)
Higashiyama et al ⁸ (case 2)	58	M	Yes	LUL	6.0 cm	metastasis to liver	LUL resection	60 (Died of disease)

NA: not available; LLL: left lower lobe; RLL: right lower lobe; RUL: right upper lobe; LUL: left upper lobe; RML: right middle lobe.

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tumor. It is necessary to note that the patient who has not developed metastasis, had the lowest tumor mitotic rate of 5/10 HPFs. Also the tumor had only mitotic rate of 1/10 HPFs in our patient, and Ki-67 nuclear proliferation index was less than 5%, and there are no recurrence and metastasis with a follow-up period of 4 months. This fact argues that mitotic rate and Ki-67 nuclear proliferation index may be an important prognostic factor of clinical outcome and survival in primary myoepithelial carcinoma of the lung.

In conclusion, a lung mass with spindle cells and clear cells should raise the suspicion of myoepithelial carcinoma; we present a case of primary myoepithelial carcinoma of lung. In our case the tumor was completely excised and bronchial margins and lymph nodes were all negative. Therefore, his surgical excision is successful and would be expected to be curative. Some reports pointed out that this tumor is not sensitive to radiotherapy and chemotherapy [6], given the rarity of these tumors, recommendations regarding chemotherapy or radiation, either pre- or post-operatively, are difficult to formulate, close long-term follow-up of this patient may help elucidate the natural history of this rare tumor.

Disclosure of conflict of interest

None.

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