Two Consecutive Cases of Platinum-Refractory Pulmonary Pleomorphic Carcinoma that Showed Dramatic Responses to MAID (Mesna, Doxorubicin, Ifosfamide and Dacarbazine) Chemotherapy

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When oncologists encounter patients with pulmonary pleomorphic carcinoma, most cases have recurrent disease after surgery or metastatic disease. Previous studies have suggested that patients with pleomorphic carcinoma have extremely poor responses to chemotherapy regimens commonly used for non-small cell lung cancer and have a dismal prognosis. This report describes two consecutive patients with platinum-refractory pulmonary pleomorphic carcinoma who received doxorubicin, ifosfamide plus dacarbazine chemotherapy. Both patients showed dramatic responses to this combination chemotherapy and the treatment effect was sustained for 7 and 9 months, respectively. Our report strongly suggests that the treatment approaches to patients with pulmonary pleomorphic carcinoma should differ from the approaches to patients with other common types of non-small cell lung cancer. Doxorubicin, ifosfamide plus dacarbazine chemotherapy may have an important role in the treatment of patients with pulmonary pleomorphic carcinoma.

Key words: non-small cell lung cancer – pulmonary pleomorphic carcinoma – chemotherapy

INTRODUCTION

Pulmonary pleomorphic carcinoma (PPC) is a rare subtype of non-small cell lung cancer (NSCLC), which has dual cell components (spindle or giant cells and epithelial cells). Herein we report two consecutive patients with platinum-refractory PPC who had dramatic responses to mesna, doxorubicin, ifosfamide and dacarbazine (MAID) chemotherapy.

CASE REPORT

The first case was a 51-year-old woman who presented with persistent cough and shortness of breath of 2 months duration. She had never smoked cigarettes. Computed tomography (CT) of the chest and abdomen showed a mass in the right upper lobe of the lung with mediastinal lymph node enlargement and a left adrenal mass. Based on a percutaneous needle biopsy of the lung mass, a diagnosis of PPC was made. The tumor cells had a biphasic appearance with epithelioid and spindle cell sarcomatous components (Fig. 1A). Antibody against cytokeratin (CK) was reactive for both epithelioid and sarcomatous components (Fig. 1B). She was treated with the standard chemotherapeutic regimen for NSCLC as a first-line therapy [gemcitabine plus cisplatin (GC)] in December 2007 (Fig. 1C). Shortly after one cycle of GC chemotherapy, however, her dyspnea worsened and a chest CT showed a rapid progression of disease (Fig. 1D). In January 2008, she received MAID chemotherapy [doxorubicin (15 mg/m² over 1 h, days 1–4); dacarbazine (250 mg/m² over 2 h, days 1–4); ifosfamide (2000 mg/m² over 2 h, days
1–3); and mesna (days 1–3) as a second-line treatment every 3 weeks. She achieved a partial remission (Fig. 1E). During chemotherapy, mild anemia (Grade 1) and leukopenia (Grade 1) were developed. However, as chemotherapy was continued, general weakness (fatigue) became worse and Grade 2 fatigue was developed after seventh cycle of MAID. Thus, she stopped receiving chemotherapy after a total of seven cycles of MAID in the status of continued remission. After cessation of MAID chemotherapy (June 2008), the tumor progressed 2 months later (August 2008). Although docetaxel was administered as a third-line therapy, she died of tumor progression in November 2008.

The second case was a 61-year-old man with a chief complaint of persistent cough of 2 months duration. He was an ex-smoker with a 20 pack-year smoking history. A chest CT showed a lung mass with pleural and pericardial effusions. The tumor consisted of cells with an epithelioid arrangement and a sarcomatous area (Fig. 2A). On immunohistochemical staining, vimentin (a panmesenchymal marker) was diffusely positive, which indicated mesenchymal differentiation (Fig. 2B). Additional immunohistochemical results were as follows: demsin, focally positive; smooth muscle actin, weakly positive; and CK, negative. He was diagnosed with PPC based on the morphologic findings of the tumor cells admixed with sarcomatoid (spindle) and epithelioid cells. He received GC chemotherapy in November 2007 (Fig. 2C), but the tumor progressed rapidly after one cycle of therapy (Fig. 2D). MAID chemotherapy was administered as a second-line treatment in November 2007. A partial remission was achieved with MAID therapy (Fig. 2E). During MAID chemotherapy, severe leukopenia (Grade 3) and neutropenia (Grade 4) were developed. However, neutropenic infection was not accompanied. Severe non-hematologic toxicities were not developed. He received eight cycles of MAID until June 2008. After discontinuing MAID therapy and a 2-month rest period, the tumor progressed rapidly (August 2008). Although he received pemetrexed and docetaxel as a later-line therapy, the tumor did not respond to treatment and he died of tumor progression in March 2009.

DISCUSSION

According to the 2004 World Health Organization (WHO) classification, PPC is classified as a subgroup of sarcomatoid carcinomas in NSCLC and characterized by a poorly differentiated adenocarcinoma, squamous cell carcinoma or large cell carcinoma containing at least 10% sarcomatoid components of spindle or giant cells (1). Sarcomatoid carcinoma was previously called ‘carcinoma with pleomorphic, sarcomatoid or sarcomatous elements’ in the 1999 WHO classification (2). PPC is extremely rare and accounts for 0.1–0.4% of all pulmonary malignancies (3–5). Due to its rarity, few reports are available on PPC. The majority of previous reports has focused on the clinicopathologic characteristics of PPC and investigators have consistently concluded that PPC has a more aggressive clinical course and a poorer survival compared with other histologic types of NSCLC.

When oncologists encounter patients with PPC, most cases have recurrent disease after surgery or metastatic
disease. Therefore, palliative chemotherapy is an important option for the treatment of PPC. However, information on the efficacy of palliative chemotherapy is extremely rare and, to our knowledge, only two studies have been reported on the treatment outcomes of chemotherapy in patients with PPC (4,5). The response rate to chemotherapy regimens commonly used for NSCLC is in the range of 0–17% and the median overall survival (OS) is only 5–8 months (4,5). Together, these studies (4,5) suggest that patients with PPC have extremely poor responses to chemotherapy regimens commonly used for NSCLC and have a dismal prognosis.

The two patients reported herein were diagnosed with PPC during a similar time period, and received GC chemotherapy as first-line therapy. However, the tumors had rapidly progressive courses in spite of GC therapy and a salvage regimen was required for both patients. We hypothesized that the sarcomatoid component of PPC may respond to regimens effective in sarcomas. The efficacy of MAID chemotherapy has been established in the treatment of sarcomas. In one phase II study, 105 patients with unresectable sarcoma received palliative MAID chemotherapy [doxorubicin (20 mg/m², days 1–3); dacarbazine (300 mg/m², days 1–4); ifosfamide (2500 mg/m², days 1–3); and mesna (days 1–4)]. The response rate (RR) and median OS were 47% and 16 months, respectively. The median time to progression in responders was about 9 months (6). In another study (phase III), 170 patients with sarcoma received MAID chemotherapy [doxorubicin (15 mg/m², days 1–4); dacarbazine (250 mg/m², days 1–4); ifosfamide (2500 mg/m², days 1–3); and mesna (days 1–4)]. The RR and median progression-free survival and median OS were 32%, 6 months and 13 months, respectively (7). In both studies (6,7), MAID regimen showed very frequent severe neutropenia (79–85%) and required clinicians’ careful attention. As there is no standard chemotherapeutic regimen for PPC, we chose MAID for the treatment of our patients with rapidly progressive and platinum-refractory PPC. Considering toxicities of MAID chemotherapy in previous reports (6,7), we used modified MAID regimen. Both patients had dramatic responses to MAID and the treatment effect was sustained for 7 and 9 months. Our report strongly suggests that the treatment approaches to PPC patients should differ from the approaches to patients with other common types of NSCLC. MAID chemotherapy may have an important role in the treatment of patients with PPC. Further studies to evaluate the effect of MAID therapy are clearly warranted.

Conflict of interest statement
None declared.

References


