**Case
Report**

Resection of a Second Primary Lung Cancer in a Lobe Where Small-Cell Lung Cancer was Previously Treated with Chemoradiotherapy: Report of a Case

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There are few reports of resected cases of second primary lung cancer in post-treatment survivors of small-cell lung cancer. Here, we report a surgical case of a 62-year-old female with second primary lung adenocarcinoma after chemoradiotherapy against small-cell lung cancer. She had been treated for small-cell lung cancer 2 years earlier, and achieved complete response after the treatment. A new nodular lesion was detected at a different segment in the right lower lobe. We performed a right lower lobectomy accompanied with systemic mediastinal nodal dissection. Histopathological findings revealed that the new nodular lesion was a second primary lung adenocarcinoma. No metastatic tumor was seen in the dissected lymph node; the initial tumor had disappeared completely. The postoperative course was uneventful, and she was discharged on day 10 after the operation. Ten months after the operation, she was free of recurrent tumor.

Keywords: small-cell lung cancer, second primary lung cancer, lobectomy

Introduction

Although survivors of small-cell lung cancer have increased risk for second primary lung cancers,¹⁾ patients in whom both initial small-cell lung cancer and second primary lung cancer were resected and examined histopathologically are little reported.²⁾ Here, we report a case of a survivor of small-cell lung cancer with second primary lung adenocarcinoma in the same lobe. Both tumors were removed and investigated histopathologically.

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Case Report

A 62-year-old female presented to our hospital with a tumor shadow in the right lung field, shown by chest X-ray (**Fig. 1A**); followed by a mass lesion in the right lower lobe, shown by chest computed tomography scan (**Fig. 1B**); small-cell lung cancer without other histological cancer components, by transbronchial biopsy (**Fig. 1C**); and an accumulation at the primary tumor and a lobar lymph node, by fluorodeoxyglucose-positron emission tomography (FDG-PET; **Fig. 1D**). After limited-disease small-cell lung cancer was diagnosed, she was treated with four chemotherapy cycles of cisplatin plus etoposide, and a total 45 Gy of concurrent radiotherapy, and the tumor shadow disappeared (**Fig. 2A**). Two years after this treatment, a new nodular lesion appeared at a different segment in the right lower lobe, and grew progressively (**Fig. 2B**). FDG-PET revealed an accumulation at only the nodular lesion. All serum tumor marker levels

Fig. 1 (A) Chest X-ray showed a tumor shadow in right lung field. (B) Chest computed tomography (CT) showed a tumor shadow in the right lower lobe. (C) Transbronchial biopsy for an initial tumor revealed small-cell lung cancer without other histological cancer components ($\times 200$). (D) Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed an accumulation at the primary tumor and lobar lymph node.

were within normal range throughout the therapeutic course.

We supposed that the nodular lesion was a recurrence of initial small-cell lung cancer or second primary lung cancer. We diagnosed and treated the new lesion using surgery. A tumor with pleural indentation was found close to the right inferior pulmonary vein in the right lower lobe. Intra-operative aspiration cytology from the nodule revealed lung adenocarcinoma. Because the initial tumor was a small-cell lung cancer without other histological cancer components, the new lesion was diagnosed as a second primary lung cancer. The tumor was completely removed with a right lower lobectomy, as it was located near the right lower pulmonary vein. Lymph node dissection was also performed. Histopathological

findings revealed adenocarcinoma and no metastatic tumor in the dissected lymph node (p-T1aN0M0 stage 1A; **Fig. 3**). The initial tumor had completely disappeared, both macroscopically and histopathologically.

Her postoperative course was good, and she was discharged from the hospital on day 10. Ten months after the operation, she has no signs of recurrent tumor.

Discussion

In the present case, preoperative differential diagnoses were intrapulmonary recurrence, pulmonary ligament lymph node recurrence, and second primary lung cancer. We performed right lower lobectomy to completely remove the tumor, and arrived at a correct diagnosis.

Fig. 2 (A) After treatment for small-cell lung cancer, an initial tumor shadow in the right lower lobe had disappeared. (B) A new nodular lesion appeared at a different area in the right lower lobe, and grew progressively larger.

An increased risk of second primary lung cancers has been reported in survivors of small-cell lung cancer. Johnson, et al., reported that six of 40 patients with small-cell lung cancer, who had been cancer-free for 2 years, had second lung cancers; they reported the distribution of second tumors to be three in the contralateral lung, one in a different lobe in the ipsilateral lung, and two in the same lobe as the initial small-cell lung cancer, respectively.¹⁾ Compared with the general population, the risk of all second cancers among these patients was increased 3.5-fold. Moreover, in survivors of small-cell lung cancer, risk of a second lung cancer increased 7-fold.²⁾ Reportedly, cumulative risk of a second primary lung cancer was 32% after 12 years, and did not appear to reach a plateau.²⁾ Several articles show that continuing to smoke is a risk factor for second primary lung cancer in survivors of small-cell lung cancer.¹⁻³⁾ Only one article discussed the relationship between second primary lung cancers and chemotherapy against initial small-cell

lung cancers,²⁾ suggesting that chemotherapy, particularly alkylating agents, contributes to the second cancer risk. These reports indicate that survivors of small-cell lung cancer are at high risk for second primary lung cancers. Long-term follow-up with careful attention to second primary lung cancer may be necessary for survivors of small-cell lung cancer.

Few reports have been published in which the initial tumor was removed and investigated histopathologically. Inoue, et al., reported a case of second primary lung cancer in the same lobe as initial small-cell lung cancer.⁴⁾ Because the initial small-cell lung cancer was located in the left S¹⁺² area and the second primary adenocarcinoma was located in left S⁴ area, they treated the case with an left upper lobectomy. The site of the initial cancer was scarred and did not contain any neoplastic cells. In the present case, however, the initial tumor disappeared completely, without even fibrous scar tissue. This difference may have been affected by whether the initial

Fig. 3 (A), (B) Histopathological findings of a new nodular lesion revealed adenocarcinoma with mixed subtype (A, $\times 40$; B, $\times 200$). (C), (D) There was normal lung tissue in the area of the initial tumor (C, $\times 40$; D, $\times 200$).

small-cell lung cancer contains other histological components. Tumors of pulmonary adenocarcinoma or squamous cell carcinoma are reportedly likely to contain scar and interstitial tissues. Whereas tumor cells disappeared after chemoradiotherapy, interstitial tissue developed scars and remained.⁵⁾ Accordingly, tumor shadow of pulmonary adenocarcinoma or squamous cell carcinoma remained after chemoradiotherapy. In the present case, the initial lung cancer was diagnosed by transbronchial biopsy as pure small-cell carcinoma. Because collected tissue via transbronchial biopsy was small, complete histological picture might not be investigated. However, the initial tumor tissue might be more likely to contain no scar or interstitial tissue.

Conclusion

We report a case of a survivor of small-cell lung cancer with a second primary lung adenocarcinoma in the same lobe. Both initial and second primary lung cancers were removed and investigated histopathologically. As the initial tumor might contain no scar or interstitial tissue, the initial cancer tissue had apparently completely disappeared after chemoradiotherapy.

Disclosure Statement

Takuma Tsukioka and other co-authors have no conflict of interest.

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