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Mucoepidermoid carcinoma of the lung with hemoptysis as the initial symptom: A case report

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**Abstract**

**BACKGROUND**

Mucoepidermoid carcinoma of the lung is a rare malignant tumor, accounting for 0.1%–0.2% of all lung malignancies. It is a primary salivary gland tumor of the lung. To date, there is no unified strategy for the treatment of PMEC, and surgical resection is recognized as the main treatment method. This article reports a case of a young woman with pulmonary mucoepidermoid carcinoma with hemoptysis as the first symptom. The patient was admitted to the interventional department of our hospital because of hemoptysis, and the possibility of a malignant tumor could not be excluded after perfect bronchoscopy and tissue biopsy. Therefore, she was transferred to thoracic surgery for lung mass resection, and based on the postoperative pathology, the tumor was clearly diagnosed as pulmonary mucoepidermoid carcinoma. In this case, the patient underwent two tissue biopsies to confirm the diagnosis of the disease. The disease is rare in the literature, so this case is hereby reported to increase the clinician's understanding of the disease.

**CASE SUMMARY**

A 24-year-old female patient presented to our hospital with "4 days of hemoptysis". The patient had no special history and denied smoking or drinking history. Physical examination: The vital signs were stable, scattered small wet rales were heard in the left
lung, and the remaining physical examination found no abnormalities. After admission, the lung tumor markers were checked, and no abnormalities were found. After completing the bronchoscopy, a new spherical organism was observed at the main bronchus 1.5 cm away from the protuberance, with obvious pulsation and little blood seepage on the surface, and histopathological biopsy results showed acute and chronic inflammation. She was transferred to the Department of Thoracic Surgery for surgical treatment on the 16th day after admission. After exclusion of surgical conjunctures, the patient underwent resection of the tumor in the left main bronchus with single-pore VATS on the 19th day after admission. The postoperative histopathological biopsy results showed mucoepidermoid carcinoma of the lung. The patient and her family refused to complete genetic testing and were discharged from the hospital on the 8th day after surgery. During the follow-up period, the patient experienced shortness of breath after feeling active and had no special discomfort.

CONCLUSION
In this paper, we report a 24-year-old female patient with moderately differentiated mucoepidermoid lung cancer who underwent surgical resection with hemoptysis as the first symptom to improve clinicians' understanding of the disease and provide a new dimension of thinking for the future diagnosis and treatment of the disease.

INTRODUCTION
Pulmonary mucoepidermoid carcinoma (PMEC) was first reported by Smetana in 1952 as a rare malignant tumor of the lung\textsuperscript{[1]}. It is the most common primary salivary gland carcinoma of the lung, originating from the small salivary gland in the submucosa of the atmospheric tract\textsuperscript{[2]}. At present, there are few reports on PMEC, and most are case reports. Its clinical symptoms and epidemiological characteristics are not specific and representative. In addition, there is no specific treatment, and surgical excision remains the main treatment. Therefore, it is necessary to increase the attention of clinicians to the disease. This paper reports the case data of a young woman with
hemoptysis as the first symptom who was clearly diagnosed with the disease after two lung histopathological biopsies and was discharged from the hospital after surgical treatment, aiming to provide some help for the diagnosis and treatment of the disease and improve the awareness of clinicians about the disease.

7 CASE PRESENTATION

Chief complaints

A 24-year-old female patient presented to our hospital with hemoptysis for 4 days.

History of present illness

Bright red blood appeared 4 days prior, the amount was approximately 20 mL/day, accompanied by cough and sputum, and the sputum was a small amount of frothy sputum.

History of past illness

Previous good health, no history of specific diseases.

2 Personal and family history

The patient’s personal history and family history were unremarkable.

Physical examination

The patient’s vital signs were stable, and the patient had a clear mind and cooperated with the physical examination. The skin mucosa color was normal, and the superficial lymph nodes of the whole body were not enlarged. Bilateral respiratory movement was normal, palpation of both lungs was normal, percussive sound of both lungs was clear, small wet rales were heard in the left lung, and pleural fricative sounds were not heard on either side. No abnormal positive signs were found in the residual physical examination.
Laboratory examinations

D-dimer was 1.17 μg/mL, and hypersensitivity C-reactive protein was 32.88 mg/L. There were no obvious abnormalities in lung tumor markers, routine blood tests, coagulation function, liver function, renal function, or Mycobacterium tuberculosis culture.

Imaging examinations

Chest CT: left lung emphysema, part of the left lung atelectasis, and part of the bronchus unclear (Figure 2).

MULTIDISCIPLINARY EXPERT CONSULTATION

Further diagnostic work-up

After admission, the patient was treated with hemostasis and anti-infection treatments, and no hemoptysis occurred. Improved contrast-enhanced CT results of the chest showed that a left main bronchial nodule was seen (Figure 2). Considering space occupation, increased soft tissue density shadows appeared in the left hilar area of the lung, and fiberoptic bronchoscopy was recommended. Left pulmonary obstructive emphysema, obstructive atelectasis and obstructive inflammation of the left lung were noted. Further improvement of the electronic bronchoscopy showed that the main bronchus grew out of a spherical new lesion 1.5 cm from the protuberance, with pulsation and slight bleeding on the surface. The considerations were as follows: 1. New lesions in the left main bronchus to be investigated. Could it be a tumor? 2. Malignant stenosis of the left main bronchus (Figure 1) was present; The painless ultrasonic bronchoscopy showed new biological properties of the left main bronchus to be investigated. The lung tumor markers improved and showed no abnormalities. Cytopathology and DNA ploidy analysis of alveolar lavage fluid (left main bronchoalveolar lavage fluid) showed no definite malignant cells. The results of the bronchial examination tissue biopsy showed that the mucosa presented acute and chronic inflammatory changes, mucinous
gland hyperplasia in the lamina mucosa, squamation of the columnar epithelium and active proliferation of epithelial cells. Some necrotic tissues were also observed, among which small clusters of proliferative glandular epithelial cells were found, the cytoplasm was vacuolar, nucleoli were visible, and no mitotic image was observed. Please refer to the clinical findings. The immunohistochemical results were as follows: CEA (+) oven, CK (+), CK5/6 + (part), CK7 (+), (-), the vera.ttf - 1 P40 (-), about (-), NapsinA (-), according to (-); The automatic immunohistochemical results were as follows: CD117(-), Ki67(5%+); Special dye: antacid (-), PAS(+)(Figure 4).

Based on the immunohistochemistry findings, the patient was transferred to the Department of Thoracic Surgery for surgical treatment on the 16th day after admission. After the exclusion of surgical conjunctures, the patient underwent resection of the tumor in the left main bronchus with single-pore VATS on the 19th day of admission (thoracotomy of the left main bronchus and trachea window for tumor resection and anastomosis). Rapid intraoperative pathological examination revealed neoplastic lesions (in the left main bronchus), which were likely to be malignant tumors from the salivating glands. Specific results were determined by paraffin wax and immunohistochemistry. The postoperative histopathological results showed the following: (in the left main bronchus) lung mucoepidermoid carcinoma, vascular invasion (-), nerve invasion (-), no tumor involvement (airway wall of tumor pedicle); (Group 4) lymph nodes (0/3), (Group 5) lymph nodes (0/1), (Group 10) lymph nodes (0/2), no tumor metastasis was found, pTNM staging: pT1bNOMX: immunohistochemical results: CK(+), CK5/6 (partial +) P40 (partial +), P63 (partial +), CK7 (+), CK-H (+), TTF1 (-), NapsinA (-), CEA (small focus.). The automatic immunohistochemical results included CD117 (part of cells+) and Ki67 (10%+); the special staining results were PAS(+) (Figure 5). Head MRI plain scan + enhancement and upper abdominal CT plain scan + enhancement showed no obvious abnormalities. After the operation, the patient was treated with anti-infection, hemostasis, cough and expectorant treatment, anti-
inflammatory treatment, and lung function recovery exercises. After repeat chest CT (Figure 3), the patient was discharged from the hospital on the 8th day after surgery.

MULTIDISCIPLINARY EXPERT CONSULTATION
After considering the pathological results of the patient's two tissue biopsies and imaging data, the pathologist believed that the lesion was a moderately differentiated pulmonary epidermal mucoid carcinoma, and the relevant genetic examination can be further improved to guide subsequent treatment. The radiologist believed that the imaging data of the patient in this case were not typical adenocarcinoma manifestations, and considering the rarity of the disease, the diagnosis was mainly based on tissue biopsy pathological nodes. The thoracic surgeon considered the patient to be a young woman, and the mass was removed locally. The lung tissue was preserved as much as possible, and close follow-up was performed to determine whether there was metastasis or recurrence. The respiratory surgeon believed that the patient should have a complete bronchoscopy at regular intervals after discharge to clarify the bronchial cavity, and reoperation could have been considered if necessary.

FINAL DIAGNOSIS
The final diagnosis of the presented case was pulmonary mucoepidermoid carcinoma (PMEC).

TREATMENT
After surgical treatment, anti-infection, hemostasis, cough and expectorant; anti-inflammatory treatments; lung function recovery exercises and other treatments were given, the patient improved and was discharged on the 8th day after surgery.

OUTCOME AND FOLLOW-UP
After surgical treatment, the patient was treated with anti-infection, hemostasis, cough and expectorant, and anti-inflammatory treatments and lung function recovery exercises, etc. The patient improved and was discharged from the hospital on the 8th
day after surgery. During the follow-up period, the patient experienced shortness of breath and no special discomfort.

**DISCUSSION**

Myxoeipidermoid carcinoma of the lung is the most common primary salivary gland cancer in the lungs, originating from small salivary glands in the submucosa of the respiratory tract[2]. As a rare malignant lung tumor, it was first reported by Smetana *et al*[1] as early as 1952, and it was found that it accounted for less than 1% of malignant lung tumors [3-5]. Due to its rarity and lack of specificity in clinical and radiological features, the diagnosis is largely dependent on pathological examination. In addition, PMECs should be distinguished from adenosquamous carcinoma, especially in tiny biopsy specimens obtained by fibrobronchoscopy or lung puncture. It is defined as a tumor composed of mucoepidermoid cells, epidermoid cells and intermediate cells[6]. At present, there is no unified standard for treatment, and surgical resection is considered the main treatment method[7].

Mucoepidermoid carcinoma is the most common malignant tumor in the salivary glands, with an incidence of 0.44 cases/100,000 people[8]. It can occur at any age but is most common between the ages of 35 and 65, with approximately 60% of cases occurring in women. Large salivary glands are frequently involved and very rarely (less than 1%) occur in the lung [9]. Patients with PMEC often have no specific clinical symptoms, but this may depend to some extent on the location of the lesion. Tumors located in the central bronchus usually present with obstructive airway symptoms, mainly cough, dyspnea, or asthma; 85% of PMECs are reported to be peripheral to the lung, characterized by cough, chest pain, and lung inflammation. Some asymptomatic patients are found during physical examination[7]. Therefore, there are challenges in the diagnosis of this disease. It is therefore necessary to improve the understanding of clinicians to achieve early detection, early treatment and accurate treatment.

In this case, hemoptysis was the first symptom, and chronic inflammatory changes were considered after the first bronchial histopathologic biopsy. However, the
immunohistochemical results suggested CEA (focal +), CK (+), CK5/6 (partial +), CK7 (+), Ki67 (5%+), and PAS staining (+). Considering the abnormal immunohistochemistry, a tumor could not be excluded, so PMEC was clearly diagnosed after surgical resection and pathological biopsy. Pathological immunohistochemistry plays an important role in the diagnosis of this disease.

The diagnosis of PMEC mainly depends on histopathological immunohistochemical examination, which is histopathologically composed of squamous epithelial cells, mucous cells, and intermediate cells with keratosis defects. PMECs are divided into low- and high-grade tumors based on histological appearance, mitotic frequency, cell atypia, and necrosis[8]. The survival rate of high-grade mucoepidermoid carcinoma was significantly lower than that of low-grade mucoepidermoid carcinoma, and the possibility of metastasis to lymph nodes of high-grade mucoepidermoid carcinoma was found to be 10 times higher than that of low-grade mucoepidermoid carcinoma[10]. In general, PMEC tumors appear as tan or light brown polypoid masses. The central bronchus may exhibit exoplastic tumors that almost completely obstruct the bronchial lumen[11]. The immunohistochemical characteristics of PMEC were retrospectively analyzed and summarized, and the positive rates of p63, CK7, Muc5Ac, p40 and CK5/6 were 58/58 (100%), 33/33 (100%), 26/26 (100%), 52/54 (96.3%) and 3/6 (50%), respectively. Napsin A, TTF-1 and human epidermal growth factor receptor 2 (HER2) were all negative[7]. However, some studies do not conform to this conclusion. Zhang et al[12] reported that TTF-1 and napsin A were positive in some PMEC cases, and one paper reported that trastuzumab treatment was effective in metastatic MEC patients with positive HER2 expression[13]. In addition, some scholars found that the Ki-67 marker index in low-grade cases was lower than that in high-grade cases and proposed that the Ki-67 marker index might be used as one of the indicators to distinguish PMEC levels[14]. At present, most studies at home and abroad mainly focus on case reports or analysis and summarize a small number of case data, and the number of studies needs to be expanded for further research.
Studies have shown that the tumor is associated with the gene t(11; 19)(q21-22; p13) chromosome translocation, which is associated with MECT1-MAML2 fusion\textsuperscript{[15]}, and some scholars have found that this fusion gene can not only activate HES1 transcription, thus destroying the Notch signaling pathway. However, it also activates the protein CREB, thus simulating the conformation activation pathway of cAMP signaling\textsuperscript{[16-17]}. Some scholars proposed that fusion genes could be used as a diagnostic basis for PMEC because they were found to exist in most patients with this disease \textsuperscript{[7]}. In addition, some studies found that fusion genes were often found in low-grade groups \textsuperscript{[18-19]}. At present, most of the genes of this disease are limited to fusion genes. There are also studies using comprehensive genome amplification to study a small number of high-grade PMECs, it was found that most patients have at least one gene mutation, and the most common genomic changes are CDKN2A and TP53. However, the reliability of this study remains questionable due to the small sample size \textsuperscript{[20]}.

More interestingly, overexpression of the EGFR protein is common in most cases of PMEC, but amplification or mutation in the tyrosine kinase region of the EGFR gene has rarely been reported \textsuperscript{[18]}. At present, there is no unified standard for the treatment of PMEC, and the main treatment mode is surgical excision. The effect of chemoradiotherapy is controversial. There have also been reports of cases effectively treated by chemotherapy, such as apatinib combined with graded stereotactic radiotherapy \textsuperscript{[14]}, carboplatin combined with paclitaxel \textsuperscript{[21]}, and EGFR-tyrosine kinase inhibitor drug therapy \textsuperscript{[22]}. However, there are individual differences due to the majority of the literature being case reports, and the specific efficacy needs to be further studied. It has been reported that PMEC is a fairly inert tumor with a relatively optimistic prognosis, and the survival rate is better than that of patients with small cell lung cancer and non-small cell lung cancer. The 5-year survival rate of PMEC is approximately 45%-70\%\textsuperscript{[5]}. Mucoepidermoid carcinoma usually involves the proximal bronchus. Therefore, the typical symptoms of mucoepidermoid carcinoma are bronchial obstruction, such as cough, hemoptyisis,
asthma, and fever [23]. Salivary gland tumors are rare primary lung lesions. The most common primary salivary gland tumors mainly include mucoepidermoid carcinoma, adenoid cystic carcinoma and epithelial-myepithelial carcinoma. Their morphology, immunophenotype and molecular characteristics are similar to those in the head and neck or other sites. Because of their rarity, research is often limited, and relevant studies are usually small or limited to individual cases. Fortunately, molecular changes such as MAML2 rearrangement in mucoepidermoid carcinoma of the lung, MYB rearrangement in adenoid cystic carcinoma, clear cell carcinoma and EWSR1 rearrangement in myoepithelial tumors have been found [24]. These molecular changes help to distinguish salivary gland tumors from other lung tumors to a certain extent and will provide great help for the diagnosis and treatment of this disease and follow-up research.

PMEC is a rare malignant tumor with no specific clinical symptoms. The diagnosis of PMEC mainly relies on pathological immunohistochemical examination. The diagnosis of the patient in this case was confirmed by two biopsies. Reporting this case is expected to improve the diagnosis rate of this disease to achieve early detection and treatment.

CONCLUSION
PMEC is a rare malignant tumor, and clinical symptoms often have no specific manifestations. Diagnosis of the disease mainly relies on pathological immunohistochemical examination. In this case, two tissue biopsies were performed to confirm the disease. When there is unexplained hemoptysis in a young patient, the disease should be considered, and diagnostic work up should be carried out as soon as possible to confirm the diagnosis.

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