

## Three Synchronous Primary Lung Cancers in a Single Lobe

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### Abstract

As a result of improved cancer detection and greater life expectancy, diagnoses of synchronous primary lung cancers are becoming more common. We present a unique example of three distinctly different histologic tumors in one lobe. A 63 year-old female with suspicious lung nodules opted for short term CT-scan follow-up for two separate right upper lobe (RUL) nodules. In the two months interval a new subcentimeter RUL nodule developed. All three nodules were hypermetabolic on PET-CT. After wedge resection, that revealed a large cell neuroendocrine carcinoma, a formal right upper lobectomy was performed. Pathology revealed: a Sarcomatoid carcinoma, an adenocarcinoma with intracellular mucine, and a large cell neuroendocrine carcinoma.

Interestingly, the third tumor was discovered during post-surgical tumor board discussion requesting a re-examination of the lobectomy specimen, emphasizing the importance of multidisciplinary review. This case might indicate that such synchronicities may occur at a greater rate than currently estimated.

**Keywords:** Synchronous primary lung cancer; Multidisciplinary approach; Tumor board; Lung cancer

### Introduction

As a result of improved cancer detection and greater life expectancy, diagnoses of synchronous primary lung cancers (SPLCs) are becoming more common [1,2], incidence estimates range from 0.2% to 20% of non-small cell lung cancers [3-5]. Multiple primary malignancies, with different histologies or similar histologies but clearly distinct histologic features [6], likely call for different treatments than single primary malignancies or multiple tumors from a single origin. However, there is no general consensus on how best to treat these cancers, driving the accumulation of many case studies and retroactive statistical analyses on the topic.

The objective of this case study is to present a unique example of SPLCs in which three distinctly different histologic tumors were detected in one lobe, is currently undocumented in the literature.

### Case Report

A 63-year-old African American female presented to thoracic surgery for workup of suspicious lesions in the right upper lobe (RUL). She was well known to the medicine service from multiple COPD exacerbation admissions and severe emphysema. Past medical history was significant for asthma, diabetes, GERD, and hypertension. She smoked ¼ PPD for 30 years (quitting at age 59). She had a family history of cancer.

During an admission for COPD exacerbation, a chest X-ray demonstrated a suspicious nodule in the right lung. Multiple axial CT-scan images were obtained, revealing a spiculated soft tissue density nodule in the periphery of the RUL (Figure 1A) as well as a second posterior pleural-based lesion (Figure 1B).

The patient opted for a short interval follow-up rather than right out surgery. Repeat CT demonstrated in only two months an interval enlargement of the two separate RUL nodules (Figures 1D and 1E) along with interval development of a new subcentimeter RUL nodule (Figure 1F). PET-CT revealed all three nodules to be hypermetabolic.

A video-assisted thoracoscopic surgery (VATS) wedge resection of the dominant anterolateral nodule was performed and returned on frozen section as large cell neuroendocrine carcinoma. Formal VATS

right upper lobectomy with mediastinal lymph node dissection was subsequently performed.

Pathology identified two primary synchronous cancers, but during review of the case at the post-surgical multidisciplinary tumor board the radiologist suggested re-examination of the pathologic specimen to investigate a subcentimeter nodule observed on the repeat CT (Comparing Figures 1C and 1F). Pathology returned to the specimen and was able to locate the additional tumor. Final pathology revealed the following three primary tumors: a large cell neuroendocrine carcinoma (pT2aN1M0, stage IIA, Figure 2A-B), a sarcomatoid carcinoma (pT1bN0M0, stage IA, Figure 2C-D), and a moderately differentiated adenocarcinoma with intracellular mucine (pT1aN0M0, stage IA, Figures 2E and 2F).

Due to her relatively young age, tumor staging, and N1 status (only intralobar disease), adjuvant chemotherapy was recommended to begin 4 weeks following surgery, with an emphasis on treating the more aggressive neuroendocrine tumor. She started chemotherapy with carboplatin/etoposide, to undergo treatment for a total of 4 cycles. She has tolerated the chemotherapy well to this point.

### Discussion

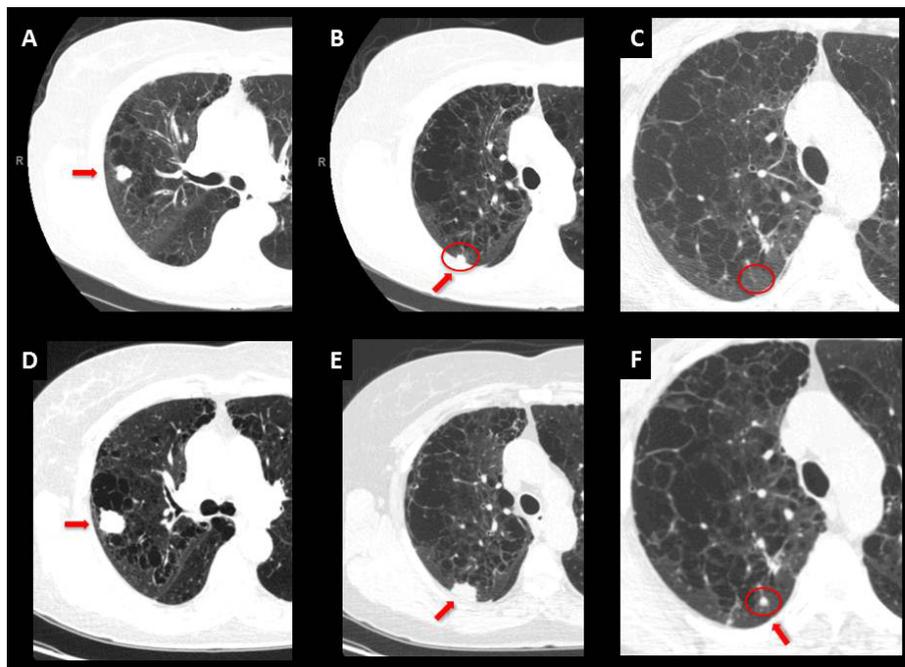
It is imperative to distinguish between synchronous primary lung cancers and pulmonary metastasis as the prognoses and treatments are different. Multiple primary lung cancers may be synchronous (initial cancer diagnoses occurring within six months of one another) or metachronous (occurring more than six months apart) [7,8], with synchronous tumors reported to be rarer than metachronous tumors [9]. The incidence of synchronous lung carcinomas has been reported

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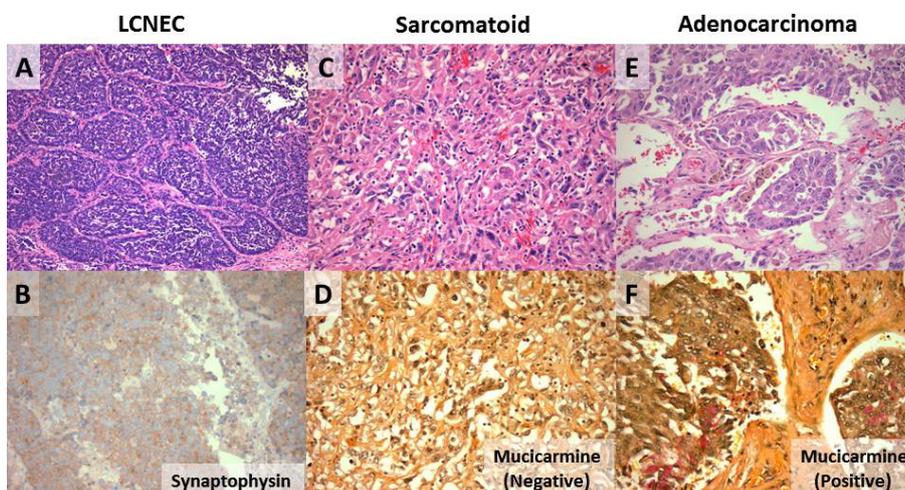
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**Figure 1:** Multiple chest CT-scans. (A): showing an anterolateral RUL 1.3 cm × 1.1 cm × 1.9 cm spiculated soft tissue density, that increased within 2 months to 2.4 cm × 2.3 cm × 2.1 cm. (B): Posterior segment RUL pleural-based lesion 0.8 × 0.5 cm × 1.2 cm, which increased within 2 months to 2.3 cm × 1.3 cm × 1.8 cm. (C): Histologically an adenocarcinoma with typical intra cellular mucine. (D): Histologically a large cell neuroendocrine carcinoma. (E): Histologically a sarcomatoid tumor. (F): New RUL nodule within the posterior segment measures 0.6 cm × 0.5 cm, which was not present 2 month prior.



**Figure 2:** A: LCNEC (large cell neuroendocrine carcinoma): islands of large, uniform cells with round/oval nuclei and scant cytoplasm (H&E, 100X). B: Synaptophysin stain: neuroendocrine marker, brown cytoplasmic stain (200X). C: Sarcomatoid tumor: spindle shaped cells (H&E, 200X). D: Mucicarmin stain: negative (a pink cytoplasmic stain to identify adenocarcinoma). E: Adenocarcinoma: Columnar cells forming glands and producing mucin (H&E, 200X). F: Mucicarmin stain: positive pink cytoplasmic stains (200X).

as being between 1% and 16% of lung cancer diagnoses [10,11], while reports of the incidence of metachronous primary lung cancers ranges between 40%-60% [10,12].

Finley et al. [3] reported a large series of surgically treated SPLCs, demonstrating overall survival rates comparable with single lung

cancers of similar stages. Adenocarcinomas accounted for a majority of synchronous primary lung cancers, with estimates ranging from 75-80% [3,7]. In fact, it seems that a majority of SPLC occurrences include only adenocarcinomas. In general, less than 20% of SPLC incidences exhibit distinct histologies [3,7]. Recently a case of synchronous triple

primary lung cancers in a 72-year-old male was described, who found to have two invasive adenocarcinomas and one squamous carcinoma, but even in this case the tumors were located in different pulmonary lobes [8].

It was therefore very unusual that our patient presented with a stage IIA large cell neuroendocrine carcinoma, a stage IA adenocarcinoma, and a stage IA sarcomatoid carcinoma, all in the right upper lobe.

Interestingly, the third tumor was discovered during post-surgical tumor board discussion, requesting a re-examination of the lobectomy specimen. This emphasizes the importance of multidisciplinary review of cancer cases. Our case might indicate that synchronic primaries may occur at a greater rate than currently estimated.

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