

Case Report

The Successful Treatment of Pulmonary Pleomorphic Carcinoma with Pembrolizumab: A Case Report

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Keywords

Pulmonary pleomorphic carcinoma · Pembrolizumab · Programmed death ligand-1 · Immune checkpoint inhibitor · Non-small cell lung cancer

Abstract

Pulmonary pleomorphic carcinomas are rare malignant tumors, and no standard treatments have been established. We herein report the successful treatment of a patient with pulmonary pleomorphic carcinoma with pembrolizumab. A 51-year-old man who was a current smoker presented to our hospital due to dyspnea and hemoptysis. Chest X-ray showed right-sided pneumothorax with pleural effusion; chest tube drainage was therefore performed. Computed tomography after chest tube drainage showed a cavitary nodule in the right upper lobe and right hilar and bilateral mediastinal lymphadenopathy. Surgery was performed for the diagnosis and treatment. He was eventually diagnosed with pulmonary pleomorphic carcinoma corresponding to clinical stage IVB (cT2aN2M1c [PLE, ADR, HEP]). The giant cells strongly expressed programmed death ligand-1, and the tumor proportion score was more than 50%. Therefore, pembrolizumab was introduced as the first-line therapy. After 3 cycles of pembrolizumab, his right hilar and bilateral mediastinal lymphadenopathy and pleural dissemination notably decreased. Pembrolizumab might be an effective therapy for pulmonary pleomorphic carcinoma.

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Introduction

Pulmonary pleomorphic carcinomas are rare and refractory to systemic chemotherapy, resulting in a poor prognosis [1–4]. No standard treatments or effective managements have been established.

We herein report the successful treatment of a patient with pulmonary pleomorphic carcinoma – in which programmed death ligand 1 (PD-L1) was strongly expressed – with pembrolizumab.

Case Presentation

A 51-year-old man who was a current smoker presented to our hospital due to dyspnea and hemoptum. He had a history of right-sided pneumothorax and pancreatitis. His chest X-ray showed right-sided pneumothorax with pleural effusion; thus, chest tube drainage was performed (Fig. 1a, b). The cytology of the pleural fluid was benign. Computed tomography on the 3rd day revealed a cavitary nodule in the right upper lobe, and right hilar and bilateral mediastinal lymphadenopathy (Fig. 1c, d). An operation was performed on the 7th day for the diagnosis and treatment of pneumothorax. The tumor was found to have macroscopically invaded the visceral pleura and air leakage persisted. Wedge resection was performed, and he was discharged on the 3rd postoperative day.

A pathological analysis of the lung tumor revealed bizarre giant multinucleate cells containing abundant eosinophilic cytoplasm (Fig. 2a). Round cells with acinar and papillary patterns (components of adenocarcinoma) were also noted. Immunohistochemical studies showed that the giant cells were positive for cytokeratin AE1/AE3, and positive cells of p53 and Ki-67 were numerous. Vascular permeation was observed. The giant cells strongly expressed PD-L1 (Fig. 2b), and the tumor proportion score was more than 50% (Dako 22C3 IHC platform). The patient was diagnosed with pulmonary pleomorphic carcinoma corresponding to clinical stage IVB (cT2aN2M1c [PLE, ADR, HEP]).

Pembrolizumab (200 mg/body) was introduced as the first-line therapy. The cytology of the pleural fluid at the initiation of therapy was malignant, and the pleural dissemination was found to have progressed in comparison to the initial medical examination (Fig. 1e). After 3 cycles of pembrolizumab, his right hilar and bilateral mediastinal lymphadenopathy and pleural dissemination notably decreased (Fig. 1f). He showed a partial response without any severe adverse events.

Discussion

Pulmonary pleomorphic carcinomas are rare and aggressive tumors; the reported incidence among all lung carcinomas has ranged from 0.1 to 0.4% [1, 2]. According to the 2015 World Health Organization (WHO) classification [5], pleomorphic carcinoma is defined as a poorly differentiated non-small cell lung carcinoma (NSCLC) in which spindle cell carcinoma and/or giant cell carcinoma form at least 10% of what would otherwise be a pure squamous cell carcinoma, adenocarcinoma or large cell carcinoma, or a carcinoma consisting only of spindle and giant cells. Pulmonary pleomorphic carcinoma has a more aggressive clinical course than other forms of NSCLC, and the response to chemotherapy is generally poor [3, 4, 6].

Recently, immune checkpoint inhibitors have shown promising results in clinical trials, and are considered to be the standard treatment for advanced NSCLC [7–9]. Pembrolizumab, a humanized monoclonal antibody against PD-1 (programmed death 1), was approved as a first-line treatment for NSCLC in cases in which PD-L1 is strongly expressed [9]. The overexpression of PD-L1 in tumor membranes is one of the predictive biomarkers of anti-PD-1 antibodies.

It is reported that 70.5–90.2% of pulmonary pleomorphic carcinomas show high levels of PD-L1 expression [10, 11], which is rather high in comparison to patients with other histological types of advanced NSCLC [7, 8]. Furthermore, the expression of PD-L1 in the giant cells of our patient was stronger than that in the adenocarcinoma cells, as was reported by Kim et al. [11]. The mechanism of mesenchymal differentiation in pulmonary sarcomatoid carcinoma is considered to be epithelial-mesenchymal transition [12], and the expression of PD-L1 is associated with the epithelial-mesenchymal transition in lung cancer [13, 14]. This mechanism may therefore explain the heterogeneous distribution of high PD-L1-expressing cells in this case.

Conclusions

To our knowledge, this is the first report to show the successful treatment of pulmonary pleomorphic carcinoma with pembrolizumab. Anti-PD-1 antibodies may be a promising therapeutic candidate for pulmonary pleomorphic carcinoma.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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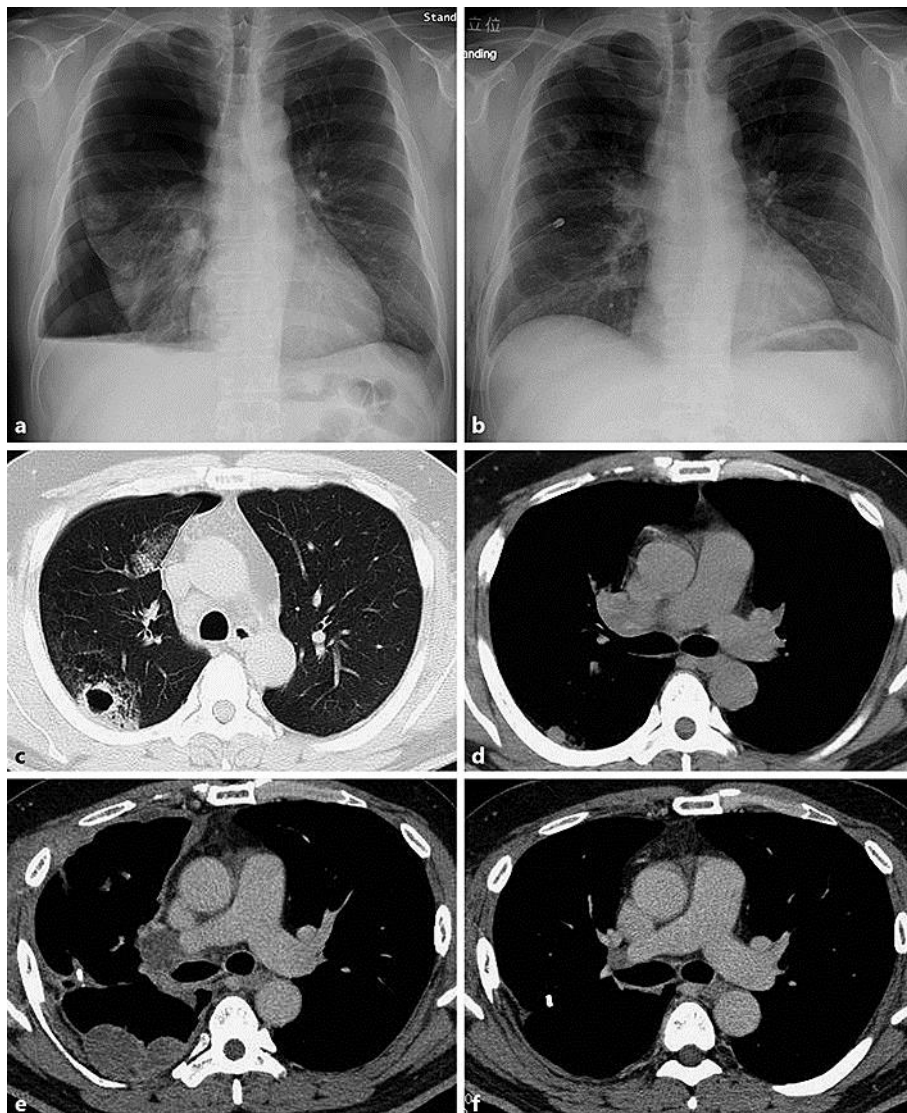


Fig. 1. Chest X-rays: on the initial medical examination (a) and after chest tube drainage (b). Computed tomography scans: before the operation (c, d), after the operation (e), and after 3 cycles of pembrolizumab (f). It was observed that the right hilar and bilateral mediastinal lymphadenopathy and pleural dissemination have decreased.

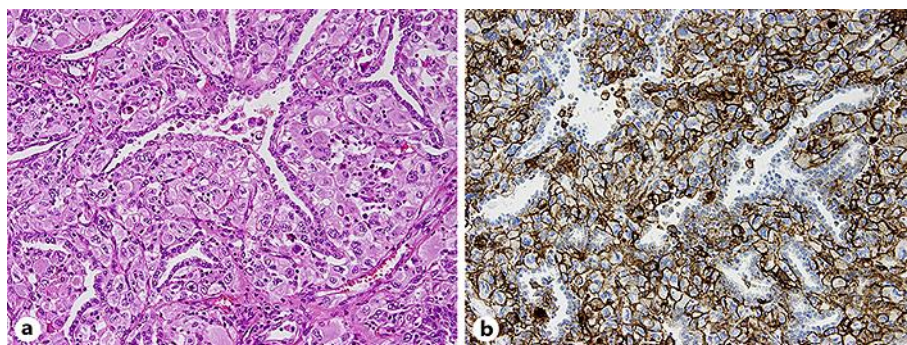


Fig. 2. The pathological analyses: hematoxylin and eosin staining (**a**) and PD-L1 staining (**b**).