Case Report

Multiple primary lung cancer comprised of adenocarcinoma and adenoid cystic carcinoma: a case report

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Background: Multiple primary lung cancer (MPLC) is a rare type of tumor, and it is necessary to differentiate it from a metastatic tumor. The type of adenocarcinoma with adenoid cystic carcinoma (ACC) is extremely rare and has not yet been reported in the literature. The initial clinical symptoms of double primary lung cancer may be nonspecific; hence, the diagnosis is often missed or incorrect.

Case Description: In this case presentation, we report the case of a 67-year-old female who had experienced persistent cough and expectoration for 8 days. Chest computed tomography (CT) revealed 2 nodules in the patient's lung. Radiographic findings could not distinguish between the 2 nodules and between primary and metastatic lesions. Thus, the patient underwent bronchoscopic biopsy and percutaneous lung puncture. We could not determine the type of the two tumors in hematoxylin and eosin (H&E) staining sections, and we subsequently performed specific immunohistochemical (IHC) staining. Combined with morphological and IHC results, we concluded that this was a case of MPLC, consisting of adenocarcinoma and ACC. The patient received symptomatic treatment because of the metastases.

Conclusions: This report reports a rare combination of MPLC and shows that a definitive diagnosis of double primary lung cancer can be based on tissue biopsy and IHC techniques.

Keywords: Multiple primary lung cancer (MPLC); adenocarcinoma; adenoid cystic carcinoma (ACC); immunohistochemistry; case report

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Introduction

Multiple primary lung cancer (MPLC) is characterized by the simultaneous or sequential occurrence of 2 or more primary malignant lung tumors. In 1932, Warren and Gates described MPLC. In MPLC, each tumor should have a definite manifestation; there should be differences between tumors, and the possibility of metastasis across lesions should be ruled out (1). The incidence of MPLC is very low. Herein, we report a case of bilateral primary lung cancer characterized by adenocarcinoma and adenoid cystic carcinoma (ACC). Primary pulmonary ACC is very rare, and then simultaneous adenocarcinoma is even rarer. In the present case, both of the locations (lower lobe of the right lung and left main bronchus) and combination (adenocarcinoma and ACC) are uncommon. We present the following case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-166/rc).

Case presentation

A 67-year-old female patient was referred to our hospital due to cough and expectoration persisting for 8 days. She had not experienced hemoptysis, fever, chest pain, dyspnea, or weight loss. She did not smoke and had no chronic diseases or family history of lung cancer. Subsequent physical examination revealed thick breathing sounds over both lungs. On bronchoscopy, a popcorn-like pedunculated mass

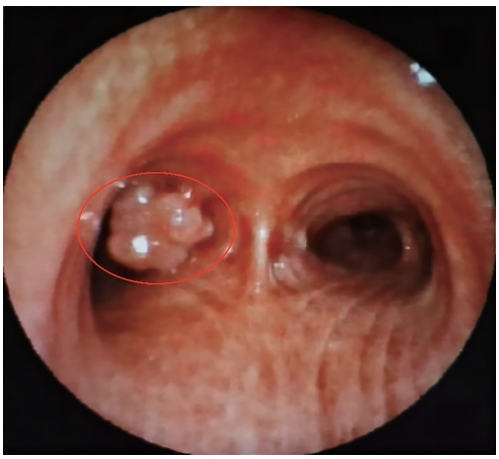

Figure 1 The popcorn-like pedunculated mass (marked with a red circle) at the opening of the left bronchus.

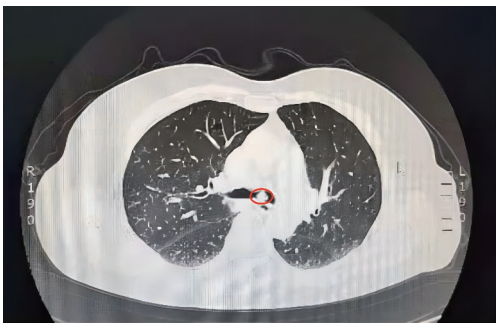

Figure 2 CT scanning of the chest revealed a small nodule (marked with a red circle) at the beginning of the left main bronchus. CT, computed tomography.

was found at the opening of the left bronchus (*Figure 1*). Chest computed tomography (CT) showed a small nodule at the opening of the left main bronchus (*Figure 2*) and a mass under the pleura in the posterior basal segment of the right lower lobe (*Figure 3*). The mediastinal lymph nodes were increased with a few calcifications. Bronchial neoplasm and lung puncture specimens were obtained for pathological examination.

Microscopically, the small gray-red nodule at the main bronchus was composed of glandular epithelial cells and myoepithelial cells. Tumor cells were haphazardly arranged in the shape of the ethmoidal foramen (*Figure 4*). The right lung mass consisted of tumor cells in an irregular glandular arrangement (*Figure 5*). Most tumor cells grew and infiltrated the stroma. To determine the types of the 2 masses, immunohistochemical (IHC)

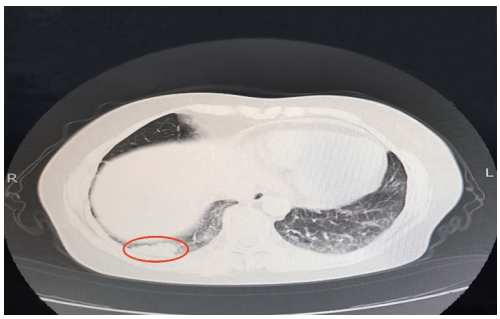

Figure 3 The irregular mass (marked with a red circle) under the pleura in the posterior basal segment of the right lower lobe.

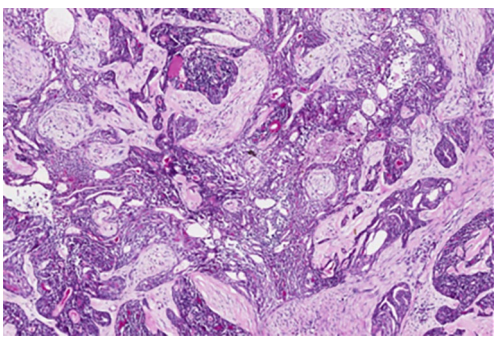

Figure 4 Microscopic picture showing that the tumor cells were haphazardly arranged and presented in the shape of ethmoidal foramen (H&E staining, ×200). H&E, hematoxylin and eosin.

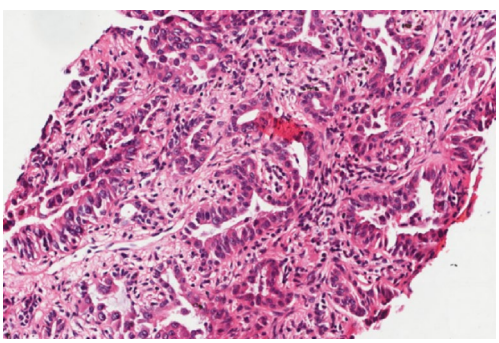

Figure 5 Microscopic picture showing that the tumor cells were arranged in an irregular glandular tube (H&E staining, ×200). H&E, hematoxylin and eosin.

staining was performed. The IHC analysis showed that the glandular epithelium expressed CK8/18, CAM5.2, and CK7 (*Figure 6*), while the basal cells were positive for P63 (*Figure 7*), P40, CK5/6, S-100, and CD117 in the nodules of the left main bronchus.

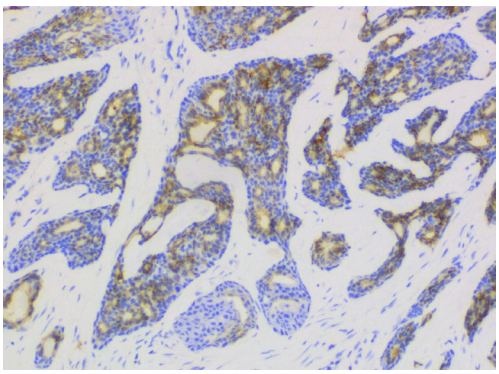

Figure 6 The tumor was positive for CK7 (IHC, ×200). IHC, immunohistochemical.

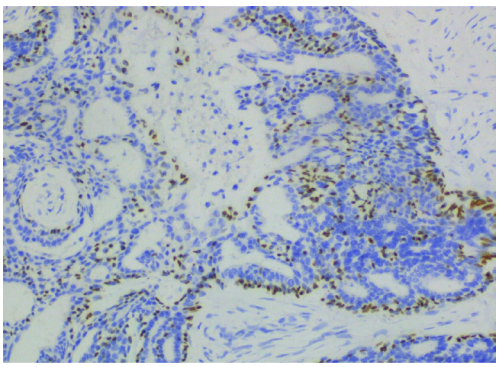

Figure 7 The tumor was positive for P63 (IHC, ×200). IHC, immunohistochemical.

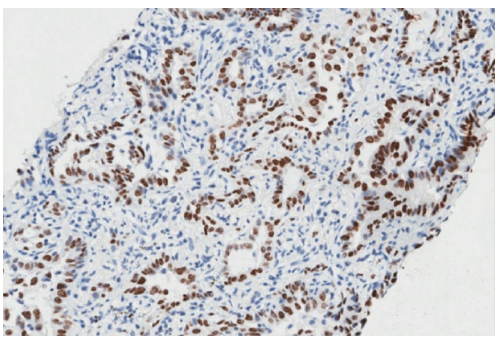

Figure 8 The tumor was positive for TTF-1 (IHC, ×200). IHC, immunohistochemical.

The IHC staining of tumor tissue in the right lung demonstrated positivity for CK7, Napsin-A, and TTF-1 (*Figure 8*). The results suggested that the tumor origins of the 2 lesions were different. After consultation, MPLC was diagnosed. In addition, on chest CT, a metastatic lesion was shown in the sixth anterior rib on the left. The patient received symptomatic treatment including anti-infection, bronchodilation, and nutritional support, as surgery was not indicated. No adverse or unexpected events happened during the treatment period. A driver gene test for lung cancer will be conducted at the upcoming follow-up, and targeted chemotherapy drugs will be selected according to the results.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

As a rare disease, MPLC has a reported incidence of 3.7–8.0%. However, the incidence rate has increased owing to the development of clinical diagnostic techniques (2). Similar to single primary lung cancer, MPLC occurs at the average age of 63.4 years, and 36.7% of patients are females (3). It usually occurs unilaterally (4). In this case, CT demonstrated that the lesions occurred in both lobes of the lungs.

It has been reported that squamous cell carcinoma plus squamous cell carcinoma is the most common type (5,6). The present case was composed of an adenocarcinoma and ACC, which is rarely reported. A rare type of tumor, ACC of the lung accounts for 0.04–0.2% of primary pulmonary tumors (7). It commonly involves the salivary glands in the head and neck (8). Histologically, ACC exhibits 3 main growth patterns: the cribriform, tubular, and solid patterns. It is characterized by its expression of myoepithelial markers, which include P63, SMA, C-kit, and S-100 protein. Once pulmonary ACC is identified, it is crucial to determine whether the lesion represents distant metastasis or primary lung cancer (9). To rule out the possibility of metastatic diseases, we conducted a general otorhinolaryngological examination to try to seek a primary salivary gland tumor. No abnormalities in the ears, nose, or throat were noted.

In clinical practice, when 2 nodules appear in the lung, doctors may easily diagnose it as metastatic cancer. As a

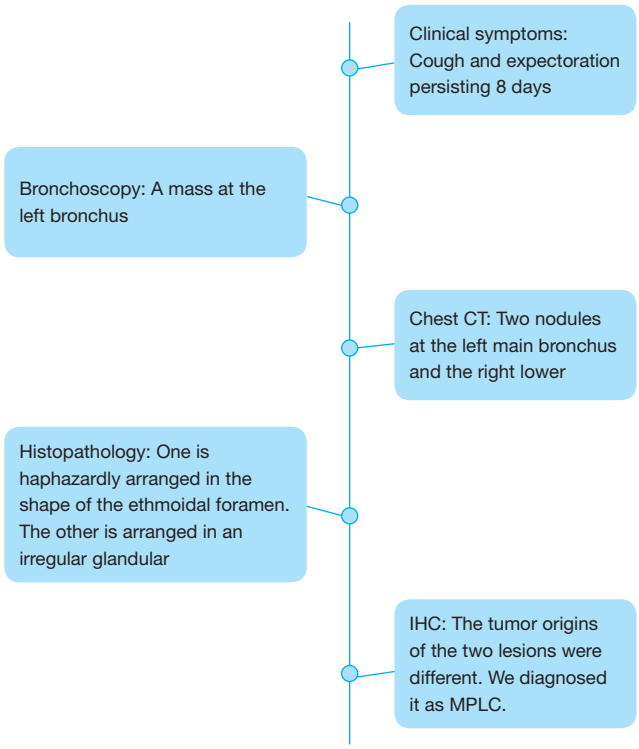

Figure 9 Timeline. MPLC, multiple primary lung cancer; ACC, adenoid cystic carcinoma; CT, computed tomography; CHA, comprehensive histologic assessment; SBRT, stereotactic body radiotherapy.

result, it is critical and challenging to distinguish whether multiple lung cancers are independent or related, that is, to differentiate multiple primary cancers from intrapulmonary metastases. The former is typically treated surgically, and the prognosis is good. However, the latter involves systemic chemotherapy, and the prognosis is poor (10). The American Joint Commission on Cancer (AJCC) has adopted comprehensive histologic assessment (CHA) as a diagnostic criterion (11). The proposal of CHA provided a new basis for differential diagnosis. The CHA includes the percentage of various histologic subtypes, nuclear features, and stromal characteristics. This is particularly useful while evaluating multiple lesions that exhibit the same tissue type. The principle of IHC technology is that antigen and antibody can combine specifically, so as to characterize and locate the specific antigen or antibody in tissues and cells. It can be used as a first-line method for differentiation and diagnosis in cases where imaging cannot distinguish between 2 tumor types. In addition, in clinical practice, the integration of radiology, histopathology, and integrated genomic features by multidisciplinary teams promotes a more accurate diagnosis of MPLC (12). With the development of molecular pathology, in 2003, the molecular genetic technique was first proposed for the diagnosis of diseases with multiple lesions in the same pathological type (13). A study indicates that sequencing of about 50 genes suggested that multiple tumors were independent if they contain different driver mutations, and that they were metastatic if they even have only one common driver mutation (14). But this detection method is very laborious and expensive. In Murphy's study, the unique genome rearrangement and breakpoint detection results for MPLCs showed a high degree of agreement with histological predictions (15). In this case, we used the histological approach. Combined with the patient's diagnosis and treatment process (*Figure 9*), we are confident in the diagnosis of MPLC. Contrary to intrapulmonary metastasis, MPLC often presents as an early-stage disease (16); thus, surgical treatment should be considered as the modality of choice for managing MPLC patients (17). To date, radical surgery is the primary therapy for MPLC. However, the optimal extent of surgical intervention has not yet been standardized (12). In Tie's article, he put forward anatomical resection, which is defined as lobectomy, double lobectomy, and pneumonectomy combined with lymph node dissection, with adequate pulmonary reserve. When the patient has limited lung function, lobectomy with sublobectomy, or sublobectomy alone, is possible. Among these, anatomic segmental resection is preferred for sublobar resection (4). During choosing surgical methods, separate or delayed resection is much safer than a first-stage procedure in patients with bilateral lung tumors (18). The purpose of the operation is to remove the tumor as thoroughly as possible and to retain as much more normal lung tissue as possible. It is also important to clean up the lymph nodes during surgery. The staging of lymph node metastasis helps to predict prognosis and develop subsequent treatment. In the study of 26 patients with MPLC, multivariate analysis showed that adjuvant chemotherapy could actively improve survival of patients (19). Unfortunately, due to the distant metastases in our patient, conservative treatment was necessary. For early-stage patients who are medically inoperable, experts have proposed stereotactic body radiotherapy (SBRT), the effectiveness and security of which have been shown (12). However, the efficacy of

SBRT for patients in advanced stage needs further research.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-166/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-166/coif). Jieyu Xu, Jinjing Wang and Xiaorong Yang report funding fees from Science and Technology Department of Guizhou Province [No. ZK (2021)383]. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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