

Case Report

Induction S-1 + Concurrent Radiotherapy Followed by Surgical Resection of Locally Advanced Non-small-cell Lung Cancer in an Elderly Patient

Hidejiro Torigoe^a, Shinichi Toyooka^{a*}, Kuniaki Katsui^b, Junichi Soh^a,
Yuho Maki^a, Katsuyuki Kiura^c, and Shinichiro Miyoshi^a

Departments of ^aThoracic Surgery, ^bRadiology, ^cRespiratory Medicine, Okayama University Hospital, Okayama 700-8558, Japan

We present the case of a 77-year-old Japanese man diagnosed with lung squamous cell carcinoma with mediastinal lymph node metastasis. He was treated with induction chemoradiotherapy for T1bN2M0 stage IIIA disease. Considering his age, we selected S-1 as the chemotherapeutic drug. Observing an objective response with no severe adverse events, we performed a left upper lobectomy with sleeve resection of the pulmonary artery. No residual tumor cells were found in the resected specimens, and no critical complication was observed in the clinical course. This case suggests that induction chemoradiotherapy using S-1 combined with concurrent radiation followed by surgery can be a therapeutic option for elderly patients with locally advanced non-small-cell lung cancer.

Key words: lung cancer, S-1, elderly, induction, chemoradiotherapy

The standard treatment of locally advanced non-small-cell lung carcinoma (NSCLC) with mediastinal lymph node metastasis is definitive chemoradiotherapy with or without consolidation chemotherapy [1]. A recent randomized phase III trial reported by Albain *et al.* did not demonstrate that surgery after induction chemoradiotherapy improves prognosis compared with definitive chemoradiotherapy. On the other hand, the possible advantages of surgical resection for selected patients with N2 disease were suggested in the same trial [2]. The standard regimen of chemoradiotherapy is a platinum-based combination, but there is no evidence that aggressive treatments used for young patients improve survival in elderly patients [3, 4].

We recently reported that concurrent treatment

with S-1 and thoracic radiation is a feasible option for NSCLC in elderly patients (aged >75 years), showing an acceptable response with manageable toxicity [5, 6]. Here we describe the case of an elderly patient who was successfully treated with induction chemoradiotherapy using S-1 followed by surgery.

Case Report

A 77-year-old Japanese man with a history of hypertension and diabetes was admitted to our hospital for the treatment of NSCLC in February 2014. Image analyses showed a 2.6-cm tumor in the left upper lobe and the positive mediastinal lymph node (Fig. 1). A transbronchial lung biopsy demonstrated squamous cell carcinoma, and endobronchial ultrasound-guided transbronchial needle aspiration from the

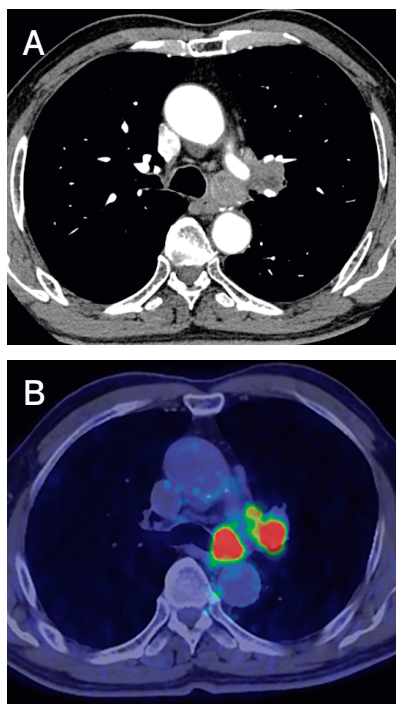


Fig. 1 Image analyses before induction chemoradiotherapy. (A) A CT scan of the chest. (B) A PET-CT scan. A lung tumor invading the pulmonary artery with a swollen left lower paratracheal lymph node is visible (strong uptake of ^{18}F -fluorodeoxyglucose).

mediastinal lymph node revealed metastasis in the left lower paratracheal lymph node. Based on these findings, we diagnosed this case as T1bN2M0 stage IIIA squamous cell carcinoma.

Considering the patient's age and good performance status (PS1), we decided to perform induction chemoradiotherapy using S-1 as the chemotherapeutic agent, followed by surgery. The induction therapy involved S-1 administration (oral S-1 at 40 mg/m^2 twice daily from days 1 to 14 and 29 to 42) with concurrent radiation (2 Gy/day; total 46 Gy). This regimen was based on our previous phase I study, except that the radiation dose was reduced in the present induction settings [5, 7].

The induction chemoradiotherapy yielded a radiological partial response (Fig. 2). The adverse effects esophagitis (grade 1) and radiation pneumonitis (grade 1) occurred and were treated conservatively. On day 35 after the end of the induction therapy, we performed a left upper lobectomy with sleeve resection of the pulmonary artery containing branches to the

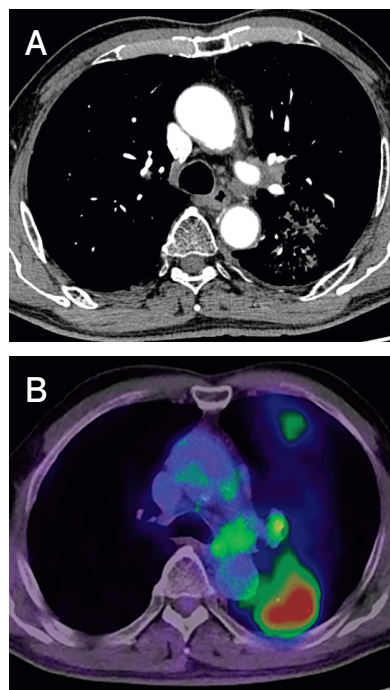


Fig. 2 Image analyses after induction chemoradiotherapy. (A) A CT scan of the chest. (B) A PET-CT scan. The lung tumor and swollen lymph node are remarkably reduced in size (decreased uptake of ^{18}F -fluorodeoxyglucose). Radiation pneumonitis is visible in the left lower lobe.

superior division and systemic lymph node dissection using a median sternotomy with fourth intercostal thoracotomy.

Microscopic examination of the resected specimens showed no residual tumor cells, demonstrating a pathological complete response. The postoperative course was uneventful except for atrial fibrillation, which was treated conservatively. Adjuvant therapy was not performed. The patient has been active daily with a stable PS1 condition and disease-free status for 1 year after surgery.

Discussion

Previous studies had indicated that radiotherapy was considered the standard treatment for elderly patients with locally advanced NSCLC [3, 8]. However, the clinical outcome was not satisfactory, with a median survival time of 13.1 months for patients aged >70 years [8]. In anticipation of the increased population of elderly NSCLC patients with

good PS, curative treatment strategies for elderly patients should be developed. A recent study conducted by the Japan Clinical Oncology Group showed that daily low-dose carboplatin with radiotherapy is superior to radiotherapy alone in patients aged >70 years with locally advanced NSCLC [9].

S-1, an oral anticancer fluoropyrimidine derivative, is considered an active single agent against NSCLC, exhibiting a radiosensitizing effect and few adverse events [5]. Recent phase I and phase II studies conducted by one of the authors (K. K.) showed the feasibility of concurrent chemoradiotherapy with S-1 and thoracic radiation, with an acceptable toxicity and median progression-free survival time (13.1 months at a median follow-up time of 23.7 months) in patients aged >75 years with locally advanced NSCLC [5, 6]. We reduced the radiation dose to 46 Gy in the present induction settings.

From the viewpoint of surgery, one of the desired effects of induction therapy is a reduction in tumor volume to facilitate surgical manipulations. This effect also helps surgeons to determine the appropriate surgical margin. On the other hand, Albain *et al.* reported a high mortality rate of pneumonectomy after chemoradiotherapy and suggested that trimodality treatment could be beneficial if a complete resection with lobectomy can be done after chemoradiotherapy [2]. In our patient's case, the primary tumor invaded the left pulmonary artery, advancing to its first branch. While we successfully performed sleeve resection of the pulmonary artery to avoid pneumonectomy, it is possible that the pneumonectomy would have been unavoidable if an initial surgery had been performed or if the induction chemotherapy had not reduced the tumor size. Even in this situation, the left pneumonectomy should be finally performed after making a maximum effort to avoid a pneumonectomy, in order to reduce critical complications and maintain the patient's activities of daily living after surgery.

The short follow-up period is one of the limitations of this case that should be considered before the usefulness of our strategy can be confirmed from the viewpoint of survival. While further follow-up is necessary, no critical complication has been observed so far, suggesting the feasibility of this modality.

In conclusion, our experience suggests that induction chemoradiotherapy using S-1 with concurrent

radiation followed by surgery can be a therapeutic option for selected elderly patients with locally advanced NSCLC.

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