



## CASE REPORT

## Case of advanced pulmonary squamous cell carcinoma cured by resection through preoperative induction of immune checkpoint inhibitor

Hideki Kawai<sup>1</sup> , Yoshitaro Saito<sup>1</sup> , Ryo Demura<sup>1</sup>, Hidesato Odaka<sup>2</sup>, Susumu Takahashi<sup>2</sup>, Kento Takahashi<sup>2</sup>, Hirokazu Kurokawa<sup>2</sup> & Katsuhiko Enomoto<sup>3</sup>

1 Department of Thoracic Surgery, Akita Red Cross Hospital, Akita, Japan

2 Department of Respiratory Medicine, Akita Red Cross Hospital, Akita, Japan

3 Department of Pathology, Akita Red Cross Hospital, Akita, Japan

### Keywords

Immune checkpoint inhibitor; induction therapy; programmed death 1 inhibitors; squamous cell lung cancer.

### Correspondence

Hideki Kawai, Department of Thoracic Surgery, Akita Red Cross Hospital, 222-1 Naeshirosawa, Saruta, Kamikitate, Akita 010-1495, Japan.

Tel: +81 18 829 5000

Fax: +81 18 829 5255

Email: [hideki\\_kawai@akita-med.jrc.or.jp](mailto:hideki_kawai@akita-med.jrc.or.jp)

Received: 20 November 2017;

Accepted: 14 December 2017.

doi: 10.1111/1759-7714.12592

Thoracic Cancer 9 (2018) 495–497

### Introduction

Recently, programmed death 1 (PD-1) inhibitors; that is, immune checkpoint inhibitors, have been used in unresectable non-small cell lung cancer. PD-1 inhibitors exert their anticancer action by a unique mechanism that is different from conventional anticancer drugs. Reactions, such as pseudo-progression, that are not seen in other cancer treatments can occur; therefore, the timing for evaluating its effect is still unclear,<sup>1,2</sup> at the same time, clinical trials have shown that this treatment is effective in squamous cell carcinoma (SCC), which has been thought to be less responsive to conventional anticancer drugs compared with adenocarcinoma.<sup>3</sup> The locally advanced type is more frequently seen in SCC than in adenocarcinoma, and if tumor shrinkage by an anticancer agent is achievable, complete curative resection can then be expected by induction therapy. We herein encountered a case in which curative

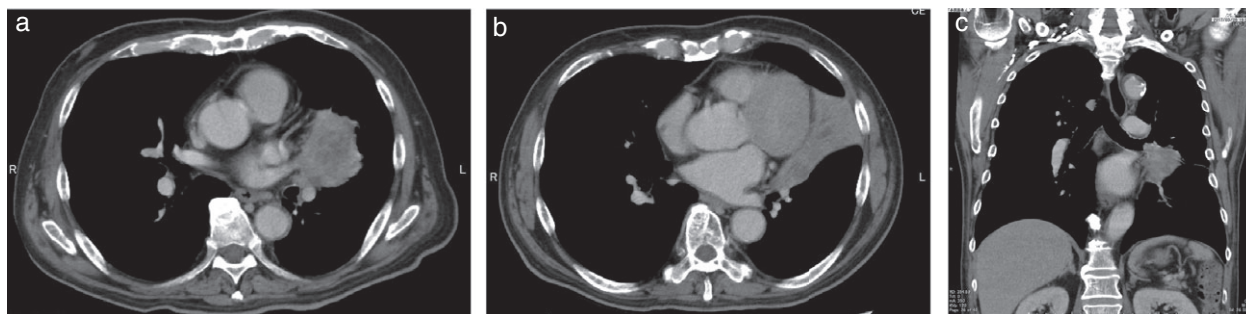
### Abstract

The options for lung cancer treatment have increased due to the development of immune checkpoint inhibitors, but there has been no report of inoperable cases whereby the treatment effects rendered the case operable, an operation was subsequently performed, and histological assessment of the surgical specimen was carried out. Here, we report a 67-year-old man who was given pembrolizumab for T3N0 lung squamous cell carcinoma suspected of pericardial infiltration and judged inoperable. Treatment effect was evaluated after four courses. Computed tomography indicated a partial response, and operability was feasible. Therefore, thoracoscopic left upper lobectomy was performed after six courses of pembrolizumab, and histological assessment of the treatment effect was determined to be Ef 3, a complete response. The postoperative course was uneventful and he was discharged on the third postoperative day. We encountered a case that could be surgically treated after pembrolizumab administration. This treatment was safe and effective for advanced lung cancer.

resection was possible for a patient with locally advanced SCC due to a partial response after pembrolizumab treatment. We also report histological evaluation after pembrolizumab administration.

### Case Report

A 67-year-old man was referred to Akita Red Cross Hospital, Akita, Japan, with diagnosis of lung cancer at another hospital. Chest computed tomography showed a 55 × 40 × 45-mm tumor in the lingular segment, and pericardial infiltration was suspected (Fig 1). Bronchoscopic examination revealed a tumor protruding from the entrance of the lingular branch, from the same site as the biopsy site, and a diagnosis of SCC was made (Fig 2a,b). Based on tumor localization and the extent of invasion, left pneumonectomy was likely required, and we therefore



**Figure 1 (a–c)** Chest computed tomography examination at pretreatment. A 55 × 40 × 45-mm tumor was found in the lingular segment, and pericardial infiltration was suspected.

decided to first carry out chemotherapy and consider operation only when tumor reduction was obtained.

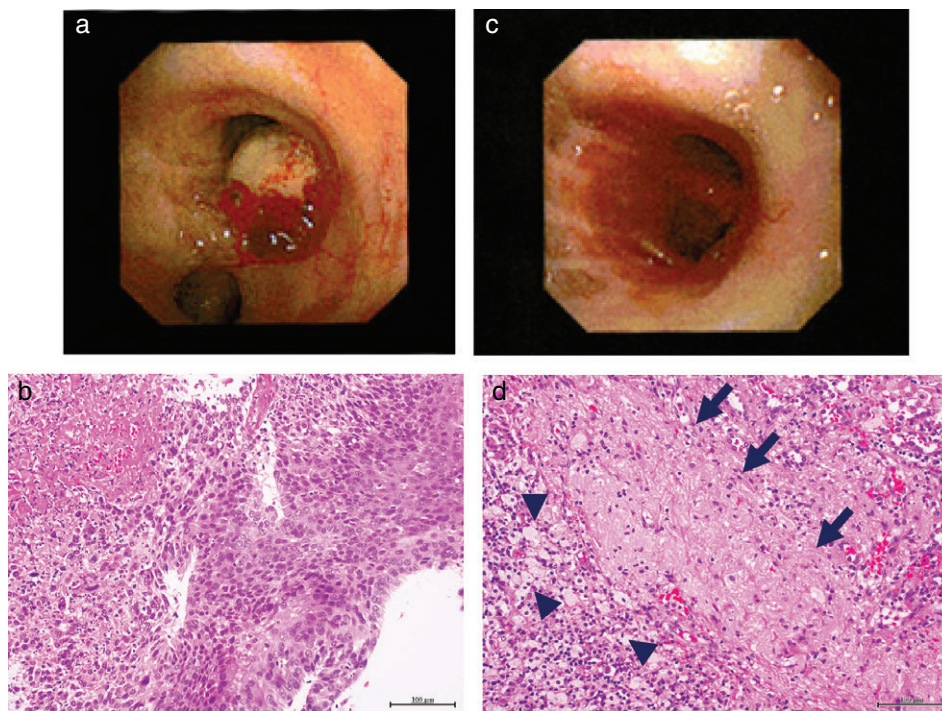
As the 22C3 test by immunohistochemical staining was positive with a tumor proportion score of 95% with the biopsy specimen, pembrolizumab was started. After four courses of pembrolizumab, a 50% reduction rate was obtained and evaluated to be a partial response based on computed tomography using the Response Criteria in Solid Tumors version 1.1. A marked reduction in tumor size was also similarly observed by bronchoscopic examination (Fig 2c, 3). At this point, it was determined that left upper lobectomy would be possible, and the operation was carried out according to the patient’s wishes. Left upper lobectomy by video-assisted thoracic surgery was carried out after six courses of pembrolizumab. Intraoperative findings included marked angiogenesis and edema near the tumor

(Fig 4). Intraoperative bleeding was 110 g and operation time was 263 minutes. Pathological diagnosis was Ef 3, which was a complete response; that is, there was no cancer cell remnant in the surgical specimen (Fig 2d).

The patient’s postoperative course was uneventful and he was discharged on the third postoperative day.

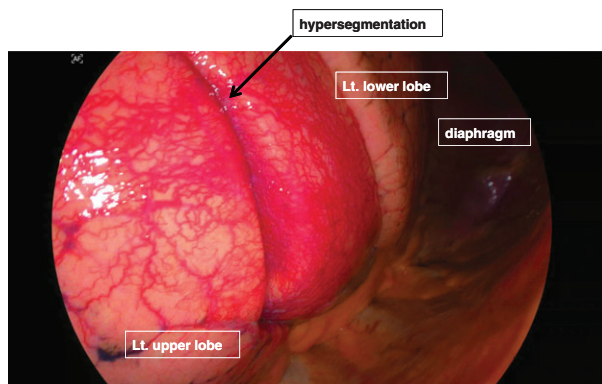
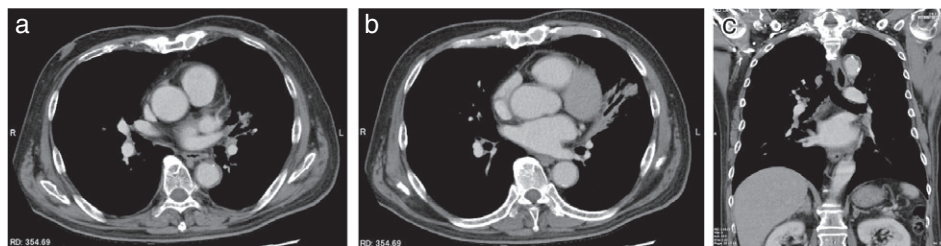
### Discussion

Pembrolizumab is a PD-1 receptor inhibitor, and it is permitted in Japan to use as a first-line treatment for cases with a tumor proportion score of ≥50% based on PD-L1 examination, and is recommended for grade A based on the 2016 edition of the Japanese lung cancer clinical practice. Among non-small cell lung cancers, SCC has fewer anticancer drug options as compared with adenocarcinoma, and in advanced



**Figure 2 (a)** Bronchoscopic examination. A tumor was protruding from the entrance of the lingular branch. **(b)** A biopsy specimen from the tumor located at the lingular branch was diagnosed as a moderately differentiated squamous cell carcinoma with necrosis. **(c)** Bronchoscopic examination. The tumor had disappeared in the observed area. **(d)** The surgically resected tissue showed the necrotic cancer cells (arrows) with reacting foamy macrophages (arrow heads). No viable cancer cell was observed in the resected tissue.

**Figure 3 (a–c)** Chest computed tomography examination after four courses of pembrolizumab. Partial response was achieved.



**Figure 4** Intraoperative findings. Marked angiogenesis and edema in the tumor vicinity.

cases of SCC, radical cure is difficult to achieve. However, in locally advanced cases without lymph node metastasis, curative operation is often possible if downstaging is obtained by preoperative chemoradiotherapy. Conventional induction therapy is mainly chemoradiotherapy; however, removal of the scar tissue by treatment is difficult. In contrast, in the present case after pembrolizumab administration, removal was relatively easy. In addition, the drug-free period was one month in conventional chemotherapy, but for pembrolizumab it was shortened by three weeks. In the present case, the preoperative evaluation was partial response, but the final pathology indicated complete response. Intraoperative macroscopic findings included angiogenesis and edema in the tumor vicinity, and it appeared that computed tomography evaluation determined this lesion to be a tumor. This phenomenon was interesting, as it might be related to pseudo-progression, which is often observed in PD-1 inhibitor treatment. For preoperative immunotherapy, there have been reports of induction therapy of immune checkpoint inhibitors in early-stage lung cancer and other cancers in Europe, and safety was not an issue.<sup>4,5</sup> Even in the present case, it was possible to be discharged from the hospital within a few days

without any postsurgical complications. Furthermore, the recovery course at the outpatient clinic after discharge was good.

As histological complete response was achieved, the postoperative therapy was only follow-up.

In conclusion, we encountered for the first time a case of induction therapy using pembrolizumab for a patient with advanced SCC. This case might open up a new therapeutic strategy for non-small cell lung cancer.

## Disclosure

No authors report any conflict of interest.

## References

- 1 Khoja L, Kibiro M, Metser U *et al.* Patterns of response to anti-PD-1 treatment: An exploratory comparison of four radiological response criteria and associations with overall survival in metastatic melanoma patients. *Br J Cancer* 2016; **115**: 1186–92.
- 2 Villaruz LC, Socinski MA. The clinical utility of PD-L1 testing in selecting non-small cell lung cancer patients for PD1/PD-L1 directed therapy. *Clin Pharmacol Ther* 2016; **100**: 212–4.
- 3 Zago G, Muller M, Yan den Heuvel M, Baas P. New targeted treatments for non-small-cell lung cancer-role of nivolumab. *Biologics* 2016; **10**: 103–17.
- 4 Forde P. Abstract LBA41\_PR-Neoadjuvant anti-PD1, nivolumab, in early resectable non-small-cell lung cancer. Proffered Paper Session, Non-metastatic NSCLC and other thoracic malignancies on Friday 7 October in Room Madrid (2016).
- 5 Elias AW, Kasi PM, Stauffer JA *et al.* The feasibility and safety of surgery in patients receiving immune checkpoint inhibitors: A retrospective study. *Frontiers in Oncology* 2017; **7**: article121.