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Synchronous Triple Primary Lung Cancers: A Case Report

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Synchronous primary lung cancers are relatively rare. The accurate diagnosis remains challenging, despite of the routine use of bronchoscopy and computed tomography (CT) of the chest. Herein we report a case of synchronous triple primary cancers of the right lung in a 72-year-old male patient in whom each tumor presented distinct CT imaging findings.

Index terms: *Neoplasms, multiple primary; Lung; Multidetector computed tomography*

INTRODUCTION

Synchronous multiple primary lung cancers are rare (1), but when they occur, it is important to distinguish metastatic deposits from independent tumors. Although the diagnostic criteria of synchronous multiple primary lung cancer and radiologic features of each primary lung cancer are well known (2-5), not all patients can be stratified in accordance to these criteria. Imaging findings frequently overlap and are difficult to differentiate. Herein we report a rare case of three synchronous, independent, histologically variant primary cancers of the right lung in a 72-year-old male patient, in whom each tumor presented distinct computed tomography (CT) imaging findings. So, preoperative multifocal biopsies were unnecessary. This report was approved by the Institutional Review Board (IRB file No. 2014-03-169), and the need for a written informed consent was waived.

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CASE REPORT

A 72-year-old man visited our institution due to abnormal chest radiograph and CT findings on routine health checkup at another hospital. He was an ex-smoker with a more than 45-pack-year smoking history and had quit smoking for 13 years. Laboratory findings including peripheral blood and urine analysis were within normal limits. The results of the pulmonary function test were within the normal range.

Posteroanterior and lateral chest radiographs revealed a 4.0-cm peripheral opacity in the right lower lobe (Fig. 1A, B). The chest CT demonstrated three malignant morphologic tumors with different radiologic features. Two masses presented in the right lower lobe: a 4.2-cm-sized, well-defined, solid mass with cavitation at the anterior-basal segment (tumor 1) (Fig. 1C) and a 3.8-cm-sized low-attenuating consolidative lesion at the posterior basal segment (tumor 2) (Fig. 1E). At the posterior segment of the right upper lobe presented a 2.5-cm-sized, lobulated, part-solid nodule (tumor 3) (Fig. 1G). Compared with the previous CT taken at another hospital two months ago, the three lesions had not changed in size or shape. Based on CT imaging findings, the tumors were interpreted as a squamous cell carcinoma (tumor 1), invasive mucinous

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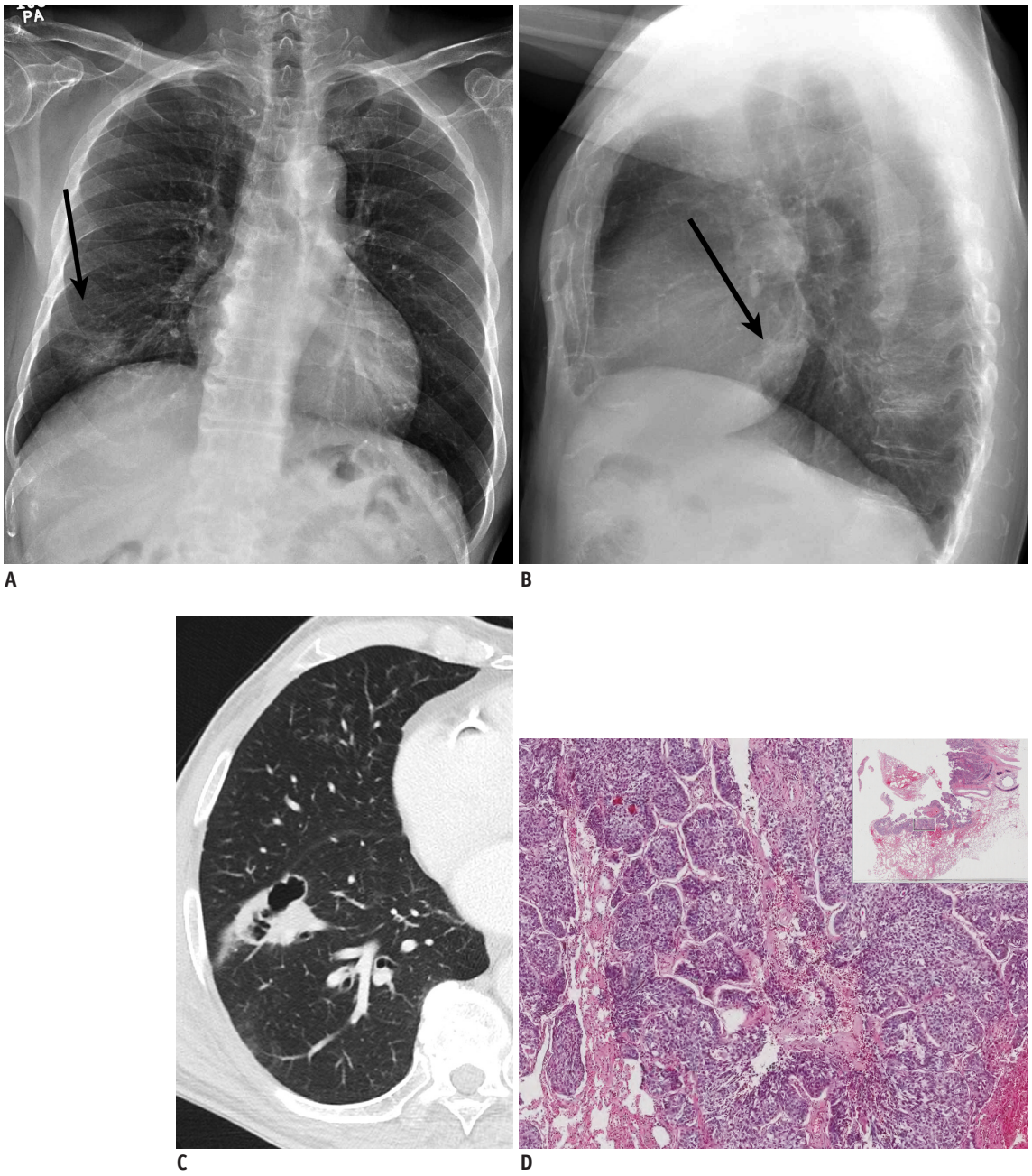

Fig. 1. 72-year-old man with synchronous triple primary lung cancers.
A, B. Posteroanterior **(A)** and lateral **(B)** chest radiographs reveal 4.0-cm ill-defined mass in right lower lobe (arrows). Lung window images (window level, -500 Hounsfield unit [HU]; window width, 1500 HU) of CT scan (2.5-mm slice thickness) of thorax and corresponding microscopic features at low magnification (hematoxylin and eosin stain, x 5 [x 1 in inset]). **C.** Anterior basal segment of right lower lobe is showing 4.2 cm irregular cavitary lesion. **D.** This lesion was confirmed to be squamous cell carcinoma with moderate differentiation exhibiting nests of polygonal cells with pink cytoplasm and distinct cell borders.

adenocarcinoma (tumor 2), and an invasive nonmucinous adenocarcinoma (tumor 3). There was no significant enlargement of lymph nodes in the mediastinum or hilar areas and no other abnormalities in both lungs. The positron emission tomography (PET)/CT revealed a mild to high ^{18}F-fluorodeoxyglucose uptake in the masses (maximum standardized uptake value [SUVmax] of 4.4, 1.7, and 0.7 for tumor 1, 2, and 3, respectively) in the right lung. Combined results obtained from abdominal ultrasonography, brain magnetic resonance imaging, radionuclide bone scanning and PET/CT scanning revealed no metastatic lesions.

A video-assisted thoracoscopic right lower lobectomy, mediastinal lymph node dissection and a wedge resection of the right upper lobe were performed without a preoperative

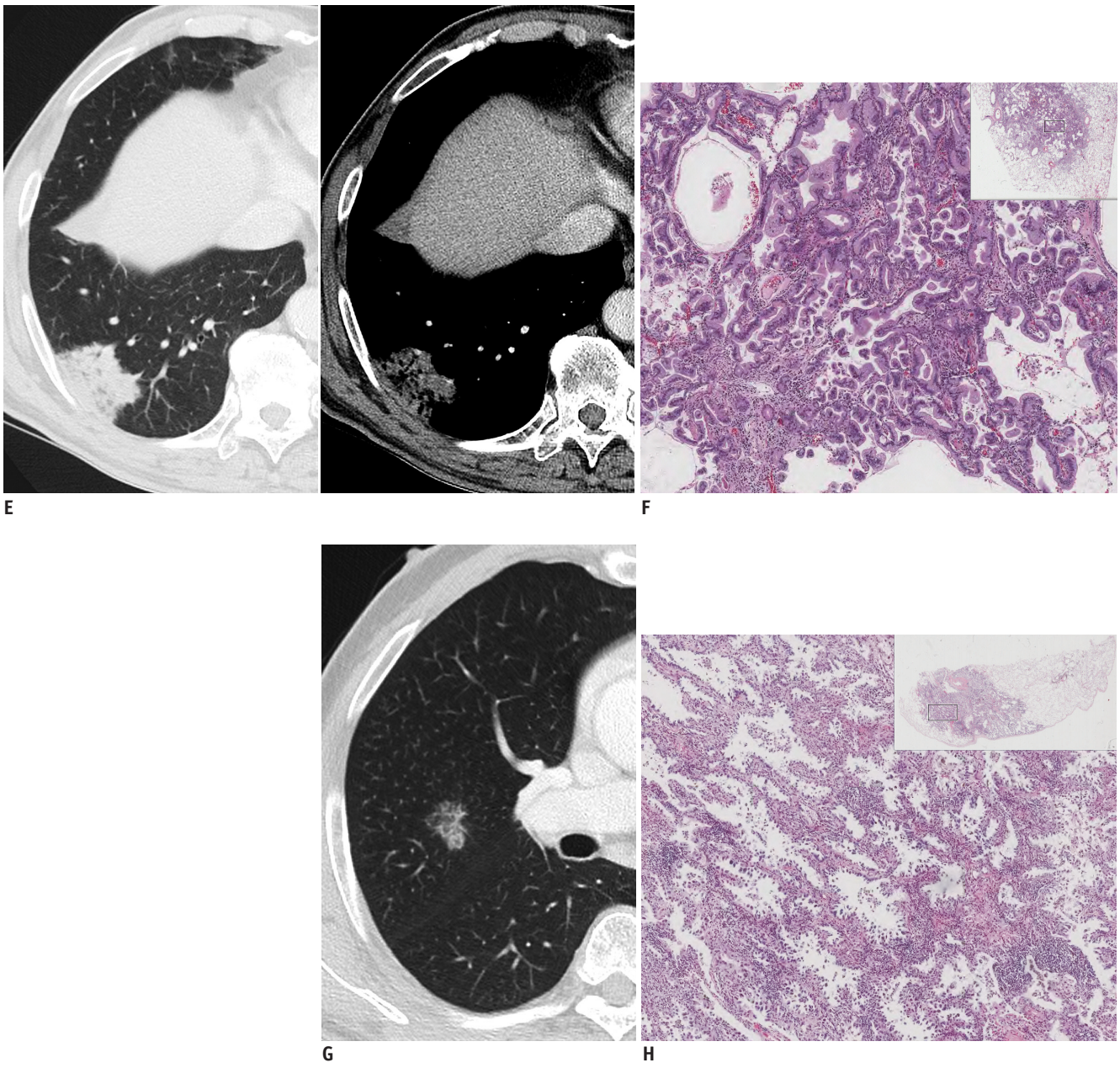

Fig. 1. 72-year-old man with synchronous triple primary lung cancers.
E. 3.8-cm parenchymal low-attenuating consolidative lesion is at posterior-basal segment of right lower lobe. **F.** This lesion was confirmed to be invasive mucinous adenocarcinoma composed of glands lined by tall columnar mucin-containing cells. **G.** 2.5-cm well-defined part-solid nodular lesion is at posterior segment of right upper lobe. **H.** It revealed adenocarcinoma with moderate differentiation and acinar pattern showing acini of polyhedral cells.

percutaneous needle biopsy for diagnosis. On the pathologic examination, two lesions were found in the right lower lobe; tumor 1 at the anterior basal segment measured 2.4 x 2.0 cm in size and was confirmed to be a squamous cell carcinoma with moderate differentiation (Fig. 1D) and tumor 2 at the posterior basal segment was 5.1 x 4.9 cm in size and was confirmed to be an invasive mucinous adenocarcinoma (Fig. 1F). Tumor 3 at the posterior segment of the right upper lobe measured 1.5 x 1.0 cm in size and was confirmed to be an invasive adenocarcinoma with a moderate differentiation and an acinar pattern (Fig. 1H). Regional lymph nodes were examined and two metastatic lymph nodes were found in the right upper paratracheal and subcarinal area involving a squamous cell carcinoma. Thus, the final TNM stage was set as pT2bN2M0. A genetic mutation analysis was performed for the largest invasive

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mucinous adenocarcinoma and it was found to be a wild type of epidermal growth factor receptor/K-ras and anaplastic lymphoma kinase. After the surgery, the adjuvant chemotherapy was planned and the patient was discharged.

DISCUSSION

Multiple primary lung cancers are divided into simultaneous (synchronous) and sequential (metachronous) tumors. Synchronous tumors are significantly rarer than metachronous tumors (1). The incidence of synchronous multiple primary lung cancer has been variably reported to range from 0.26% to 1.33% (6-8). Ferguson (9) summarized the overall incidence of histologically categorized, synchronous double primary lung cancers; over 51.3% of individual patients had identical histologic subtypes and the remaining 48.7% had different histologic subtypes. A squamous cell carcinoma is the most common cancer, comprising over 70% of synchronous cancers with identical histologic subtypes and nearly 85% of patients with tumors of different histologic subtypes. An adenocarcinoma was present in a relatively smaller percentage of patients with synchronous primary lung cancer. Nevertheless, it is not easy to evaluate the exact incidence due to the difficulties in distinguishing a synchronous multiple primary lung cancer from a single pulmonary neoplasm with intrapulmonary metastases or pulmonary metastases originating from primary cancers in different organs. However, in order to plan the appropriate treatment based on the stage it is clinically relevant during the initial workup and imaging study to assess if the second tumor is a synchronous tumor or a metastasis (10).

Generally accepted diagnostic criteria include the demonstration of synchronous masses with different histology and the proof that tumors arise from separate and distinct endobronchial foci, if histologically similar (9). The Martini and Melamed (11) criteria are based on tumor characteristics (inclusive of, but not limited to, morphology, location, presence or absence of carcinoma *in situ*, vascular invasion and metastasis), but lack the power to differentiate between metastasis and a second primary lung cancer (12). Malignant characteristics of CT imaging of primary lung cancer in various lesions may provide valuable clues for the preoperative distinction of synchronous primary tumors from primary lung tumors with intrapulmonary metastases or other metastases at the initial workup. Not all patients can be stratified in accordance with the above diagnostic criteria of synchronous multiple primary lung cancers (11). Thus, separate biopsies need to be performed for different pulmonary masses.

We reported a patient with three synchronous, independent and histologically variant lung cancers. All three tumors had different and distinct CT imaging features and all lesions displayed the malignant characteristics of a primary lung cancer. On CT, the solid nodule/mass with irregular cavitation was diagnosed as a squamous cell carcinoma, the most common histological type of lung cancer to cavitate (82% of cavitary primary lung cancer) (3, 5). An unchanged parenchymal consolidative lesion with low attenuation was diagnosed as an invasive mucinous adenocarcinoma (4) whereas a well-defined, part-solid nodule appearing as mixed areas of ground-glass opacity and solid attenuation was likely to be a nonmucinous adenocarcinoma (2). A subsequent percutaneous needle biopsy to exclude the possibility of metastasis was not necessary due to the confirmed differences in radiologic features.

Even though there are many case reports regarding synchronous multiple primary lung cancers in the literature, very few cases of triple tumors with different histologies have been investigated yet (6, 13-15). Moreover, no previously reported synchronous lung cancers have been investigated in terms of radiologic findings. To our knowledge, this is the first report on three synchronous primary lung cancers with radiologic-histopathologic correlation.

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