A Case of Pulmonary Mucoepidermoid Carcinoma Responding to Carboplatin and Paclitaxel

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A 59-year-old man was admitted to our hospital with dyspnea and cough. A large polypoid tumor was observed in the lower trachea and bronchoscopic polypectomy was performed using a snare to relieve symptoms. The tumor was diagnosed as a high grade mucoepidermoid carcinoma mainly by the histology of piecemeal specimens obtained by bronchoscopic resection. The primary lesion involved the trachea and the main bronchus, and there were multiple metastases in the lung. The patient was treated with the combination of carboplatin and paclitaxel. After four cycles of chemotherapy, the tumors were significantly reduced. He remains well without evidence of tumor progression for 25 months. This case suggests that the combination chemotherapy of carboplatin and paclitaxel can be an option for treatment of pulmonary mucoepidermoid carcinoma.

Key words: pulmonary mucoepidermoid carcinoma – high grade – polypectomy – carboplatin and paclitaxel

INTRODUCTION

Pulmonary mucoepidermoid carcinoma (MEC) was first reported by Smetana et al. (1) in 1952. MEC is uncommon, and accounts for \( \sim 0.1–0.2\% \) of all lung cancers (2). This tumor is indistinguishable histologically from its salivary gland counterpart, and it is believed to originate from the submucosal glands of the tracheobronchial tree (2).

MEC is classified into low- and high-grade tumors. Low-grade tumors are often confined to the bronchial wall, while high-grade tumors extend into the peribronchial interstitium or adjacent lung parenchyma (3). Surgery is an appropriate treatment of choice for patients with MEC, if the lesion is resectable. Low-grade tumors can be removed completely for best results, while high-grade tumors are difficult to remove completely because of aggressive tumor behavior.

We report here a case of pulmonary MEC presenting a progressive dyspnea and a persistent cough due to respiratory tract obstruction, which was highly responded with the chemotherapy of carboplatin and paclitaxel.

CASE REPORT

A 59-year-old man presented a 3-year history of cough. He was admitted to the hospital because of progressive dyspnea and persistent cough. He smoked 30 cigarettes per day for 40 years. In physical examination, there were moderate rhonchi audible in both lungs. In arterial blood gas analysis, hypoxemia was eminent: \( \text{pH} = 7.39 \), partial pressure of carbon dioxide \( = 50.7 \text{mmHg} \) and partial pressure of oxygen \( = 96.2 \text{mmHg} \) under supplemental oxygen 3 l/min on nasal
No significant abnormal value was detected in blood count and serum and biochemical data. Chest X-ray showed a mass (suspicious of a polypoid tumor) in the lower trachea. Chest computed tomography (CT) scan confirmed that the tumor located in the main carina occupied almost fully the luminal space (Fig. 1A). Multiple nodules were also found in the left lower lobe (Fig. 1C), and were diagnosed as metastases based on F-18 FDG PET/CT scan showing their abnormal uptake (SUVmax: 6.8, supplementary figure). Bronchoscopy was performed and identified a large polypoid tumor located above the carina with 90% obstruction of the tracheal lumen (Fig. 2A).

Bronchoscopic polypectomy was performed using a snare to relieve symptoms. General anesthesia and percutaneous cardiopulmonary support were needed. The procedure successfully eliminated respiratory symptoms with oxygenation improved.

In the resected tumor, there were atypical cells with hyperchromatic nuclei that varied in size and shape microscopically. Epidermoid differentiation was observed and intracytoplasmic mucin was faintly confirmed with diastase–periodic acid–Schiff and mucicarmine stain. Immunohistochemically, the tumor was negative for p-63, TTF-1 and Napsin A. EGFR mutational status was negative with high-sensitive polymerase chain reaction method. In light of the tumor location as well as the finding of hematoxylin–eosin and special staining, the tumor was diagnosed as a high-grade MEC (Fig. 3).

Even after the endoscopic treatment, the mucous membrane of the trachea and bronchi were still infiltrated by the tumor (Fig. 2B), and metastatic multiple tumors remained in the lung. Based on previous reports with advanced non-small cell lung cancer (4–6), the patient was treated with the combination of carboplatin (AUC 6, day 1) and paclitaxel (60 mg/m², days 1, 8, 15) every 4 weeks. ECOG performance status is Grade 1 at the time of chemotherapy. The treatment was effective, and the maintenance chemotherapy of the same regimen was repeated 13 times. Since currently, there is no approved chemotherapy protocol for MEC, we decided to continue the chemotherapy so far as it was beneficial to the patient. A chest CT scan performed after four cycles of chemotherapy revealed a reduction in lymphadenopathy and multiple nodules in the left lower lobe (Fig. 1F). Bronchoscopy showed recovery of the smoothness of the trachea and bronchi (Fig. 2C and D). However, since one...
nodule did not disappear, we considered the efficacy as partial response on the basis of RECIST guideline (version 1.1). After 13 cycles of chemotherapy, administration of the drug was stopped due to a progressing peripheral neuropathy (Grade 3 on CTCAE v4.0) caused by paclitaxel. No radiotherapy was performed. The patient remains well without evidence of tumor progression for 25 months after initiating systemic chemotherapy and for 6 months after the last systemic chemotherapy.

DISCUSSION

Primary MEC of the lung is a rare malignancy. According to several published reviews, patients vary in age from 3 months to 78 years, but most of the patients are younger than 30 years (7). The tumors arise from bronchial glands in the central airways, particularly in the main bronchi and trachea, and a combination of wheezing, cough, hemoptysis and dyspnea are the most common symptom. Histologically, MEC is divided into low- and high-grade types. The low-grade tumors can have a long natural history and rarely metastasize, while the high-grade tumors can be very aggressive and prone to local invasion and early metastasis (8). In one series of 18 pulmonary MECs, 15 were reported to be low grade and 3 were high-grade type tumors. The 12 patients with the low-grade tumors that had been resected were alive at the last follow-up (the mean follow-up period was 4.7 years). In contrast, all three high-grade tumors were fatal within 16 months (9).

As a treatment, surgery should primarily be chosen, especially for patients with early-stage disease. There has been no report or clear evidence in the benefit of chemotherapy for pulmonary MECs. Only a few case reports are available on chemotherapy on salivary gland tumors which are histologically identical to pulmonary MECs. Gilbert et al. (10) reported that partial responses had been obtained in 3 of 14 patients with salivary gland MEC treated with paclitaxel (200 mg/m², every 21 days). Another case series reported 2 of 14 patients with recurrent salivary gland carcinoma had shown efficacy to a treatment with carboplatin and paclitaxel (11). Our case was treated with chemotherapy based on the above reports. We chose a weekly administration of paclitaxel to avoid neurotoxicity. To our knowledge, this is the first case report of pulmonary MEC having responded well to carboplatin and paclitaxel.

Recent reports have been published focusing on epidermal growth factor receptor (EGFR) mutation of the tumor, although it is not clarified whether the mutations are significantly associated with the tumor characteristics. Yu et al. (12) examined the EGFR mutational status in 20 pulmonary MECs, and L861Q mutation in exon 21 was confirmed in five patients. Tamaki and colleagues (13) also reported a case of pulmonary MEC with EGFR mutation (exon 19 deletion mutation) that was successfully treated by gefitinib. In our case, EGFR mutation was not detected; however, molecular screening of the tumor is considered to be required for the selection of treatment and to accumulate scientific evidence.

The diagnosis of MEC is sometimes challenging. According to the WHO Classification (14), criteria more typical of high-grade mucoepidermoid tumors include: (i) exophytic endobronchial growth, (ii) surface epithelium lacking changes of in situ carcinoma, (iii) absence of individual cell keratinization and squamous pearl formation and (iv) transitional area to low-grade MEC. In our case, both (i) and (iii) are evident. However, the bronchoscopic snare dissection material, which consisted of the tumor itself, was insufficient to examine the presence/absence of in situ lesion and transitional area to low-grade tumor. We recognized that adenosquamous carcinoma should be ruled out in order to make a definite diagnosis of pulmonary MEC. The double-negative result of TTF-1 and Naspin A suggested that adenosquamous carcinoma was an unlikely diagnosis (15). In light of the WHO criteria, the immunohistochemical results and the tumor location, we diagnosed the tumor as high-grade MEC.

This patient remains well without evidence of recurrence for 25 months. We speculate that the biological character related to the degree of differentiation of tumors influences the response rate of chemotherapy instead of the degree of differentiation. It has been previously reported that the expression of excision repair cross-complementation group 1 (ERCC1) isoform is a potential biomarker of the efficacy of cisplatin-based chemotherapy (16). Also, Zhang et al. (17) showed the expression of the class III β-tubulin was associated with chemosensitivity of paclitaxel. We did not check the expression of these proteins in our case, and further study may be required.

In conclusion, we reported a case of a high-grade MEC, in which surgery had not been conducted due to the multiple pulmonary metastases and highly invasive nature of the tumor. The diagnosis was made mainly by the histology of bronchoscopically obtained piecemeal specimens. Although it was difficult to observe a whole appearance of the tumor, other pathologic findings, including the location and histochemical and immunohistochemical results, proved an accuracy of the diagnosis. After the successful bronchoscopic procedure, this patient was treated with carboplatin and paclitaxel. Although
currently, there is neither evidence of effectiveness nor a guideline in the treatment for pulmonary MEC, this case suggests that the combined chemotherapy of carboplatin and paclitaxel can be a treatment option for the tumor.

Supplementary data
Supplementary data are available at http://www.jjco.oxfordjournals.org.

Conflict of interest statement
None declared.

References