Reversible Restrictive Lung Disease in Pseudomesotheliomatous Carcinoma in a Lung Harboring a HER2-mutation

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Abstract:
Pseudomesotheliomatous carcinoma of the lung is very rare, and reversible restrictive lung disease with pseudomesotheliomatous carcinoma has not yet been previously reported. We herein report a patient with HER2-positive non-small-cell lung cancer (NSCLC) showing pseudomesotheliomatous carcinoma who was successfully treated with bevacizumab combination chemotherapy. A 56-year-old Japanese woman with advanced NSCLC presented with dyspnea. We administered chemotherapy with cisplatin (75 mg/m²) plus pemetrexed (500 mg/m²) plus bevacizumab (15 mg/kg), followed by pemetrexed plus bevacizumab. After eight cycles of maintenance chemotherapy, chest CT demonstrated a marked tumor reduction and an improvement of the right lung volume. The vital capacity was thereafter found to have significantly increased according to pulmonary function tests.

Key words: HER2, lung cancer, pseudomesotheliomatous carcinoma, restrictive lung disease

Introduction

Pseudomesotheliomatous carcinoma of the lung is very rare, with a reported incidence among all lung cancers of 0.46% (1). Reversible restrictive lung disease with pseudomesotheliomatous carcinoma in non-small cell lung cancer (NSCLC) patients harboring HER2-mutation has not yet been previously reported. Because of its rarity and clinical features, there are fewer evidence-based therapies available for pseudomesotheliomatous carcinoma of the lung compared to other types of NSCLC. A novel, effective treatment for NSCLC with pseudomesotheliomatous carcinoma is therefore needed.

We herein describe a patient with HER2-positive lung cancer showing pseudomesotheliomatous carcinoma who was successfully treated with bevacizumab combination chemotherapy and thereafter demonstrated a significant improvement in the symptoms of restrictive lung disease.

Case Report

A 56-year-old Japanese woman presented with dyspnea. She was not occupationally exposed to asbestos and had never smoked. Chest radiography and computed tomography (CT) revealed diffuse pleural thickening and a reduced volume of the right lung and narrowing of the intercostal spaces (Fig. 1A, C and D). A transbronchial lung biopsy of the mass was performed; the pathological diagnosis was adenocarcinoma. 18F-fluorodeoxyglucose (FDG) positron-emission tomography (PET) demonstrated FDG accumulation in an area of diffuse pleural thickening (Fig. 1B). Molecular testing with next-generation sequencing revealed a human epidermal growth factor receptor-2 (HER2) mutation in exon 20 insertion. We administered chemotherapy with cisplatin (75 mg/m²) plus pemetrexed (500 mg/m²) and bevacizumab (15 mg/kg) every 3 weeks, followed by pemetrexed plus bevacizumab. After eight cycles of maintenance chemotherapy, CT and PET demonstrated a marked increase in the volume of the right lung and a significant improvement in the symptoms of restrictive lung disease.
tumor reduction and an improvement of diffuse pleural thickening and the right lung volume (Fig. 2A-D). The vital capacity and peak expiratory flow then was observed to significantly increase according to pulmonary function tests (Fig. 3A and B).

Discussion

Reversible restrictive lung disease of lung cancer patients is generally observed in cases with malignant pleural effusion or obstructive atelectasis due to the presence of a tumor. However, reversible restrictive lung disease with pseudomesotheliomatous carcinoma as observed in our patient has not yet been reported. Pseudomesotheliomatous carcinoma was first reported by Harwood et al. in 1976, among lung cancer patients with extension to the pleura (2). Pseudomesotheliomatous carcinoma of the lung is very rare, with a reported incidence among all lung cancers of 0.46%. It was reported that 87% of pseudomesotheliomatous carcinoma patients had a smoking history and 76% of such cases had an asbestos exposure history (3). Smoking and asbestos have thus been considered as causes of pseudomesotheliomatous carcinoma carcinogenesis.

A case of pseudomesotheliomatous carcinoma harboring an epidermal growth factor receptor (EGFR) mutation without occupational asbestos exposure was recently reported, with narrowing of the intercostal spaces (4). Although previous pseudomesotheliomatous carcinoma reports did not describe the incidence of oncogenes, such as EGFR mutation or HER2 mutation, the present case might indicate that the HER2 mutation could play an important role in the development of pseudomesotheliomatous carcinoma of the lung, as our patient had no other risk factors (e.g., smoking history, asbestos exposure).

HER2 mutation is a rare somatic mutation that represents 2%-3% of lung cancers, and there has been no report of its comorbidity with pseudomesotheliomatous carcinoma showing intercostal space narrowing (5, 6). Regarding the outcomes of chemotherapy for advanced HER2-mutant lung cancers, Mazieres et al. reported the outcomes with conventional chemotherapy excluding HER2 targeted drugs. The response rate and the median progression free survival for patients receiving first-line chemotherapy were 43.5% and 6.0 months (95% CI: 5.0-7.1), respectively (n=93) (7). In addition, Falchook et al. reported a case of advanced non-small cell lung cancer harboring a HER2 mutation which achieved
a sustained antitumor effect to lapatinib and trastuzumab in combination with bevacizumab (8). In the present case, we performed bevacizumab combination chemotherapy. The findings of this case suggest that bevacizumab containing chemotherapy may play an important role in the successful treatment of pseudomesotheliomatous carcinoma of the lung.
harboring a HER2-mutation.

Regarding prognostic factors, Tomizawa et al. reported that HER2 mutations were not associated with the prognosis of non-small-cell lung cancer patients, suggesting a negative prognostic role for the co-existence of a TP53 mutation (9).

The present report is the first to described a case of HER2-positive lung cancer showing pseudomesotheliomatous carcinoma that was successfully treated with cisplatin plus pemetrexed and bevacizumab chemotherapy with a significant improvement in the symptoms of restrictive lung disease.

The authors state that they have no Conflict of Interest (COI).

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