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Case Report

Successful Treatment of Pulmonary Pleomorphic Carcinoma with Nivolumab: A Case Report

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Pulmonary pleomorphic carcinoma · Nivolumab · Programmed cell death ligand-1

Abstract
Pulmonary pleomorphic carcinoma (PPC) has a poor prognosis due to the poor results of treatment with systemic chemotherapy. We report the case of a 73-year-old woman with PPC who showed a favorable response to nivolumab. As first-line treatment for postoperative recurrence, she received carboplatin and nanoparticle albumin-bound paclitaxel. However, 12 months later, a new metastatic lymph node appeared. Nivolumab was administered as second-line treatment, and the patient showed a favorable prolonged response. The effects of treatment of PPC with nivolumab seem promising. The results of a future prospective study are expected to identify indicators for the treatment of PPC.

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Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide [1]. However, the treatment strategies for patients with advanced non-small cell lung cancer (NSCLC) have shown improvements, and immune checkpoint inhibitors, such as nivolumab and pembrolizumab, which are anti-programmed cell death-1 (PD-1) monoclonal antibodies, have improved the prognosis of patients with advanced NSCLC; these agents have already been approved for clinical use.

Pulmonary pleomorphic carcinoma (PPC), a rare malignancy that accounts for 0.1–1.6% of all cases of thoracic malignancies [2, 3], shows rapid progression and is associated with a poor prognosis due to the poor results of treatment with systemic chemotherapy [4, 5]. There are no standard chemotherapy regimens established by verification clinical trials, and the treatment that is often provided is based on the treatment of NSCLC. Moreover, there are few published reports on systemic chemotherapy for the treatment of PPC. Here, we report a patient with PPC who showed a favorable treatment response to nivolumab.

Case Report

A 73-year-old woman visited our hospital in July 2012 due to the presence of a nodular shadow in her left lung (S1 + 2) that was detected on a chest computed tomography (CT) scan. The size and fluorodeoxyglucose (FDG) uptake of the shadow appeared to increase on positron emission tomography/CT scans (maximum standardized uptake value, 9.9; Fig. 1). Therefore, lung cancer was suspected, and the patient underwent a bronchial fibroscopy in March 2013. Although no malignant findings were observed in a biopsy specimen obtained by bronchial fibroscopy, the patient underwent surgery (left upper lobectomy and lymph node dissection) in May 2013 and was diagnosed with PPC (pT2aN0M0, stage IB) (Fig. 2).

Following surgery, she was administered a 1-year regimen of oral tegafur-uracil as adjuvant chemotherapy. However, 29 months after the surgery, a morbid fracture occurred in her right femur, and she underwent artificial head replacement surgery. Based on a surgical specimen, a diagnosis of a bone tumor that had metastasized from PPC was established.

The patient was administered 6 courses of carboplatin (CBDCA) and nanoparticle albumin-bound paclitaxel (nab-PTX) as first-line systemic chemotherapy and achieved a partial response after 3 courses. However, 12 months later, a thoracic CT scan revealed a new right pelvic lymph node, confirming disease progression. As the PD ligand-1 (PD-L1) tumor proportion score (TPS) was 50%, treatment with nivolumab was chosen as second-line therapy. Nivolumab was administered at a standard dose (3 mg/m^2, biweekly) from January 2017 onward, with no adverse events. Following the administration of 6 courses of nivolumab, the FDG uptake in the right pelvic lymph node significantly declined, and the tumor showed a treatment response to nivolumab (Fig. 3). The tumor has been controlled to date. The current regimen includes the administration of 25 courses of nivolumab; no adverse events have been observed.

Discussion

PPC, which is classified as a sarcomatoid cancer, is a relatively rare disease. It is highly malignant and resistant to chemotherapy and radiotherapy; therefore, the prognosis of patients is poor, even if diagnosed during the early stages [6]. Many patients experience a recurrence within 6 months following resection, and the median survival period following the confirmation of recurrence has been reported to be 2.6 months [2].

However, some studies have reported successful outcomes of chemotherapy. Bae et al. [7] reported that the median overall survival in cases of advanced or recurrent lung sarcoma-like cancer treated with chemotherapy was 5 months. Kaira et al. [3] retrospectively analyzed the effectiveness of chemotherapy for advanced and recurrent PPC and reported a median progression-free survival of 1.75 months and 1.0 month in patients treated with first- and second-line chemotherapy, respectively.

It has been reported that PPC treated with CBDCA plus PTX, with or without bevacizumab, showed a good treatment response [8, 9]. In our patient, CBDCA plus nab-PTX was very effective, and the antitumor effect continued for >1 year.

Nivolumab, an anti-PD-1 antibody, has shown superior results to docetaxel as second-line chemotherapy in advanced squamous and nonsquamous NSCLC. Moreover, the expression of PD-L1 is thought to be a predictive biomarker for its efficacy [10–12]. Previous studies showed that PD-L1 is strongly expressed in PPC with a TPS of 69.2–90.2% [13, 14]. Moreover, in PPC, PD-L1 expression is significantly higher in localized sarcomatous areas than in the corresponding carcinomatous ones [14]. The PPC in the present case likewise showed high PD-L1 expression, with a TPS of 50%.

Based on these results, nivolumab is expected to be beneficial for patients with PPC. Several case reports indicated that nivolumab was an effective treatment for PPC [15]. In our case, we treated the patient with nivolumab as second-line treatment. The tumor showed a good response, and long-term tumor control was achieved.

The effects of the treatment of PPC with nivolumab seem promising. However, the lack of data on the effectiveness and the side effects of this treatment remains a concern. A prospective study to evaluate the efficacy and safety of nivolumab for PPC is ongoing (UMIN000023433), and the results of this trial are expected to reveal indicators for the treatment of PPC.

In conclusion, we report a case of advanced PPC with a favorable prolonged response to nivolumab as second-line therapy.

Statement of Ethics

The patient gave written informed consent to the publication of this case report and the accompanying images.

Disclosure Statement

Dr. Yokoi has received honoraria from Chugai Pharmaceutical Co., Ono Pharmaceutical Co., and Bristol-Myers Squibb Co. The remaining authors declare no conflict of interest.

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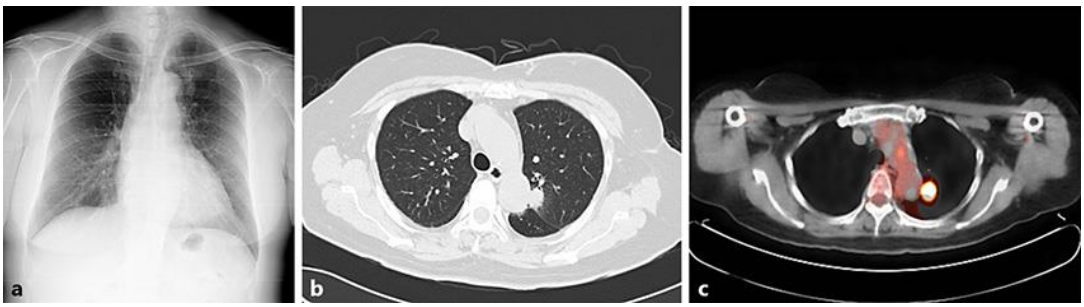

Fig. 1. Chest radiography (**a**), chest computed tomography (**b**), and fluorodeoxyglucose positron emission tomography/computed tomography scans (**c**) obtained during the initial medical examination of the patient. A 20-mm nodule with a maximum standardized uptake value of 9.9 was observed in the left lung (S1 + 2).

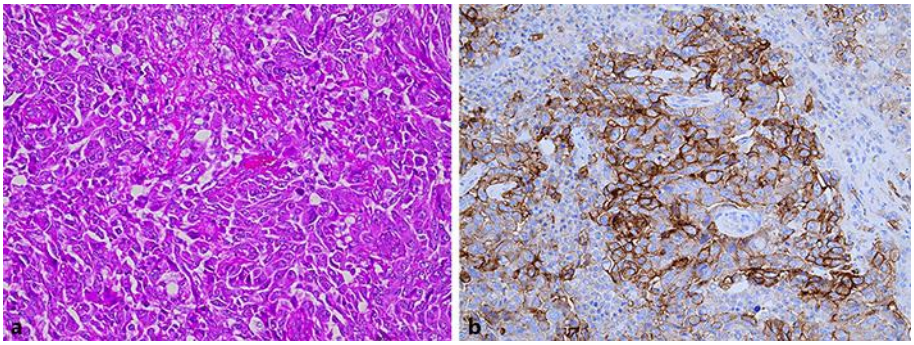

Fig. 2. Pathological analyses using hematoxylin and eosin staining (**a**) and programmed cell death-ligand 1 (PD-L1) staining with Dako 28-8 (**b**).

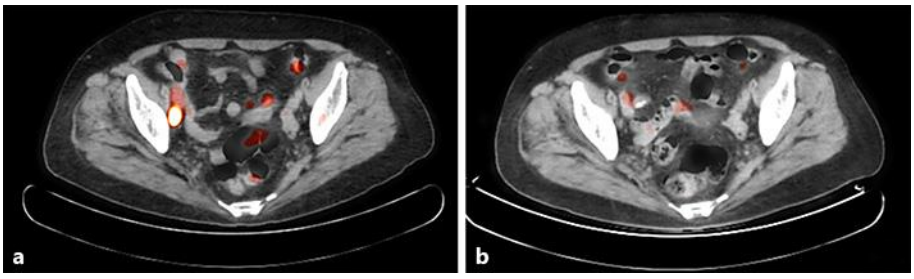

Fig. 3. Prior to the treatment of the patient with nivolumab, the fluorodeoxyglucose positron emission tomography (FDG-PET) scans showed a high level of uptake in the right pelvic lymph node (**a**). After the patient had been treated with 6 courses of nivolumab, the FDG-PET scans showed a decrease in uptake in the right pelvic lymph node (**b**).