Case Report
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Synchronous Triple Primary Lung Cancer: A Rare Case with Radiologic-Pathologic Correlation

동시성 삼중성 원발성 폐암: 증례 보고 및 영상의학적–조직병리학적 비교

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Synchronous multiple primary lung cancer is uncommon. They present at the same time, but are distinct and have different histologic features. Synchronous triple primary lung cancer is rare and only few cases have been reported previously. We described a case of synchronous triple primary lung cancers in an asymptomatic 64-year-old man that showed different radiologic features of lung tumors on chest computed tomography images. Anatomical resection and histological analysis revealed 3 different types of lung carcinoma with radiologic-pathologic correlation.

Index terms
Neoplasms, Multiple Primary
Lung Neoplasms
Carcinoma
Multidetector Computed Tomography

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INTRODUCTION

According to the diagnostic criteria of Martini and Melamed (1), synchronous multiple primary lung cancers are physically distinct, separate, and originate from different carcinomas *in-situ* or show different histologic types without involvement of common lymphatics or extrapulmonary metastases. Multiple synchronous primary lung cancer is rare with a low and variable incidence rate of 1–16% (2). Furthermore, the reported incidence of synchronous triple lung cancers is approximately 0.02% (3). We reported the case of a patient with synchronous triple and histologically different primary lung cancers. Furthermore, we determined the correlation of the radiologic features with pathology.

CASE REPORT

The Institutional Review Board of our hospital approved the study. The requirement for patient informed consent was waived because of the retrospective nature of the study.

A 64-year-old man presented with incidentally detected pulmonary nodules on chest computed tomography (CT) images. He had a history of total thyroidectomy for thyroid cancer, 3 years prior, without recurrence. He was on medication for hypertension and asthma for 10 years. He was a non-smoker and did not have any pulmonary symptoms. Routine laboratory tests were within normal range. There were 3 lesions in both lungs on the CT images. Lesion 1 was a 0.7 cm solid nodule in the right lower lobe (RLL) superior segment (Fig. 1A). Lesion 2 was a 1.4 cm pure ground-glass opacity nodule located in the RLL lateral basal segment (Fig. 2A). Lesion 3 was an irregular-shaped 1.2 cm cavitary nodular lesion located in the left upper lobe (LUL) (Fig. 3A). There were no enlarged lymph nodes in the mediastinum.

At the 9-month follow-up, CT images showed enlargement of lesion 1 to 1.8 cm and the appearance of lobulation and spicule

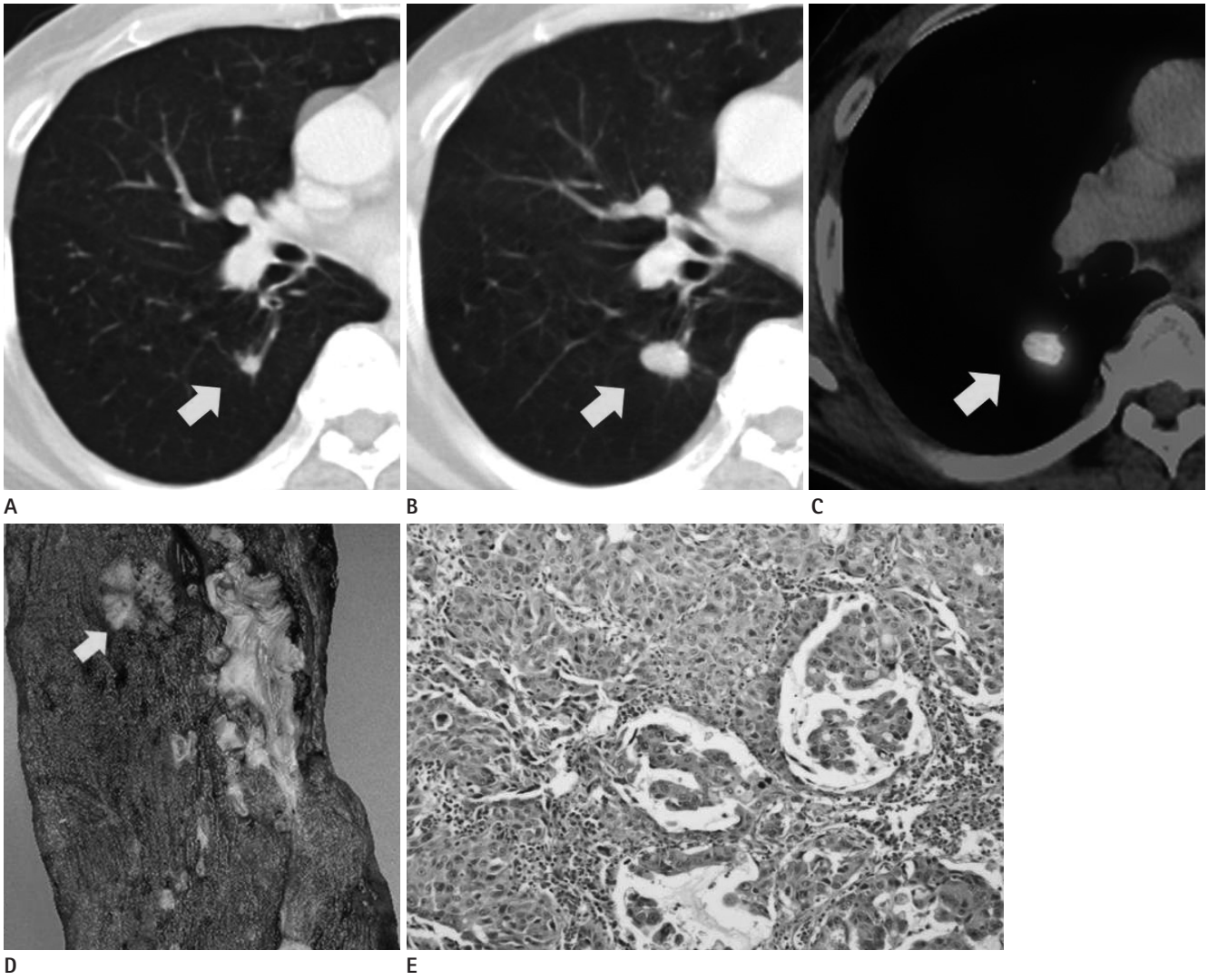

Fig. 1. A rounded solid nodule in the right lower lobe superior segment of the lung (lesion 1).
A. An initial axial computed tomography (CT) scan shows a 0.7 mm solid nodule (arrow).
B. A 9-month follow-up CT image shows an enlargement of the nodule in right lower lobe (RLL) superior segment to 1.8 cm with evidence of lobulation and spicule formation (arrow).
C. A positron emission tomography-CT image shows 18F-fluorodeoxyglucose uptake (standardized uptake value = 7.4) in lesion 1 (arrow).
D. Macroscopic examination of the superior segment of the RLL of the lung reveals a 1.6 cm solid mass (arrow).
E. This lesion was confirmed as adenocarcinoma composed of solid and micropapillary patterns (× 200).

formation (Fig. 1B), whereas lesion 2 remained unchanged (Fig. 2B). The lesion 3 was also increased in size to 1.4 cm (Fig. 3B). Whole-body positron emission tomography-CT showed increased 18F-fluorodeoxyglucose (FDG) uptake in lesions 1 [standardized uptake value (SUV) = 7.4] and 3 (SUV = 3.8), but no FDG uptake in lesion 2 (Figs. 1C, 2C, 3C).

Pathological examination on biopsy specimens retrieved by CT-guided needle aspiration indicated that lesion 1 was non-small cell lung carcinoma. One week after biopsy, lobectomy of the RLL with mediastinal lymph node dissection, and wedge resection of the LUL of the lung were performed by video-assisted thoracic surgery. Macroscopic examination of the RLL of the lung revealed a 1.6 cm solid mass in the superior segment (Fig. 1D) and a 1.0 cm ill-defined lesion with discoloration in the lateral basal segment (Fig. 2D). Histopathologically, lesion 1 was confirmed as adenocarcinoma composed of solid (90%) and micropapillary (10%) patterns (Fig. 1E). Lesion 2 was adenocarcinoma, acinar predominant type (Fig. 2E). A 1.7 cm solid mass extending beyond the resection margin was found on cut sections of the LUL of the lung (Fig. 3D). Microscopic examination

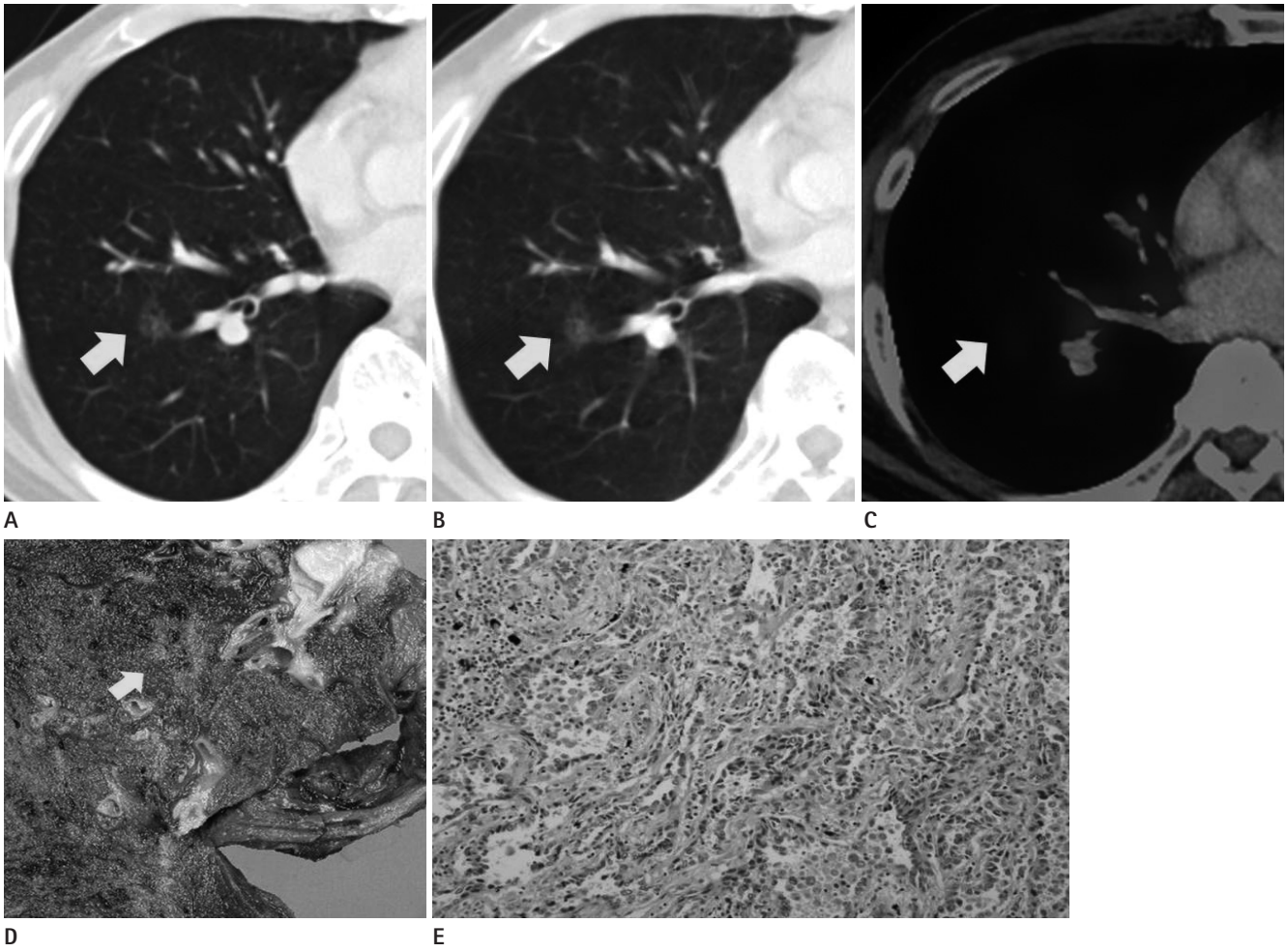

Fig. 2. A ground-glass opacity nodule in the right lower lobe (RLL) lateral basal segment of the lung (lesion 2).
A. On an axial computed tomography (CT) scan, a 1.4 cm subsolid nodule (arrow) is detected at the basal segment of the RLL.
B. There is no change in the lesion size on a 9-month follow-up CT image (arrow).
C. A positron emission tomography-CT image shows that there was no focal 18F-fluorodeoxyglucose uptake by the nodule (arrow).
D. A gross image in the lateral basal segment of the RLL of the lung reveals a 1.0 cm ill-defined nodule with discoloration (arrow).
E. Lesion 2 was confirmed as adenocarcinoma, acinar predominant type (× 200).

showed moderately differentiated squamous cell carcinoma (SCC) with visceral pleural involvement (Fig. 3E). Angiolymphatic invasion or lymph node metastasis was not detected.

There was no evidence of local recurrence on follow-up chest CT at 6 months post-chemotherapy.

DISCUSSION

The occurrence of synchronous triple primary lung cancers is very low and only a few cases have been reported previously (4, 5). When detected simultaneously, only histologically different tumors are classified as multiple synchronous primary lung cancers; and in the case of the same histology, they should be considered as synchronous primary tumors based on features such as associated carcinoma *in-situ* or no evidence of lymphatic involvement or extrapulmonary metastases (1). During pre-operative staging, the importance of differentiating between multiple metastatic lesions and synchronous tumors is essential for tumor staging and appropriate treatment planning, but there is a lack of universal guidelines for diagnosing multiple synchronous lung cancers based on histopathological characteristics (5, 6). However, the distinct radiologic features of multiple lung cancers could provide clues in the differential diagnosis of multiple synchronous versus metastatic lung cancers.

We reported the case of 3 synchronous tumors of the lung with different histology and radiologic features.

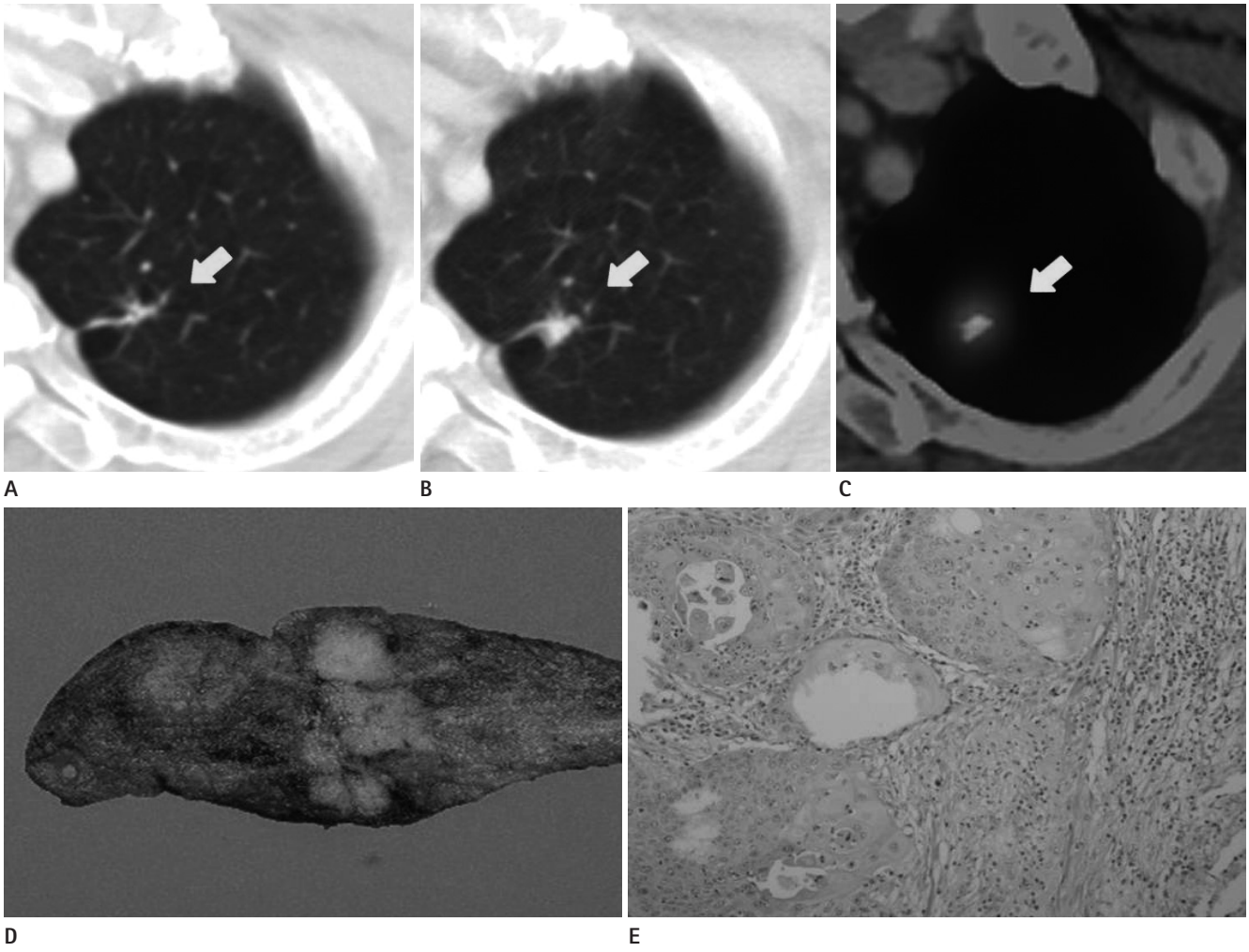

Fig. 3. A cavitary nodular lesion in the left upper lobe (LUL) of the lung (lesion 3).
A. A 1.2 cm irregular-shaped cavitary nodular lesion without calcification (arrow) is located in LUL on an axial computed tomography (CT) image.
B. CT images taken at a 9-month follow-up indicate that lesion size is increased to 1.4 cm (arrow).
C. A positron emission tomography-CT image shows focal 18F-fluorodeoxyglucose uptake (standardized uptake value = 3.8) in this lesion (arrow).
D. On gross findings, a solid mass in the wedge resection specimen of the LUL of the lung extends to the resection margin.
E. This lesion was confirmed as moderately differentiated squamous cell carcinoma (× 200).

The lesion 1 was confirmed as a solid, predominant-type of adenocarcinoma. It appeared as a round solid nodule with a tumor doubling time of 203 days concomitant with lobulation and spicule formation, which are characteristic imaging findings of adenocarcinoma due to its desmoplastic reaction (7).

The lesion 2 was a persistent part-solid ground-glass nodule with a solid component in the central area, confirmed as acinar component predominant adenocarcinoma. On CT findings, part-solid nodular ground glass opacity suggests a malignancy rate of 64% including adenocarcinoma *in-situ*, minimally invasive adenocarcinoma or invasive adenocarcinoma (8).

The lesion 3 contained a cavity and had an irregular margin without calcification, compatible with SCC. The cavitary nodule with an irregular or lobulated border is one of the radiologic abnormalities of SCC (9). In SCC, approximately 10% show cavitation on CT because of central necrosis.

According to the Martini-Melamed criteria, these tumors are triple primary lung cancers owing to different morphologic patterns between lesions 1 and 2 (solid predominant vs. acinar predominant) and a different histologic subtype of SCC for lesion 3. There are some attempts to make up for the limitations in diagnosis of multiple synchronous lung cancers according to the criteria of Martini and Melamed (4). However, only a few reports deal with the imaging findings of each lesion in synchro-

nous triple lung cancers (5). In our patient, the different microscopic findings for each of the synchronous triple primary lung cancers could be explained by their distinct radiologic characteristics, which correlated to the histologic subtypes reported in other studies (7-9). In addition to histopathologic criteria, distinguishing the different radiologic features of each lesion in synchronous primary lung cancer may be beneficial for diagnosis of the cancer.

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동시성 삼중성 원발성 폐암: 증례 보고 및 영상의학적–조직병리학적 비교

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동시성 다발성 원발성 폐암은 조직학적으로 서로 다른 두 개 이상의 원발성 폐암이 발생부위를 달리하여 동시적으로 발생하는 흔치 않은 질환이다. 동시성 삼중성 원발성 폐암은 매우 드물며, 이에 대한 보고는 많지 않다. 이에 64세 무증상 남자 환자에서 발생한 동시성 삼중성 원발성 폐암을 보고하고자 한다. 흉부 전산화단층촬영상, 세 개의 병소는 서로 다른 영상소견을 보였다. 수술적 절제 후 동시성 삼중성 원발성 폐암으로 진단되었으며, 세 병소 각각은 영상의학적-병리학적 연관성을 보였다.

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