

Pulmonary Metastasis of Combined Hepatocellular and Cholangiocarcinoma: A Unique Radiographic Presentation with Air-space Consolidation Masquerading as Pneumonia and Primary Pulmonary Adenocarcinoma

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Abstract

Lung metastasis showing radiographic findings of air-space consolidation is considered to be rare. This report describes the case of a man with progressive left lower lobe air-space consolidation with a history of hepatocellular carcinoma. The pulmonary lesion was initially suspected to be infection and later clinically diagnosed as primary adenocarcinoma of the lung. Although the patient was treated with systemic chemotherapy, the disease progressed very rapidly. A postmortem examination revealed that the alveolar spaces were filled with neoplastic cells subsequently proven to be metastases of combined hepatocellular and cholangiocarcinoma.

Key words: metastatic lung tumor, liver, air-space consolidation, combined hepatocellular and cholangiocarcinoma

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Introduction

The typical radiographic pattern of metastatic lung tumors includes multiple nodules in both lung fields. In contrast, primary lung cancer often expresses an air-space consolidation pattern. It has been reported that metastasis in the gastrointestinal tract, pancreas, ovaries and/or breast occasionally present with air-space consolidation. However, pulmonary metastasis originating from liver tumors exhibiting this presentation has not been previously reported. Furthermore, pathological findings of alveolar filled neoplastic cells are uncommon in cases of metastatic lung cancer. We herein describe the case of a man with a history of hepatocellular carcinoma (HCC) that presented with radiological findings of progressive air-space consolidation in the lung. The patient was diagnosed with and treated for primary lung adenocarcinoma, and a postmortem examination revealed the lung can-

cer to be metastases derived from combined hepatocellular and cholangiocarcinoma.

Case Report

A 68-year-old man with a history of HCC (cT4N0M0) treated with transcatheter arterial chemoembolization, ethanol injection, right hepatectomy and adjuvant chemotherapy with sorafenib was admitted to our department for an investigation of air-space consolidation in the left lower lobe of the lung and swelling of the mediastinal lymph nodes on chest computed tomography (CT). Small nodules in the left lower lobe were found on CT three months before admission and eight months after right hepatectomy (Fig. 1a). The nodules were accompanied by peribronchovascular consolidation and mediastinal lymph node swelling, suggesting an infection. The laboratory findings on admission were as follows: WBC: 4,900/ μ L, C-reactive protein (CRP): 0.13 mg/

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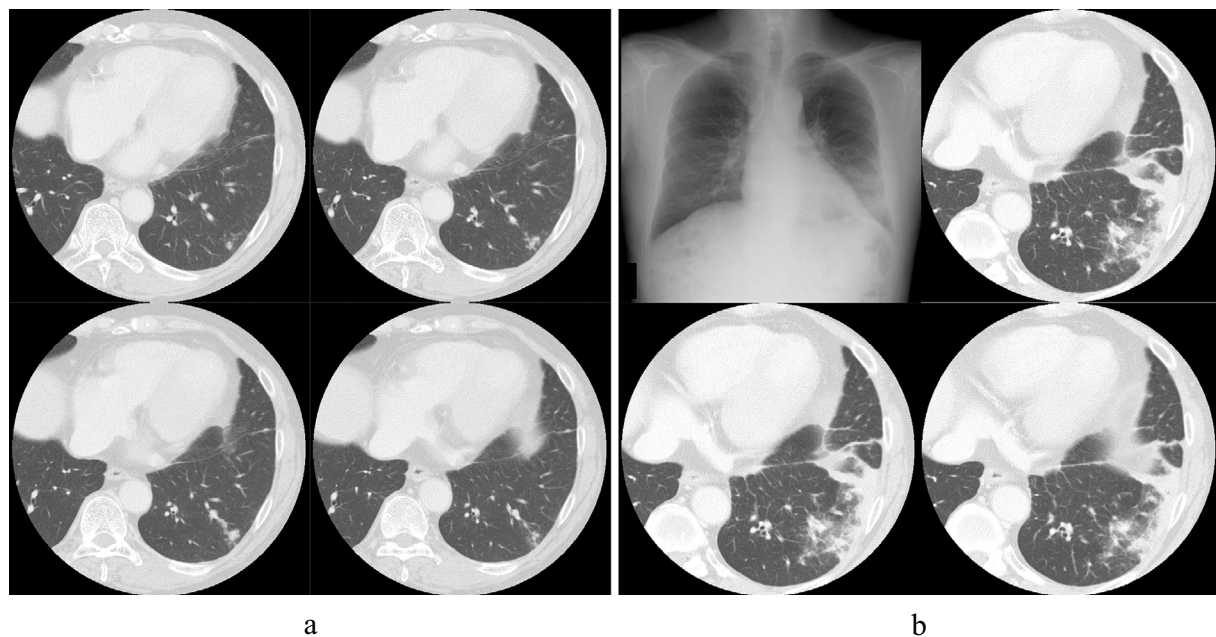


Figure 1. Serial CT findings of the lung tumor: a: A small centrilobular nodule was observed in left S9. b: Three months later, the shadow rapidly became enlarged and multifocal, and confluent air-space consolidation was detected in the left lower lobe.

dL, lactate dehydrogenase (LDH): 373 U/L, alpha-fetoprotein (AFP): 9.1 ng/mL (-ng/mL before treatment for HCC), carcinoembryonic antigen (CEA): 5.1 ng/mL and carbohydrate antigen (CA)19-9: 24 U/mL. The lesions grew rapidly and became multifocal, with confluent air-space consolidation on CT at the time of admission (Fig. 1b). Swelling of the mediastinal and supraclavicular lymph nodes was also noted with left pleural effusion. Sputum, bronchial fluid and pleural effusion cytological examinations revealed adenocarcinoma. Because immunocytochemical staining for thyroid transcription factor-1 (TTF-1) was positive on sputum cytology, the patient was diagnosed with primary lung cancer (cT4N3M1a), and chemotherapy with carboplatin and paclitaxel was initiated. However, the treatment was ineffective, and metastasis to the right adrenal gland developed in addition to tumor progression within the thorax. The patient died of respiratory failure due to progressive disease two months after diagnosis, and an autopsy was performed.

Pneumonia-like tumor spread with no scarring (Fig. 2a) was observed macroscopically in the left lower lobe of the lung, which was thought to be the site of the primary lesion. A microscopic examination showed that the tumor was composed of a tubular adenocarcinoma component that produced mucin and a HCC component exhibiting solid or trabecular growth with focal bile production. Tumor cells filled the alveolar space without destroying the original alveolar structure (Fig. 2b-d), and extensive venous invasion and lymphangitic spread with tumor cells were observed. An immunohistochemical examination revealed that the tumor cells were positive for hepatocytes, cytokeratin (CK)7 and CK19 but negative for TTF-1.

Multiple tumor nodules were observed in the liver. The

morphological characteristics of the tumor cells and results of the immunohistochemical examination were the same as those for the lung tumor cells, and the liver tumor was considered to be composed of combined hepatocellular and cholangiocarcinoma.

The right hepatectomy surgical specimen was reexamined, and typical HCC and atypical HCC components were identified. An immunohistochemical examination revealed that the former was positive for hepatocytes and glypican-3 and negative for CK7 and CK19, while the latter displayed features similar to those of the liver and lung tumors on the postmortem examination.

The final diagnosis after the postmortem examination was combined hepatocellular and cholangiocarcinoma with local recurrence and pulmonary metastases.

Discussion

Typical CT findings of pulmonary metastasis of HCC comprise non-calcified soft tissue nodules or masses (1). In general, air-space consolidation, with a “pneumonic mimicry” pattern of metastasis to the lungs, is atypical. Seo et al. (2) reviewed and described the “air-space pattern” of metastasis with pathological characteristics of lepidic growth of tumor cells along intact alveolar walls. The differential diagnosis of this radiographic pattern includes pneumonia, cryptogenic organizing pneumonia and bronchioloalveolar carcinoma. Frequently reported primary tumor sites consist of the gastrointestinal tract, including the intestines and pancreas, as well as the ovaries and breast (3-5). Rosenblatt et al. (3) and Rossmann et al. (6) reported a series of cases of metastatic “alveolar-cell tumors.” According to their descriptions,

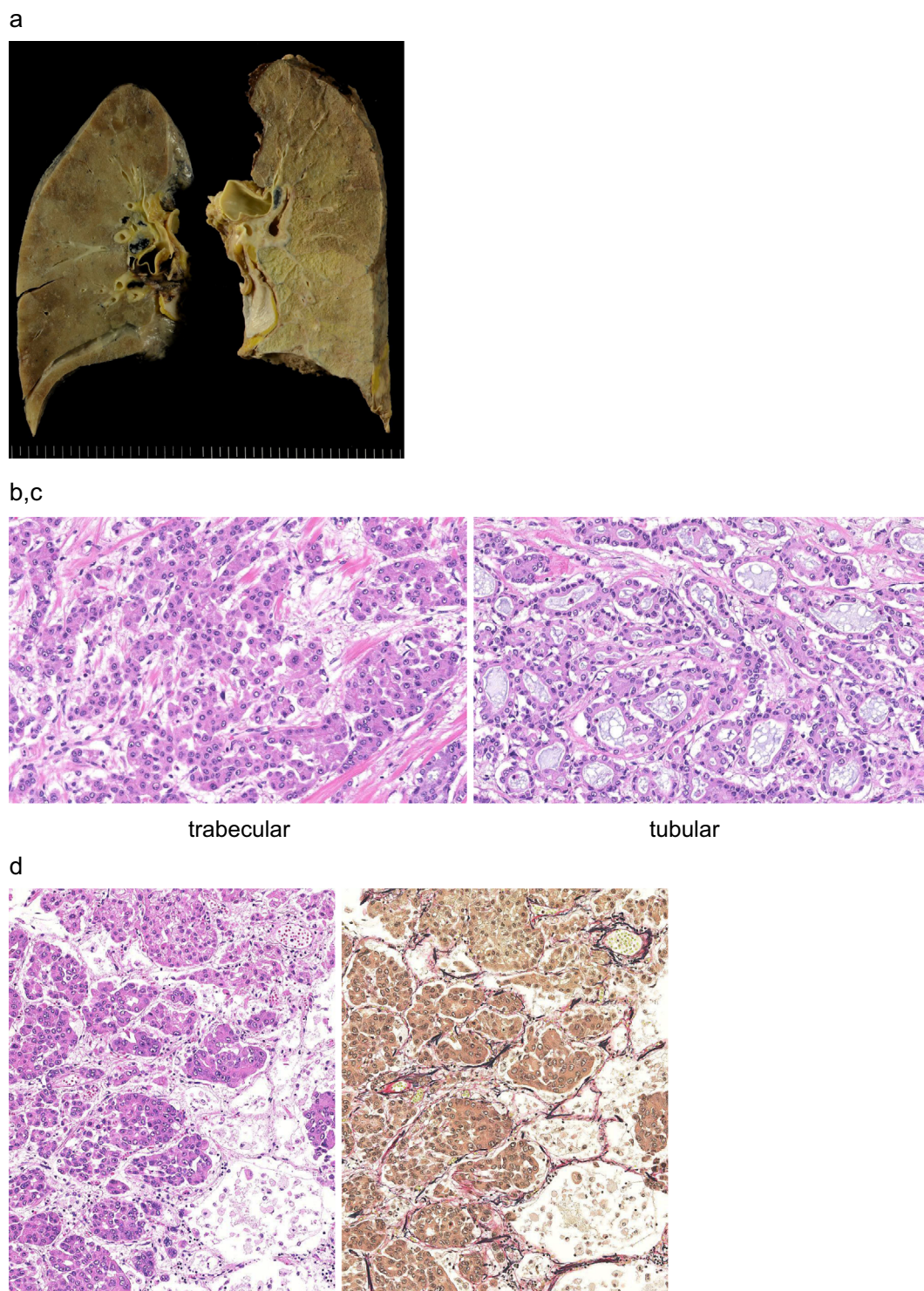


Figure 2. Pathological findings on the postmortem examination: a: The frontal cut surface of the bilateral lungs showed the tumor proliferating along the bronchial walls with a pneumonia-like appearance in the left lower lobe (red circle), measuring 7.0×5.0×5.0cm in size. b, c: Trabecular growth (indicating HCC components) and tubular growth (adenocarcinoma components) patterns of tumor cells were noted in the left lower lobe. (Hematoxylin and Eosin staining). d: Photomicrograph (original magnification ×400, Elastica van Gieson stain) showing alveolar filling with tumor cells without destruction of the alveolar structure.

the histopathological findings vary for the lining of the alveolar wall, ranging from a single layer of malignant cells to total filling of the alveolar space with tumor cells and invasion of lymphatic vessels. Namely, the metastatic pattern

of alveolar filling is thought to reflect the progressive phase of lepidic growth, and lymphatic tumor invasion may precede the spillover of tumor cells into the alveolar space with filling of the alveoli. In the current case, the metastatic

spread was distinctive in that extensive alveolar filling with tumor cells was observed without an apparent lepidic growth pattern. The detection of extensive alveolar filling with tumor cells noted in this case may explain the findings of air-space consolidation observed on the CT images. This is the first reported case of an alveolar-filling type of metastatic lung tumor derived from primary liver cancer that included HCC and cholangiocarcinoma.

Combined hepatocellular and cholangiocarcinoma is rare, accounting for <1% of all liver cancers (7). The prognosis is poor compared with that of HCC but similar to that of cholangiocarcinoma (8). The lungs are a relatively frequent organ for metastasis of this type of tumor, based on a Japanese survey (9), although its pathological and radiological findings have not been well described. In the present case, it was difficult to obtain a pathological diagnosis of a hepatic tumor in the surgical specimen because scant viable tumor tissue was available after transcatheter arterial chemoembolization and ethanol injection, and almost all of the remaining viable tumor was composed of HCC.

The clinical diagnosis in this case prior to the postmortem examination was primary adenocarcinoma of the lung. The reasons for this clinical diagnosis are as follows. First, the cytological sputum examination revealed adenocarcinoma, consistent with the results for the bronchial fluid and pleural effusion, and immunocytochemical staining of the sputum disclosed TTF-1-positive tumor cells. Second, the course of progression of the tumor, including the metastatic sites, was consistent with a typical case of primary lung cancer. Third, although the patient had been treated for HCC and exhibited an elevated serum alpha-fetoprotein level before undergoing right hepatectomy, we did not observe serum alpha-fetoprotein re-elevation at the time of development of the lung lesions or recurrence of the tumor on postoperative liver CT images. The discrepancy in the TTF-1 immunoreactivity status of the tumor cells between the sputum cytology and postmortem examinations deserves comment. Obtaining a correct morphological assessment may be difficult

when conducting immunocytochemical examinations of the sputum. In the current case, it is possible that the TTF-1-positive cells were normal bronchial epithelial cells.

We were unable to make a correct antemortem diagnosis in this case; however, even if we could, there was no alternative effective treatment, considering that the tumor was aggressive and sorafenib had already been administered as adjuvant chemotherapy.

This case suggests that a histopathological diagnosis should be obtained in order to distinguish primary lung tumors from pulmonary metastasis, particularly in patients with a history of extrapulmonary tumors, even when other findings coincide with those of a primary lung tumor.

The authors state that they have no Conflict of Interest (COI).

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