Synchronus Presentation of Early-stage Small Cell Carcinoma and Adenocarcinoma in the Same Lung Lobe

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Abstract

A 73-year-old man with no symptoms was admitted to our hospital with a nodular shadow (>2 cm) in the left upper lung field on chest X-ray. A histological diagnosis (small cell carcinoma) was obtained by bronchoscopic examination including a transbronchial lung biopsy (TBLB). The preoperative clinical staging was T1N0M0 (StageIA). After preoperative chemotherapy (CDDP + CPT-11) was carried out, a nodule in the left S1+2 diminished remarkably, but a smaller nodule in the left S3 (>8 mm) remained unchanged. While the nodule in the left S1+2 (small cell carcinoma) had become completely necrotic by the time the final diagnosis was made after resection of the left upper lobe, histological diagnosis of the nodule in the left S3 revealed a well differentiated adenocarcinoma. Synchronous presentation of early-stage lung cancer consisting of small cell carcinoma and adenocarcinoma was identified in the same left upper division of the lung. Because there have been the few previous reports regarding cases of synchronous presentation of early-stage lung cancer in the same lung lobe, we also report on the clinical characteristics, thus adding this case to the five previously reported cases.

Key words: synchronous, multiple early-stage lung cancer, same lung lobe

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Introduction

Whereas double cancer has commonly been defined as malignant tumors transferred from separate organs, multiple cancer has been defined as malignant tumors of more than two different types appearing in one organ (1). Although the diagnosis of multiple lung cancer has previously been made at the advanced stage, it has recently been diagnosed at the early stage because of advances in radiological diagnosis.

We report a rare case presenting with synchronous early-stage lung cancer consisting of both small cell carcinoma and adenocarcinoma in the same left upper division of the lung.

Case Report

A 73-year-old man was admitted to our hospital with suspected lung cancer because of an abnormal finding in the left lung on a chest X-ray during a periodical health examination on November 26, 2004. He had a past history of hypertension, cerebral infarction and hyperlipidemia. He had no family history of lung cancer and no respiratory symptoms, but had a smoking history (Brickman index: 500). Physical examination revealed no abnormalities. Laboratory data on admission are shown in Table 1. Although there were no abnormal peripheral blood and blood chemistry findings, tumor markers such as carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE) were mildly elevated. Arterial blood gas analysis showed mild hypoxia. A chest X-ray on admission showed a nodular shadow (>2 cm)
in the left upper lung field (Fig. 1). Chest computed tomography (CT) revealed a nodule (2x2 cm) with homogeneous density and a clear margin in the left S_{1+2} (Fig. 2a). In addition, a smaller nodule (<1 cm) was recognized in the left S_{3} (Fig. 2b). There was no hilar or mediastinal lymph node swelling. Bronchoscopic examination showed no abnormal findings within the visible area. The histopathological diagnosis of a specimen taken by transbronchial lung biopsy (TBLB) from the left S_{1+2} was a small cell carcinoma consisting of small atypical cells (Fig. 3). However, there were no significant bronchoscopic findings regarding a smaller nodule in the left S_{3}.

Because there were no obvious metastases to other organs after the diagnosis of small cell lung cancer of the lung by bronchoscopy examination after admission, we diagnosed it as Stage IA (T1N0M0) for preoperative clinical staging and carried out two courses of preoperative chemotherapy [Cisplatin (CDDP) + Irinotecan (CPT-11)]. Although bone marrow suppression was observed as a side effect of the chemotherapy, the nodule of the left S_{1+2} was remarkably diminished on chest CT (Fig. 4). However, the smaller nodule in the left S_{3} was unchanged. Afterwards, a left upper lobectomy was performed on February 18, 2005.

Regarding the macroscopic findings of the resected lung specimen (Fig. 5), the nodule in S_{1+2} of the left upper lobe had become necrotic and was diminished. However, the smaller nodule in the left S_{3} was unchanged (10x8 mm) in size before and after the treatment. Regarding microscopic findings, the nodule in the left S_{1+2} consisted of small atypical cells and the final diagnosis was small cell carcinoma. Most of the tumor cells had become necrotic. The histological effect due to chemotherapy was complete response. The nodule in the left S_{3} was finally diagnosed as a well differentiated adenocarcinoma with a tubular structure of tumor cells, replacement of the alveolar epithelium, or interstitial fibrosis [type E in Noguchi’s classification (2)]. Because there were no lymph node metastases in the histological diagnosis after complete surgical resection, the final diagnosis with regards to postoperative clinical staging was Stage IA (T1N0M0) for both the small cell carcinoma and the adenocarcinoma (Fig. 6).
Figure 2. Chest CT on admission showing a nodule (2×2cm) with a homogeneous density and clear margin in the left S1+2 (a) and a smaller nodule (<1cm) in the left S3 (b) (arrowhead).

Figure 3. Microscopic findings of TBLB specimen showing small atypical cells diagnosed as small cell carcinoma in the left S1+2 (HE staining, ×100).

Figure 4. Chest CT after two courses of preoperative chemotherapy shows a diminished nodule in the left S1+2.

Figure 5. Macroscopic findings of a resected lung specimen show that the nodule in the left S1+2 had become necrotic and it was diminished (a) (arrows), but the smaller nodule in the left S3 was unchanged (b) (arrows).

This patient was transferred to our division after the surgical procedure and two courses of postoperative chemotherapy (CDDP + CPT-11) were performed. He was followed-up as an outpatient without complications.

DISCUSSION

Recently, due to the increasing numbers of lung cancer patients and the advances in radiological diagnostic techniques, multiple cancer has sometimes been detected. Multiple lung cancers have been reported to make up 10% or less
Figure 6. Microscopic findings of a resected lung specimen shows the smaller nodule diagnosed as well differentiated adenocarcinoma with a tubular structure of tumor cells, replacement of alveolar epithelium, and interstitial fibrosis in the left S3 (HE staining, ×100).

Table 2. Synchronous Multiple Early Lung Cancer in the Same Pulmonary Lobe Reported in Japan

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Preoperative diagnosis</th>
<th>Site</th>
<th>Tumor size</th>
<th>Histological type</th>
<th>Surgical procedure</th>
<th>pTNM</th>
<th>Outcome (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>M</td>
<td>Multiple Lung cancer</td>
<td>Lt S1/2</td>
<td>Unknown</td>
<td>Sq (Wall)</td>
<td>Lobectomy (Lt upper lobe)</td>
<td>TINOMO</td>
<td>Alive(4 years)</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>M</td>
<td>Multiple Lung cancer</td>
<td>Lt S1/2</td>
<td>1.6 cm</td>
<td>Ad (Wall)</td>
<td>Lobectomy (Lt upper lobe)</td>
<td>TINOMO</td>
<td>Alive(1 year)</td>
</tr>
<tr>
<td>3</td>
<td>85</td>
<td>F</td>
<td>Multiple Lung cancer</td>
<td>Rt S3</td>
<td>1.5±2.0 cm</td>
<td>Ad (Wall)</td>
<td>Lobectomy (Rt lower lobe)</td>
<td>TINOMO</td>
<td>Alive(3 years)</td>
</tr>
<tr>
<td>4</td>
<td>68</td>
<td>M</td>
<td>Multiple Lung cancer</td>
<td>Lt S1/2</td>
<td>2.2±1.1 cm</td>
<td>Ad (Wall)</td>
<td>Lobectomy (Lt SP)</td>
<td>TINOMO</td>
<td>Alive(10 months)</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>M</td>
<td>Multiple Lung cancer</td>
<td>Rt S1/2</td>
<td>1.7±1.7 cm</td>
<td>Ad (Wall)</td>
<td>Lobectomy (Rt upper lobe)</td>
<td>TINOMO</td>
<td>Unknown</td>
</tr>
<tr>
<td>This case</td>
<td>73</td>
<td>M</td>
<td>Multiple Lung cancer</td>
<td>Lt S3</td>
<td>2.5±2.0 cm</td>
<td>Sm (intermediate)</td>
<td>Lobectomy (Lt upper lobe)</td>
<td>TINOMO</td>
<td>Alive(3 months)</td>
</tr>
</tbody>
</table>

L: Left, R: Right, Sq: Squamous cell carcinoma, Ad: Adenocarcinoma, Sm: Small cell carcinoma
M: Male, F: Female, S: segment, B.I.: Brockman index

of total lung cancers (3-5). Among them, those of the bilateral type comprise 60-70% (3-5). The unilateral type has been comparatively rare. In our investigation of previously reported cases in Japan, we found only five cases which showed the synchronous early lung cancers in the same lung lobe (6-9) (Table 2). The clinical characteristics of those reported cases and our case with two synchronous early lung cancers in the same lung lobe were as follows; the patients were elderly males, a portion of the left upper lobe was involved, the histological diagnosis was well differentiated adenocarcinoma, and the prognosis was good with all cases still alive. Because the tumor size was too small to distinguish between benign and malignant disease, there were few characteristic findings, except for case 1, in which one of the two nodules showed malignant findings, including an irregular margin, spicula, and pleural indentation on radiological findings.

As for the differentiation between multiple early lung cancer and metastatic lung cancer, we were able to make the clinical diagnosis of multiple early lung cancer comparatively easily because the histological types of the two nodules were quite different in this case. Regarding multiple lung cancer, Martini and Melamed (1) indicated that synchronous multiple cancer requires the existence in different portions of an organ and different histological types, or the existence in a different lobe or segment. Its genesis should be recognized to be from carcinoma in situ, with no metastasis in the common lymphatic systems, and no metastasis from other organs. Other authors have also indicated that to be defined as multiple lung cancer, the tumor cells must be present in a different lobe among cases with the same histological diagnosis (10, 11). However, Tanimura et al (12) considered that it was possible to distinguish multiple lung cancer from metastatic lung cancer based on: 1) the connection to bronchial epithelium, 2) the subepithelial spreading and vascular invasion in cases with squamous cell carcinoma, 3) the degree of differentiation and 4) the subtype of tumor cells in cases with adenocarcinoma. Ichinose et al also indicated that further genome analysis should be performed, because there have been reports of study of the DNA flow cytometry of tumor cells (13).

Regarding the combination of histological types of multi-
ple lung cancer, squamous cell carcinoma + adenocarcinoma has been most frequently reported in Japan, followed by squamous cell carcinoma + small cell carcinoma, and squamous cell carcinoma + squamous cell carcinoma. In western countries, in contrast, the occurrence of squamous cell carcinoma + squamous cell carcinoma has been most frequent, followed by squamous cell carcinoma + small cell carcinoma, and squamous cell carcinoma + adenocarcinoma due to smoking or circumstantial factors. The combination of small cell carcinoma + adenocarcinoma, as in the present case, has been very rare. We could not determine whether the nodule in the left S I2 was benign or malignant on admission from the radiological findings because there was no hilar or mediastinal lymphadenopathy. However, after we diagnosed it as a small cell carcinoma of the lung from the specimen obtained by TBLB, preoperative chemotherapy was successfully performed and there was no recurrence after surgical resection. As for the small nodule in the left S I, we could not rule out a benign or malignant tumor and synchronous multiple lung cancer in the preoperative diagnosis because it was small (10x8 mm). We removed the adenocarcinoma in the left S I completely with a left upper lobectomy. Fortunately, we restricted the lobectomy to the left upper division of the lesion because there were no suspected primary lesions in any other organs on radiological findings.

Concerning the treatment of synchronous multiple lung cancer, Martini and Melamed reported that the survival rate five years later was 28% in cases in which the lesion could be surgically removed, while Tanimura et al reported it to be 37.5%. Because the prognosis has commonly been poor in cases with lung metastases, it is important to distinguish multiple lung cancer from lung metastases. Although Ferguson et al reported that the preoperative diagnostic rate of multiple lung cancer was relatively high (48%) in their cases, almost all of them had bilateral lesions. One reason it was difficult to make a correct preoperative diagnosis in this case with two neighboring small nodules was the fact that two adequate tissues could not be obtained at the same time by bronchoscopic examination alone.

An invasive examination, such as a CT-guided lung biopsy or video-assisted thoracoscopic surgery (VATS), was considered necessary in this case since two abnormal nodules were obviously separated in the same lobe on chest CT. The invasive examination led us to conclude that one nodule was a synchronous early-stage small cell carcinoma and the other was adenocarcinoma.

References