Case Report

Docetaxel for High-Grade Mucoepidermoid Carcinoma of the Lung

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Abstract.

Mucoepidermoid carcinoma is considered to be one of the salivary gland-type cancers, which seldom originate from the lung. Herein, we report a 69-year-old female with primary pulmonary high-grade mucoepidermoid carcinoma. The disease progressed rapidly and reached an unresectable status. We treated the patient with bi-weekly doses of docetaxel and the clinical response allowed for the disease to become more stable. The patient survived for only six months from the onset of the symptoms. The case demonstrated that single use of docetaxel would appear to be a treatment option for mucoepidermoid carcinoma of the lung.

Keywords: pulmonary mucoepidermoid carcinoma, docetaxel

INTRODUCTION

Mucoepidermoid carcinoma (MEC) is an uncommon tumor of the lung that accounts for 0.1 to 0.2% of all pulmonary cancers [1]. Primary pulmonary MEC often appears as lobulated and intraluminal nodules with distinct margins, and is primarily located in the segmental bronchi as opposed to the trachea or main bronchi [2].

MEC can develop at almost any age, ranging from 3 to 78 years, but most patients are generally young adults [3]. Most MECs are benign with an indolent clinical course, but some presented with malignant behaviors involving multiple metastasis and visceral invasion. Currently, there is no consensus regarding
optimal treatments for malignant or high-grade MECs. Herein, we report a case of primary pulmonary MEC receiving systemic chemotherapy with docetaxel.

CASE REPORT

A 69-year-old female with a history of diabetes mellitus was followed-up from the cardiology outpatient department. In August 2013, she presented with right-sided chest pain and dry cough for one month. In addition, she also suffered from weight loss of more than 10 kilogram over a period of three months. A chest X-ray revealed a mass lesion over the right lower lung. Then she was transferred to the department of thoracic surgery. The patient underwent a computed tomography (CT) scan in September 2013, which showed a bronchogenic tumor and obstructive pneumonia at the right lower lobe with pleural invasion and right hilar lymphadenopathy (Figure 1A,1B). Other exams including magnetic resonance imaging of the brain, abdominal sonography, and Tc-99m whole body bone scan revealed no evidence of distal metastasis.

This patient underwent video-assisted thoracoscopic wedge resection of the right lower lobe. The pathology revealed cancer cells with pleomorphic nuclei, prominent nucleoli, and moderate cytoplasm arranged in sheets or a nest pattern with desmoplastic stroma. The immunohistochemical stains were shown to be positive for CK7, CK5/6, mucin, and p40, but negative for TTF-1, synaptophysin, and CD56 (Figure 2). Review of the available data and diagnostic information indicated the patient had a primary pulmonary mucoepidermoid carcinoma, cT3N1M0, stage IIIA. However, an episode of acute cerebral infarction and sepsis occurred after operation. Subsequent systemic chemotherapy was postponed due to poor performance status (Eastern Cooperative Oncology Group (ECOG): 3). The patient received supportive care and was followed-up in our hematology department.

In November 2013, the patient was evaluated for further chemotherapy. Her performance was slightly improved (ECOG: 2). A follow-up CT scan revealed multiple nodules over the bilateral lung with an invasion of the mediastinum and right lateral chest wall, and right hilar and mediastinal lymphadenopathies (Figure 1C,1D). The disease worsened and progressed to cT4N2M0, stage IIIB.

She received palliative chemotherapy with docetaxel, 40 mg/m2 every two weeks, starting in December 2013. A CT scan in January 2014 (8 weeks after treatment) revealed mild shrinkage of the right lower lung tumors (Figure 1E,1F), and we considered its efficacy as "stable disease" according to RECIST guidelines (version 1.1). During her chemotherapy treatment, the patient didn’t experience febrile neutropenia or sepsis. Nevertheless, the patient requested to discontinue chemotherapy due to general malaise with deterioration of performance status. The patient then died from cardiac arrest related to a choking episode in February 2014.

DISCUSSION

MEC is considered to be one of the salivary gland-type cancers, which are rare lung neoplasms including MEC, adenoid cystic carcinoma (ACC), and epithelial-myoepithelial carcinoma (EMC) according to the World Health Organization (WHO) classification [4]. Salivary gland-type lung cancers are a group of low-aggressive entities with a higher likelihood of recurrence and metastasis [4]. These tumors are slow growing and arise from the submucosal glands of the bronchial tree [5].

MEC is classified into two groups according to its pathological features and clinical behaviors. Low-grade tumors are composed mostly of cysts, are confined to the bronchial wall, and it is unusual for
Figure 1. A CT scan of the chest in September 2013 (A and B) showed a bronchogenic tumor and obstructive pneumonia at the right lower lobe with pleural invasion and right hilar lymphadenopathy (maximal diameter: 14.37 cm). In November 2013 (C and D), multiple nodules were progressively enlarged over the bilateral lung with an invasion of mediastinum and right lateral chest wall, and right hilar and mediastinal lymphadenopathies (maximal diameter: 15.98 cm). The follow-up CT scan after treatment in January 2014 revealed mild shrinkage of the right lower lung tumors (maximal diameter: 14.98 cm)
Figure 2. The pathology revealed cancer cells with pleomorphic nuclei, prominent nucleoli, and moderate cytoplasm arranged in sheets or a nest pattern with desmoplastic stroma (A,B) with positive for CK7(C), CK5/6(D), mucin (E), and p40(F), but negative for TTF-1(G) in immunohistochemical stains.
metastasis to progress to regional lymph nodes [5-8]. High-grade tumors display sheets or nests of mucus-secreting, squamous and intermediate cells mixed with mitotic activity and necrosis, and they also exhibit aggressive patterns with invasion to regional lymph nodes, interstitium, or lung parenchyma [5-7]. Heitmiller et al. reported one series with 18 pulmonary MECs, where 15 patients were low-grade type and 3 patients were high-grade type tumors. All 15 patients with low-grade tumor were alive without recurrence at a mean follow-up of 4.7 years, and all patients with high-grade tumors were deceased within 16 months [7].

Although pulmonary MEC is rare, it shares a similar pathology to the relatively more common salivary MEC [3]. MEC of the salivary gland and lung also share similar reciprocal translocation involving chromosome 1q32, 5p15, 7q22, and 15q22 [9]. Recurring t(11;19) translocation with an associated CRTC1-MAML2 fusion oncogene is present in 38-81% of such tumors [10]. This translocation may exist in all grades of MEC [11], and fusion protein is associated with the regulation of cell-cycle pathways, activation of EGFR signaling, and increased expression of amphiregulin (EGFR ligand) [12].

Surgery consisting of radical resection of the primary tumor is still the current treatment of choice, especially for low-grade tumors that are at an early stage of the disease [13]. The definitive benefits of chemotherapy are lacking at this time for MEC. Chemotherapy has been used in locally advanced or metastatic mucoepidermoid carcinoma of the salivary glands [14,15]. The response rates vary from 10% to 46% [14-17]. Combined therapy with anthracycline and platinum agents would appear to be more promising than the use of single agents [16,17]. Taxane agents have been shown to have an impressive anti-tumor activity especially in squamous cell carcinoma of the head and neck cancers with a response rate of 32% (95% confidence interval 17-47%), median duration of response of 4.5 months (range, 2-20 months), a median survival of 9.2 months, and a 1-year survival rate of 33% [18,19]. Since such a positive response has been observed, taxane agents have been used in cases of MEC of the salivary glands. One report showed a surprising response to docetaxel in four cases that had MEC of the salivary glands, but showed the patients remained stable for at least 18 months after six cycles of chemotherapy [20,21]. Another report showed a partial response lasting 5 and 12 months to carboplatin and paclitaxel in 2 of 14 patients with recurrent MEC of the salivary glands [22]. Our case was treated with the single use of docetaxel (40 mg/m² every two weeks) chemotherapy for the aged patient that suffered from a poor performance status, anti-tumor activity of docetaxel, and the acceptable safety profile. The response was favorable with the patient continuing to have stable disease for at least 2 months. Therefore, single use of taxane appears to be an alternative treatment to consider for MEC of the lung.

Recently published reports put an emphasis on epidermal growth factor receptor (EGFR) mutation of the tumor. Although a definite association between mutation and MEC is not clearly established at this time, mutations of EGFR including L861Q mutation in exon 21 and exon 19 deletion have been found in some patients [23]. Some reports demonstrated that patients lacking a sensitizing EGFR mutation revealed clinical response of pulmonary MEC to tyrosine kinase inhibitors of EGFR [24,25].

Here, we report on a case of primary pulmonary MEC treated with single use docetaxel chemotherapy. Although we discontinued treatment due to the patient’s senescence and weakness, the patient continued to have stable disease for at least 2 months without chemotherapy-associated febrile neutropenia. Further studies are necessary to investigate the role of systemic chemotherapy in high-grade MEC.

REFERENCES


