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CASE REPORT

Left lower lobe sleeve resection for the clear cell variant of pulmonary mucoepidermoid carcinoma: A case report

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Abstract

BACKGROUND

Pulmonary mucoepidermoid carcinoma (PMEC) is a rare malignancy that arises from minor salivary glands within the tracheobronchial tree. The clear cell variant of PMEC is exceptionally uncommon and presents notable diagnostic challenges, primarily attributable to its morphological similarity to other tumors containing clear cells.

CASE SUMMARY

A 22-year-old male, formerly in good health, came in with a two-month duration of persistent cough and production of sputum. Subsequent imaging and bronchoscopy examinations revealed a 2 cm tumor in the distal left main bronchus, which resulted in complete atelectasis of the left lung. Further assessment *via* positron emission tomography/computed tomography scans and endoscopic biopsy confirmed the primary malignant nature of the tumor, characterized by clear cell morphology in most of the tumor cells. The patient underwent a left lower lobe sleeve resection accompanied by systematic mediastinal lymph node dissection. Molecular pathology analysis subsequently revealed a *CRTC3-MAML2* gene fusion, leading to a definitive pathological diagnosis of the clear cell variant of PMEC, staged as T2N0M0. After surgery, the patient experienced a smooth recovery and exhibited no signs of recurrence during the one-and-a-half-year follow-up period.

CONCLUSION

This article describes an unusual case of a clear cell variant of PMEC characterized by the presence of a *CRTC3-MAML2* gene fusion in a 22-year-old male. The

patient underwent successful left lower lobe sleeve resection. This case underscores the distinctive challenges associated with diagnosing and treating this uncommon malignancy, underscoring the importance of precise diagnosis and personalized treatment strategies.

Key Words: Pulmonary mucoepidermoid carcinoma; Clear cell variant; *CRTC3-MAML2* gene fusion; Sleeve lobectomy; Case report

Core Tip: Pulmonary mucoepidermoid carcinoma (PMEC) is an uncommon malignancy originating from the minor salivary glands of the tracheobronchial tree. Its clear cell variant, even rarer, presents distinctive diagnostic challenges due to its morphological similarity to other clear cell tumors. This report describes the case of a 22-year-old male diagnosed with the clear cell variant of PMEC characterized by the *CRTC3-MAML2* gene fusion. The patient successfully underwent a left lower lobe sleeve resection without the need for adjuvant therapy. At the one-and-a-half-year postoperative follow-up assessment, he exhibited no signs of recurrence.

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INTRODUCTION

Pulmonary mucoepidermoid carcinoma (MEC) is an uncommon malignant neoplasm that accounts for only 0.1%-0.2% of all lung malignancies[1]. Originating from minor salivary glands within the tracheobronchial tree, Pulmonary MEC (PMEC) is histologically characterized by mucous-producing, epidermoid, and intermediate cells[2]. The clear cell variant of PMEC, distinguished by prominent cytoplasmic clearing, poses diagnostic challenges due to its similarity to other clear cell-containing tumors[3]. Recent genetic advancements have identified *MAML2* as a critical driver gene in MEC, establishing the *CRTC1/3-MAML2* gene fusion as a valuable diagnostic biomarker[4]. Despite these genetic insights, there is currently no standardized therapeutic strategy for PMEC; however, complete surgical resection remains the primary treatment approach[5]. This case report discusses the case of a patient who was diagnosed with the clear cell variant of PMEC harboring the *CRTC3-MAML2* gene fusion and underwent left lower lobe sleeve resection. The objective is to highlight the distinctive challenges associated with diagnosing and managing this rare malignancy, emphasizing the critical importance of accurate diagnosis and personalized treatment strategies.

CASE PRESENTATION

Chief complaints

A 22-year-old Chinese male sought medical attention, presenting at the hospital with a persistent 2-mo history of coughing coupled with the production of sputum.

History of present illness

A 22-year-old male presented with symptoms that started approximately two months earlier without identifiable precipitating events or triggers. Initial complaints included a persistent cough and the production of white, mucoid sputum, occasionally encompassing streaks of blood. He sought medical attention at a local facility after experiencing these symptoms for a month, and the initial assessment suggested bronchopneumonia, which led to treatment with cephalosporin antibiotics. However, over subsequent days, symptoms not only persisted but also worsened. The cough intensified and was accompanied by dyspnea and intermittent left-sided chest pain. Due to the lack of improvement, additional diagnostic investigations were initiated. High-resolution chest computed tomography (CT) and bronchoscopy revealed a 2 cm contrast-enhanced nodule in the left main bronchus, causing complete atelectasis of the left lung and a mediastinal shift to the left. Biopsy was challenging due to the necrotic surface of the lesion. In response, the hospital's respiratory team implemented an interventional approach, which included a high-frequency snare technique combined with cryotherapy to excise a section of the lesion. Subsequent histopathological examination revealed that the tumor was a primary lung carcinoma with clear cell morphology, although the exact pathological classification was indeterminate. Following the intervention, the patient reported significant alleviation of respiratory symptoms. However, a subsequent CT scan indicated left lower bronchus obstruction despite re-expansion of the upper left lung. Given the malignancy, comprehensive positron emission tomography (PET)/CT revealed metabolic activity confined to the known mass in the left main bronchus, with no distant metastases, classifying the clinical stage as cT2N0M0. In addition to respiratory

complaints, the patient denied fever, night sweats, hoarseness, dizziness, headache, or pain in his spine or extremities since symptom onset. Additionally, he maintained a consistent mental state, appetite, sleep pattern, urinary and bowel habits, and weight. Given his diagnosis and the need for specialized treatment, he was referred to our institution for potential surgical management and further evaluation.

History of past illness

The patient reported no history of surgery, trauma, significant infections, or other notable medical conditions. Furthermore, he confirmed no prior encounters with coronavirus disease 2019 infection.

Personal and family history

The patient reported no significant family history of related illnesses. When employed as an automotive welder for four years following high school graduation, he suggested possible occupational exposure to dust during this period.

Physical examination

The patient's vital signs were recorded: Body temperature, 36.5 ˚C; height, 175 cm; weight, 64 kg; respiratory rate, 20 breaths/min; heart rate, 89 beats/min; and blood pressure, 122/78 mmHg. No palpable superficial lymph nodes were observed in the supraclavicular or neck regions. Symmetry characterized the chest wall, devoid of any deformities. Although breath sounds were reduced in the left lung, the patient maintained a regular breathing pattern. No other notable abnormalities were evident.

Laboratory examinations

The laboratory findings were as follows: A white blood cell count of 7.8 × 10^9/L, a neutrophil percentage of 58%; a hemoglobin level of 149 g/L; a hematocrit of 47.3%; a fasting blood glucose level of 4.3 mmol/L; a total protein level of 81 g/L; and a globulin level of 34.2 g/L. A comprehensive panel of 12 tumor markers, including alpha-fetoprotein, carcinoembryonic antigen, neuron-specific enolase, cancer antigen (CA) 125, CA 15-3, CA 242, CA 19-9, prostate-specific antigen (PSA), free PSA, ferritin, and beta-human chorionic gonadotropin, was assessed *via* protein biochip detection in serum, with all the values falling within normal ranges. Pulmonary function tests revealed a forced vital capacity of 2.7 L (53.4% predicted) and a forced expiratory volume in one second of 2.5 L (57.7% predicted). Additional routine laboratory examinations, encompassing analyses of urine and stool, liver and kidney functions, and electrolyte levels, were within normal limits. Furthermore, screenings for infectious diseases such as hepatitis B, hepatitis C, syphilis, and human immunodeficiency virus yielded no abnormalities.

Imaging examinations

A chest CT conducted at a local hospital revealed a 2 cm contrast-enhanced nodule of soft tissue density within the left main bronchus. This nodule caused complete obstruction, resulting in total atelectasis of the left lung and a leftward mediastinal shift (Figure 1A). Consistent with the CT findings, the results of electronic bronchoscopy revealed a polypoid tumor in the left main bronchus. The tumor surface exhibited gray-yellow necrotic material, preventing further biopsy *via* bronchoscopic forceps (Figure 1B). In the local hospital's respiratory department, a segment of the tumor was excised using a high-frequency snare combined with a cryotherapy approach and was subsequently subjected to histopathological evaluation. Following endoscopic intervention and airway secretion clearance, a noticeable improvement in the patient's respiratory symptoms was observed. An examination revealed a patent left upper lobe bronchus with a healthy mucosal appearance, while the left lower lobe bronchus remained obstructed. Subsequent CT scanning revealed re-expansion of the left upper lung postintervention, but the mass in the left main bronchus persisted, continuing to obstruct the left lower lobe (Figure 1C). The patient subsequently underwent whole-body PET/CT at the same local hospital, at which the mass in the left main bronchus was identified and considered a metabolically active lesion, suggesting malignancy. Importantly, no abnormal metabolic activity was detected elsewhere, providing no evidence of metastatic spread (Figure 1D).

MULTIDISCIPLINARY EXPERT CONSULTATION

A multidisciplinary team (MDT) comprising thoracic surgeons, oncologists, anesthetists, radiologists, and pathologists was assembled to assess the conditions of the patients. Imaging and bronchoscopy examinations revealed a tumor in the distal left main bronchus. Comprehensive evidence from whole-body PET/CT and endoscopic biopsy confirmed that the tumor was primary malignant and predominantly exhibited clear cell morphology. While the exact pathological type has yet to be determined, consideration should be given to the potential diagnosis of a primary pulmonary salivary gland tumor. Clinical staging revealed no signs of local or distant metastasis, and the tumor was categorized as cT2N0M0. Routine blood test results and tumor marker levels were within normal limits. Pulmonary function tests demonstrated moderate restrictive ventilation impairment. Based on these findings, the MDT recommended a timely curative surgical approach, specifically left lower lobe sleeve resection. The tissue obtained from this procedure will further inform the diagnosis and subsequent therapeutic decisions.

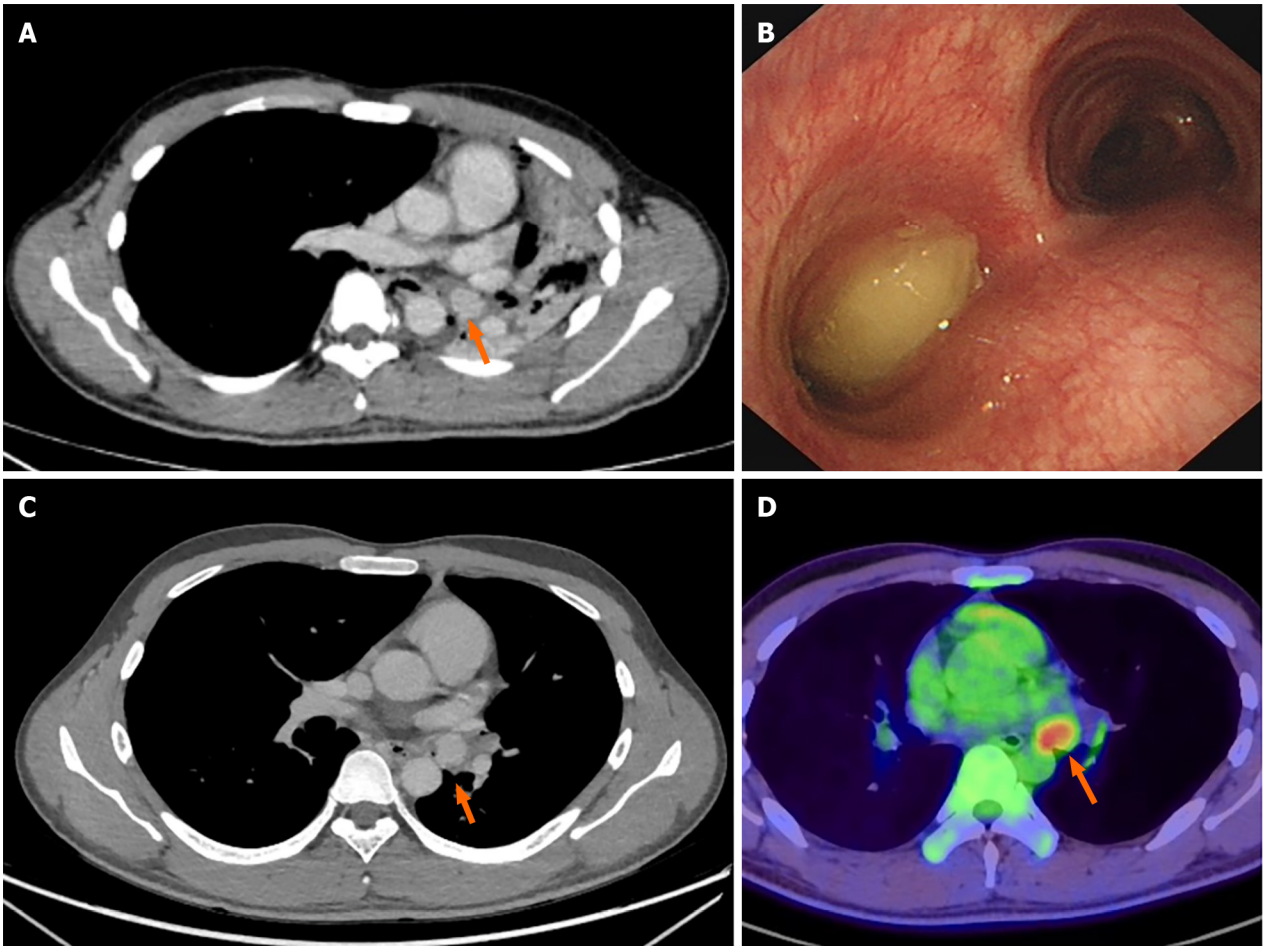

Figure 1 Preoperative patient examination. A: Chest computed tomography (CT) scan with enhanced imaging revealed a 2-cm soft tissue density nodule situated in the left main bronchus, resulting in complete atelectasis of the left lung; B: Electronic bronchoscopy image showed a polypoid tumor obstructing the left main bronchus, featuring a surface covered with gray yellow necrotic material; C: CT imaging demonstrated signs of recruitment in the left upper lung after endoscopic treatment, while the mass in the left main bronchus persisted; D: Whole-body positron emission tomography/CT scan revealed metabolically active lesions indicative of malignancy, with the tumor location highlighted by a red arrow.

FINAL DIAGNOSIS

Pathological examination of the specimen retrieved *via* bronchoscopy biopsy revealed tumor cells arranged in nest-like and papillary patterns. These cells exhibited clear, abundant cytoplasm with pronounced, deeply basophilic nuclei, indicative of malignancy. Immunohistochemically, the tumor tissue tested positive for cytokeratin, cytokeratin 7 (CK7), and vimentin; focal regions also exhibited P63 expression. Conversely, the cells tested negative for thyroid transcription factor-1 (TTF-1), Napsin A, calponin, paired box gene 2, paired box gene 8 (PAX-8), carbonic anhydrase IX, cluster of differentiation 117 (CD117), cluster of differentiation 10 (CD10), human melanoma black-45, melanoma antigen-A, inhibin A, cytokeratin 20, Villin, caudal type homeobox transcription factor 2, cytokeratin 5/6 (CK5/6), and P40. Antigen Kiel 67 (Ki-67) staining revealed a proliferation index of approximately 40%. Based on these findings, the primary diagnosis was a bronchogenic malignancy with a clear cell phenotype. A comprehensive assessment incorporating both immunohistochemical data and PET/CT scan results indicated that metastasis from renal, gastrointestinal, or other clear cell carcinomas was unlikely. Key differential diagnoses under consideration included pulmonary salivary gland tumor, pulmonary squamous cell carcinoma with clear cell differentiation, and hyalinizing clear cell carcinoma.

TREATMENT

At our institution, the patient underwent both left lower lobe sleeve resection and systematic mediastinal lymph node dissection. An anterolateral incision measuring 12 cm was made in the fourth intercostal space. Intraoperatively, observations revealed smooth visceral and parietal pleura with no nodular presence. Mild adhesions were observed within the thoracic cavity, and the oblique fissure was prominent. While the left upper lobe was hyperinflated, the left lower lobe was entirely obstructed and consolidated. After adhesions were appropriately resolved, the pulmonary hilum and mediastinal lymph nodes were effectively cleared. The left lower pulmonary vein and artery were sequentially exposed, sealed, and sectioned using an endoscopic linear cutting stapler. A subsequent incision in the left lower lobe

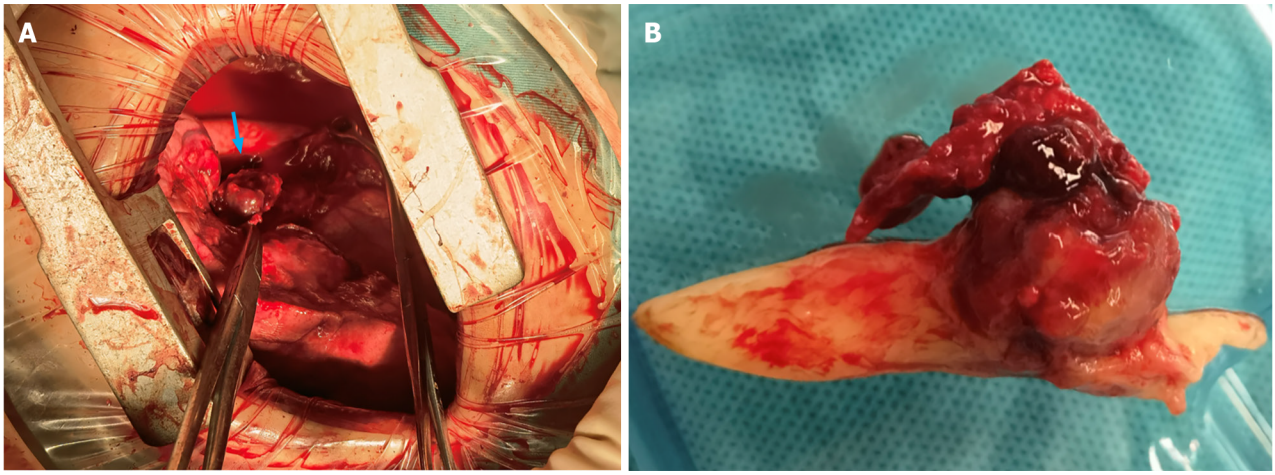

Figure 2 Intraoperative images. A: An anterolateral incision facilitated sleeve resection of the left lower lobe and systematic mediastinal lymph node dissection. The image depicts the hyperinflated left upper lung, the severed left lower lobe bronchus, and a 2 cm dark red spherical tumor obstructing the bronchial opening in the left lower lobe while infiltrating the bronchial wall (indicated by a blue arrow); B: The tumor was accompanied by a white, tongue-shaped, clotted sputum plug extending into the left upper bronchus and obstructing a substantial portion of the lumen.

bronchus exposed a 2 cm dark-red spherical tumor blocking the bronchial orifice and permeating its wall. Attached to the tumor, a white, tongue-shaped coagulum extended into the left upper bronchus, significantly occluding its diameter (Figure 2). After removal of the left lower lobe, the left main and left upper lobe bronchi were trimmed to ensure tumor-free margins, as validated by rapid intraoperative pathologic assessment. To reconstruct the left upper lobe bronchus, an end-to-end anastomosis was created using 3/0 Prolene sutures. The surgical procedure lasted 2.5 h, with a recorded blood loss of 100 mL and no intraoperative complications. The patient's postoperative recovery was uneventful; the drainage tube was removed on the 4th day after surgery, and the patient was subsequently discharged the following day.

OUTCOME AND FOLLOW-UP

The results of the postoperative pathological analysis were consistent with those of the preoperative bronchial biopsy, indicating a malignant invasive tumor in the left main bronchus with clear cell morphology. The tumor, measuring approximately 2.5 cm, had breached the bronchial wall. Lymph nodes from the hilar and mediastinal areas tested negative for malignancy. Immunohistochemical staining was positive for CK7, pan-cytokeratin, epithelial membrane antigen, and Ki-67 (approximately 30%). Conversely, markers such as carbonic anhydrase 9, calponin, CD10, CD117, napsin A, P40, P63, PAX-8, PSA, S-100, synaptophysin, TTF-1, CK5/6, smooth muscle actin, lysozyme, α-methylacyl-CoA racemase, SRY-Box transcription factor 10, and GATA binding protein 3 were not detected (Figures 3 and 4).

Diagnosing clear cell malignancy in the left main bronchus is challenging due to its uncommon presentation. Traditional pathological and immunohistochemical evaluations are often limited in providing a definitive diagnosis. To overcome this limitation, we utilized molecular pathology and next-generation sequencing of the tumor tissue. While DNA sequencing did not reveal any prevalent driver mutations, RNA sequencing revealed a gene fusion between *CRTC3* (NM_022769.4: exon 1) and *MAML2* (NM_032427.1: exon 2). Reports highlight the pivotal role of *MAML2* in MEC, in which the *CRTC1/3-MAML2* gene fusion is considered a significant diagnostic marker. As a result, our conclusive pathological evaluation identified PMEC in the left main bronchus, specifically the clear cell variant, and it was staged as T2N0M0. Based on these insights and the current therapeutic literature, we do not recommend postoperative adjuvant therapy for these patients. At the 1.5-year follow-up assessment, there were no signs of recurrence (Figure 5).

DISCUSSION

Primary salivary gland-type tumors of the lung (PSGTTL) represent a rare subset of lung cancers, constituting less than 1% of all primary lung tumors[6]. The most common PSGTTL subtype is PMEC. While salivary gland tumors typically occur in the head and neck, PMEC is very rare in the lungs and is currently thought to have its origin in the salivary glands of the tracheobronchial tree, specifically within the proximal bronchi[1].

The clinical manifestations of PMEC vary, and patients commonly display symptoms related to airway obstruction or irritation, such as cough, dyspnea, and shortness of breath[7]. The diagnosis of PMEC heavily relies on high-resolution CT imaging, which detects nodules or masses with well-defined borders, appearing round, oval, or lobulated. These lesions generally present densities similar to muscle tissue, and enhanced scans commonly reveal visible enhancement[8].

As a result of the infrequency of PMEC and the nonspecific nature of clinical and imaging diagnostic approaches, the primary diagnostic method remains histological examination. It is imperative to distinguish PMEC from other

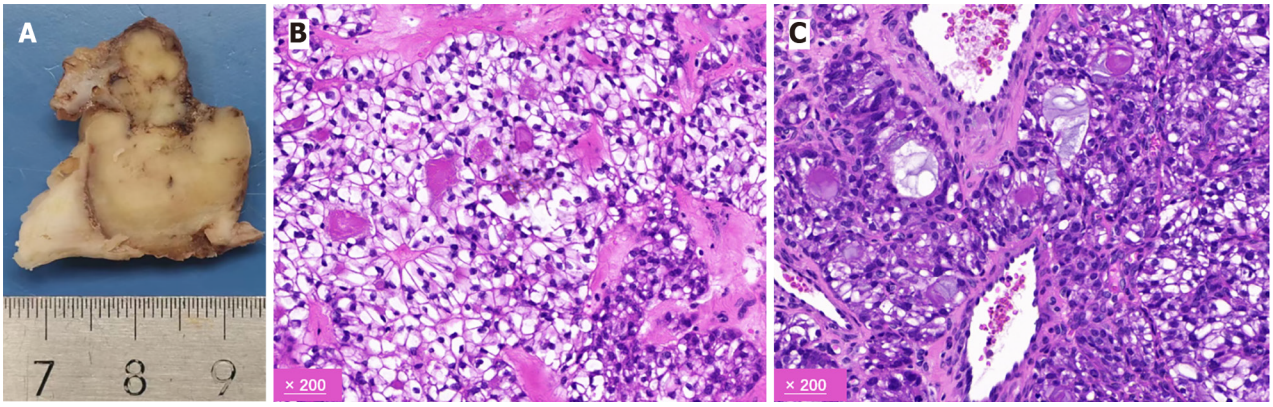

Figure 3 Gross and microscopic hematoxylin-eosin staining examination of the mass. A: The mass, measuring 2.5 cm × 2 cm × 1 cm, was well circumscribed and displays a gray white color after formalin fixation; B: The mass was predominantly composed of clear cells with abundant clear or slightly eosinophilic cytoplasm and small round nuclei. The mass contains variable amounts of amorphous eosinophilic material interspersed between clear cells; C: Additionally, some areas of the neoplasm feature foci of mucus-secreting cells were intermixed with clear cells.

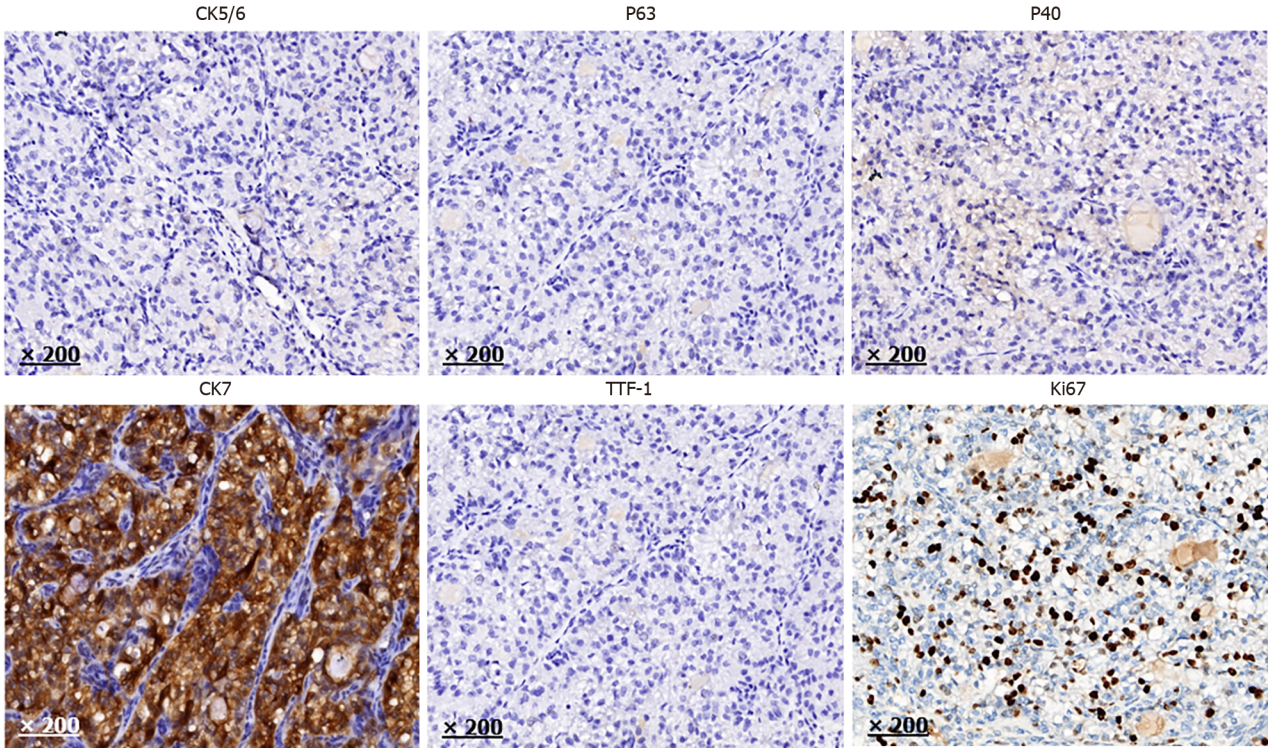

Figure 4 Immunohistochemistry. The tumor cells showed diffuse positivity for cytokeratin (CK) 7 and negativity for cytokeratin 5/6, P63, P40, and thyroid transcription factor-1. The Kiel 67 proliferation index of tumor cells in hotspots were relatively high. CK: Cytokeratin; TTF-1: Thyroid transcription factor-1.

malignancies, particularly when dealing with small biopsy specimens acquired through fiber optic bronchoscopy or lung puncture[1]. A conclusive PMEC diagnosis necessitates the identification of mucoepidermoid, epidermoid, and intermediate cells. Additional diagnostic techniques, such as immunohistochemistry, cytochemical staining, and analysis of *MAML2* gene translocation, can further contribute to the diagnostic process[9].

PMEC is primarily managed with surgical intervention, and complete resection and lymph node dissection is necessary for optimal long-term survival. Postoperative chemotherapy and/or radiation therapy may be deemed necessary for patients exhibiting positive lymph node metastases, involved tumor margins, or a high tumor grade[10]. Thorough surgical resection is paramount for an enhanced prognosis, and techniques such as bronchoplasty and extended resection are considered valuable in the surgical management of this disease[10]. Additionally, preoperative endobronchial interventions are considered potentially useful in cases of obstructive pneumonia to mitigate complications preceding surgery[11].

This case report highlights the unique challenges associated with diagnosing and managing this clear cell variant of PMEC. The clear cell variant can be particularly challenging to diagnose due to its resemblance to other clear cell-containing tumors. In this case, RNA sequencing plays a pivotal role in identifying the *CRTC3-MAML2* gene fusion,

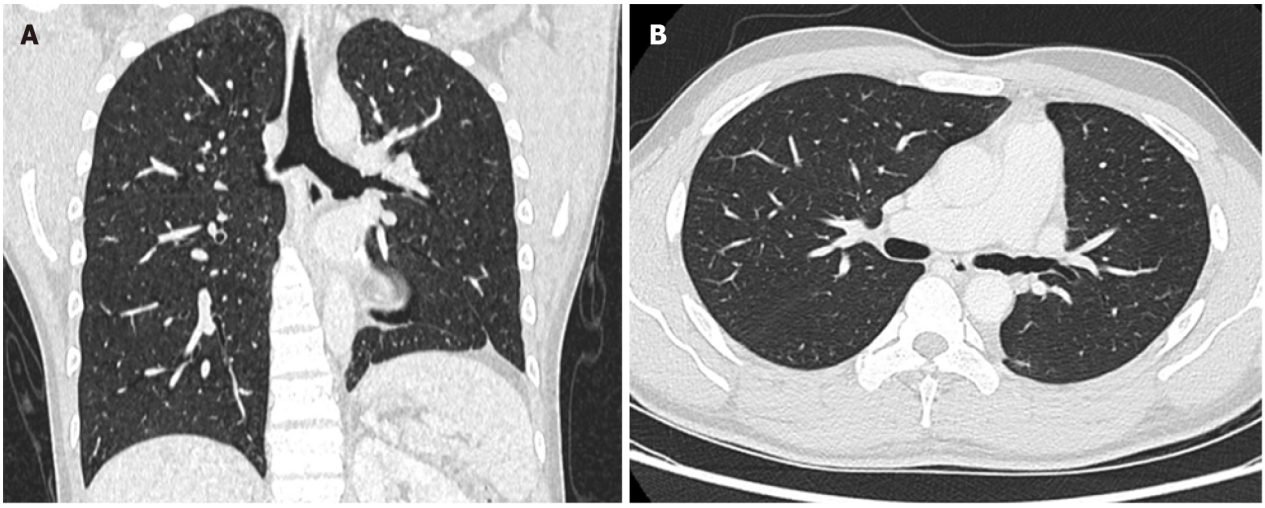

Figure 5 High-resolution chest contrast-enhanced computed tomography. A: Coronal plane; B: Transverse plane. A re-examination *via* computed tomography 1.5 yrs after the operation revealed that the lungs were in good condition, with no evidence of recurrence.

thereby enabling a definitive diagnosis of the clear cell variant of PMEC. These findings underscore the importance of molecular pathological analysis for accurately diagnosing rare malignancies.

Regarding treatment outcomes, the 5-year overall survival rate for PMEC patients who undergo lobectomy or sleeve resection is approximately 85%, with a more favorable prognosis associated with complete resection, younger age, female sex, early stage, smaller tumor size, lower histological grade, and the presence of the *MAML2* fusion gene[11,12]. In this case, a 22-year-old male patient with the *CRTC3-MAML2* fusion gene underwent left lower lobe sleeve resection and exhibited no lymph node metastasis, suggesting a positive prognosis.

In conclusion, this case report underscores the importance of an accurate diagnosis, primarily through molecular pathological analysis, in guiding personalized treatment strategies for the clear cell variant of PMEC. Surgical intervention remains the primary treatment modality, and while the prognosis is generally favorable for PMEC patients, individual characteristics such as gene fusion status, age, sex, tumor stage, and histological grade play crucial roles in determining long-term outcomes.

CONCLUSION

This article presents an uncommon case of a clear cell variant of PMEC featuring a *CRTC3-MAML2* gene fusion in a 22-year-old male. The patient underwent successful left lower lobe sleeve resection, and the postoperative outcome was notably favorable. This outcome reiterates the significance of surgery as the primary therapeutic approach for early-stage PMEC. This case highlights the unique challenges in diagnosing and treating this uncommon malignancy, thus emphasizing the critical role of accurate diagnosis and personalized treatment strategies.

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