Dramatic Response to Pembrolizumab with Chemotherapy Followed by Salvage Surgery in a Lung Cancer Patient

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Case report

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Abstract

Background: Immune checkpoint inhibitors with chemotherapy have been shown to exhibit remarkable efficacy for advanced non-small-cell lung carcinoma and are under investigation as an induction therapy. But the significance of preoperative therapy with pembrolizumab + chemotherapy for surgically resected non-small-cell lung carcinoma still remains unclear.

Case presentation: We herein report a case of stage IIIB non-small-cell lung carcinoma who underwent salvage surgery after three cycles of pembrolizumab + carboplatin + nab-paclitaxel. Computed tomography revealed the remarkable decrease in tumor volume by 81%. A pathological examination showed that viable neoplastic cells were observed in less than one percent of the total tumorous lesion suggesting near pathological complete response.

Conclusions: This case suggests that this regimen might be a good option as induction therapy for non-small-cell lung carcinoma.

Background

Immune checkpoint inhibitors (ICIs) are under investigation in the neoadjuvant setting. Several trials suggested that neoadjuvant ICI with chemotherapy exhibits remarkable efficacy for non-small-cell lung carcinoma (NSCLC); however, significance of the preoperative pembrolizumab with chemotherapy has yet to be clafiried.1-4 We report a case of a patient with locally advanced NSCLC who were successfully treated with surgical resection following pembrolizumab + carboplatin + nab-paclitaxel. Pathologically, viable neoplastic cells were observed in less than one percent of the total tumorous lesion, suggesting a near pathological complete response.

Case Presentation

The patient was a 50-year-old man with a 32 pack-year smoking history. Chest X-ray of the medical check-up showed a mass shadow in the left upper lung field (Figure 1A) without any pain in the chest and back, and the patient was referred to our hospital. Laboratory examinations revealed remarkable elevation of the serum level of carcinoembryonic antigen (CEA; 1253.2 ng/ml). Chest computed tomography (CT) revealed a huge mass shadow of 132 mm in size (Figure 1B), in the left upper lobe with invasion into the lower lobe and main pulmonary artery. The hilar and mediastinal lymph nodes were also swollen. Positron emission tomography/CT revealed a high uptake in the mass, with a maximum standardized uptake value of 19.85 (Figure 1C). The patient underwent transbronchial biopsy and was diagnosed with NSCLC (cT4N2M0, cStage IIIB; Figure 2A). No genetic alterations were identified in epidermal growth factor receptor, anaplastic lymphoma kinase or c-ROS oncogene 1. Two percent of the tumor cells exhibited the expression of programmed death-ligand 1 (PD-L1; 22C3; Figure 2B). Then, carboplatin + nab-paclitaxel + pembrolizumab were administered. During the second cycle, an adverse event (neutropenia: grade three) occurred and the patient could not receive nab-paclitaxel on day 15. After

the second cycle, the patient's serum level of CEA decreased to 202.6 ng/ml. After the administration of pembrolizumab in the third cycle, an immune-related adverse event (infusion reaction: grade 2) occurred and we judged that drug therapy could not be continued. After the third cycle, laboratory examinations revealed that the patient's serum level of CEA had decreased to 20.8 ng/ml. CT revealed that the mass shadow was reduced to 104 mm in size (-21%: stable disease) and three-dimensional CT showed a remarkable decrease in tumor volume from 448859 mm3 to 85081 mm3 (-81%). No distant metastasis was present. The patient's good physical capacity, including his pulmonary function, suggested that he could undergo left pneumonectomy. Left pneumonectomy combined with resection of the parietal pleura due to adhesion between the left upper lung and parietal pleura was performed (Figure 2C). The hilar and mediastinal lymph nodes were also dissected. The postoperative course was uneventful with no postoperative complications. The tumorous lesion in the left upper lung exhibited massive necrosis, fibrosis with hyalinization and inflammation. Viable neoplastic cells were observed in less than one percent of the total tumorous lesion, suggesting a near pathological complete response (pCR; Figure 2D, arrow). In addition, no viable cells were identified in the dissected lymph nodes. After surgery, a laboratory examination revealed a further decrease in CEA (1.3 ng/ml; Figure 3). Because of the occurrence of an infusion reaction, we decided to follow-up without postoperative therapy.

Discussion And Conclusions

ICIs are generally administered to patients with advanced-stage NSCLC and their significance in induction therapy is under investigation.5-11 Forde et al. reported that neoadjuvant nivolumab therapy led to a major pathological response (MPR) in 9 of 20 patients (45%) and a pCR in 3 of 20 patients (15%).1 After this trial, several trials tested the significance of neoadjuvant ICI in resectable NSCLC and suggested that neoadjuvant ICI with chemotherapy exhibits remarkable efficacy for NSCLC.2 Neoadjuvant therapy with atezolizumab + carboplatin + nab-paclitaxel was tested in patients with resectable NSCLC.3 Among 22 patients, 12 (54.5%) and 7 patients (32%) demonstrated an MPR and pCR, respectively. Furthermore, preoperative therapy with nivolumab + paclitaxel + carboplatin was investigated in patients with resectable stage IIIA NSCLC.4 Among 46 patients, an MPR was achieved in 35 (76%) and a pCR was achieved in 25 patients (54%). Thus, ICI + chemotherapy may have a remarkable efficacy as induction therapy for resectable NSCLC, although the survival benefits are yet to be determined. Some studies showed that pCR after neoadjuvant chemotherapy bring long overall survival for the patients with NSCLC.12-14 Pembrolizumab and chemotherapy are also being examined in patients with resectable NSCLC, but the result has not been reported (NCT03425643).

The present case was initially diagnosed as stage IIIB NSCLC and pembrolizumab + carboplatin + nab-paclitaxel were administrated. Paz-Ares et al. reported that the addition of pembrolizumab to standard chemotherapy with carboplatin and either paclitaxel or nab-paclitaxel, in comparison to chemotherapy alone, prolonged median overall survival by 4.6 months (15.9 months vs. 11.3 months) and median progression-free survival by 1.6 months (6.4 months vs. 4.8 months) in patients with untreated metastatic squamous NSCLC.15 Because of the immune-related toxicity, we considered that it was not possible to continue this regimen any further and performed salvage surgery. The achievement of a near

pCR with pembrolizumab with carboplatin + nab-paclitaxel indicates that this combination therapy might be a good option for induction therapy for NSCLC, although this regimen is not currently being investigated for this application. In summary, we report the case of a patient with NSCLC who was successfully treated with carboplatin + nab-paclitaxel + pembrolizumab followed by salvage surgery. This regimen might be a good option for induction therapy for NSCLC.

Abbreviations

ICIs: Immune checkpoint inhibitors

NSCLC: non-small-cell lung carcinoma

CEA: carcinoembryonic antigen

CT: computed tomography

PD-L1: programmed death-ligand 1

pCR: pathological complete response

MPR: major pathological response

Declarations

Ethics approval and consent to participate:

This study was conducted according to the principles of the Declaration of Helsinki.

Consent for publication:

The patient gave his consent for information about himself to be published.

Availability of data and materials:

The datasets generated and analysed during the current study are not publicly available because individual privacy could be compromised but are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

All authors read and approved the final manuscript.

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Figures

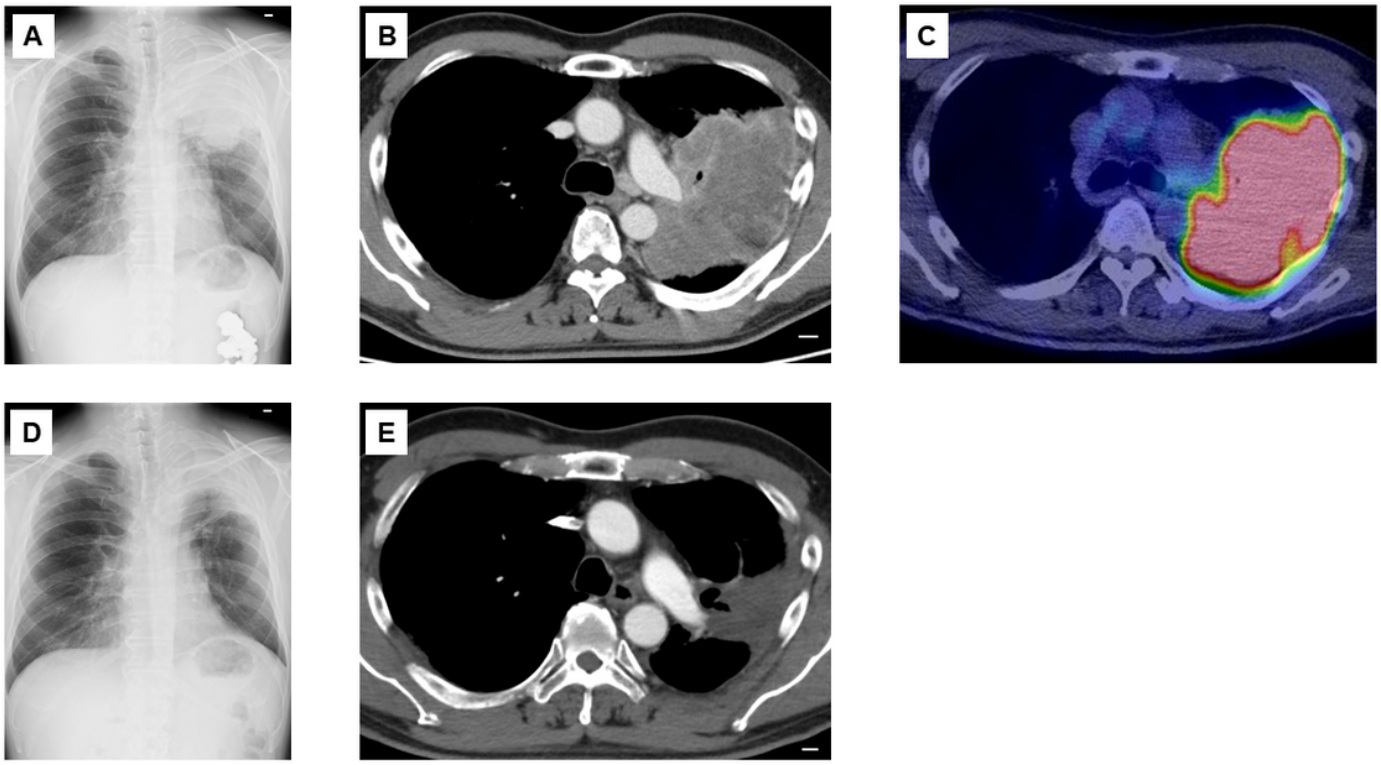

Figure 1. Saito et al.

Figure 1

Chest X-ray revealed a mass shadow in the left upper lung field (A). Chest computed tomography (CT) revealed a huge mass shadow, measuring 132 mm in size, in the left upper lobe with invasion into the lower lobe and main pulmonary artery (B). Positron emission tomography/CT revealed an avid uptake in the mass, with a maximum standardized uptake value of 19.85 (C). After three cycles of carboplatin + nab-paclitaxel + pembrolizumab, chest X-ray revealed that the mass shadow in the left upper lung field had decreased in size (D), and CT revealed that the mass shadow reduced to 104 mm in size (-21%: stable disease) (E). Scale bar: 1.0 cm.

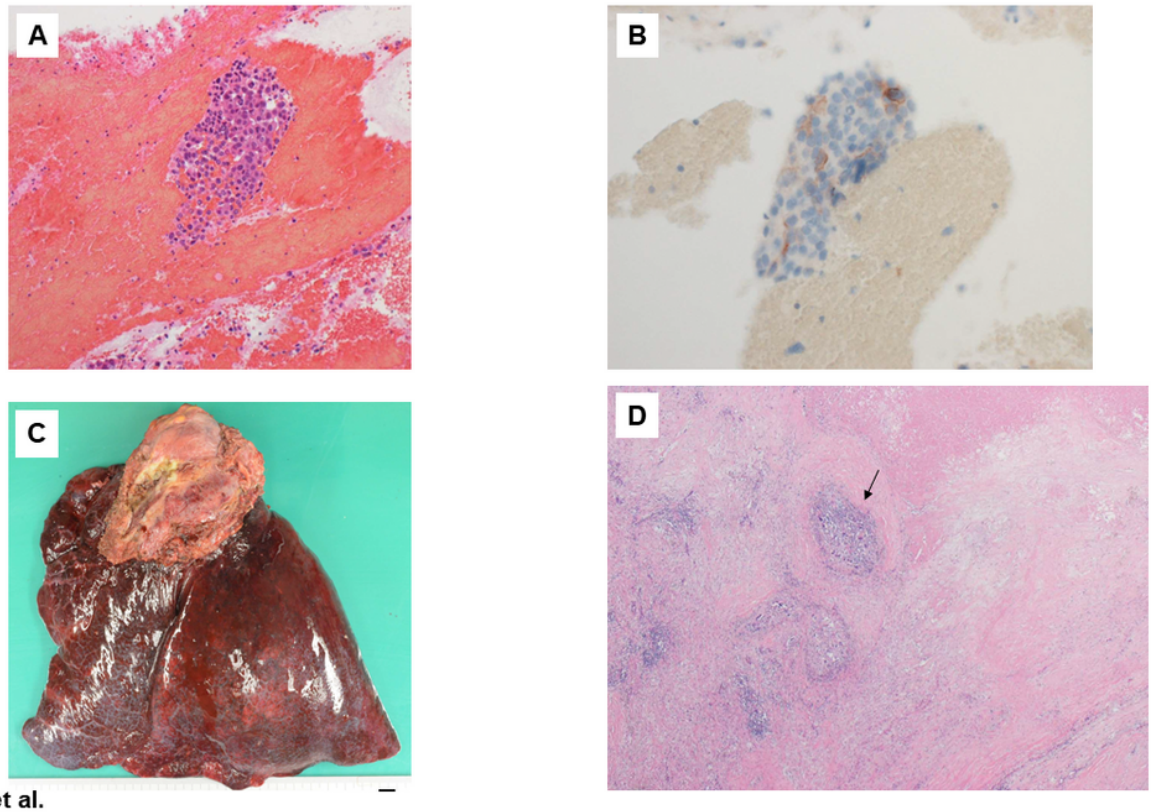

Figure 2. Saito et al.

Figure 2

The pathological examination of a transbronchial biopsy specimen revealed non-small-cell lung carcinoma (NSCLC; A), and two percent of the tumor cells expressed programmed death-ligand 1 (22C3; B). The patient underwent left pneumonectomy combined with the resection of the parietal pleura (C). The tumorous lesion in the left upper lung exhibited massive necrosis, fibrosis with hyalinization and inflammation. Viable neoplastic cells were observed in less than 1% of the total tumorous lesion (D, arrow).

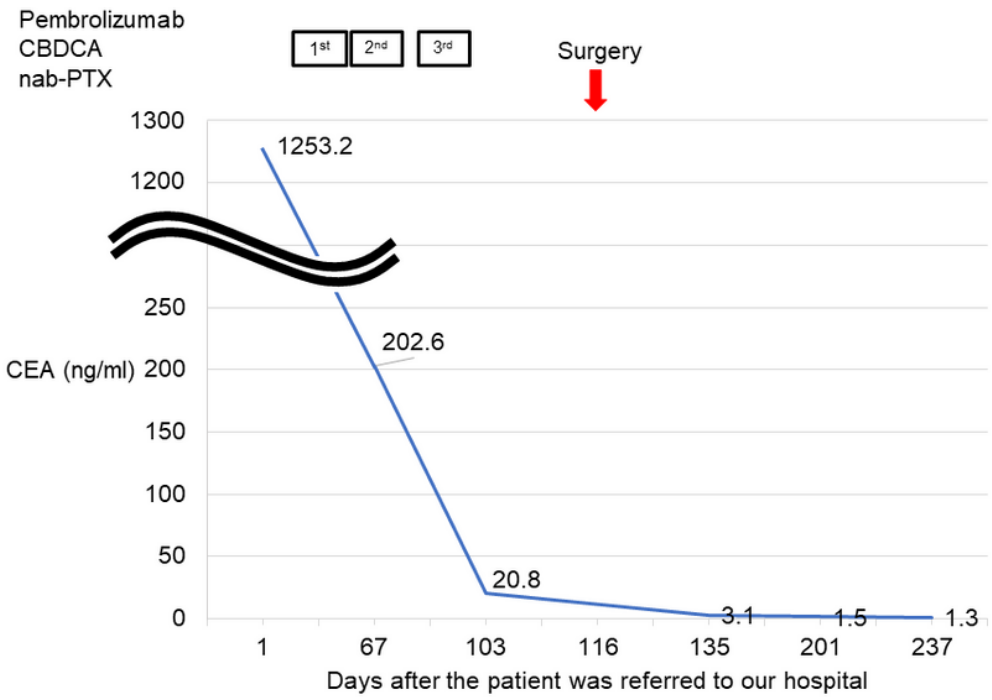

Figure 3. Saito et al.

Figure 3

Changes in carcinoembryonic antigen. CEA, carcinoembryonic antigen; CBDCA, carboplatin; nab-PTX, nab-paclitaxel