

# Giant Metastatic Liver Tumor of Unknown Primary Origin: Thoracic Autopsy Solves the Mystery

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## ABSTRACT

A 59-year-old male patient was hospitalized in the Internal Medicine Department for investigation of hepatic metastases from an unknown primary neoplasm. During the hospitalization the patient died from acute myocardial infarction. The autopsy revealed a 8.2 kilograms (kg) liver that was diffusely infiltrated by whitish metastatic masses. No other tumor was detected, apart from a 2.5 centimeters (cm) pulmonary nodule next to the right intermediate bronchus that was histologically compatible with small cell lung cancer (SCLC). Despite the fact that hepatic metastases from SCLCs are common, diffuse metastatic hepatomegaly from a malignant pulmonary nodule are rarely seen. Given that the most common cause of malignancy-related death is lung cancer, early diagnosis and appropriate management of pulmonary nodules is of paramount importance.

## KEYWORDS

pulmonary nodule; lung cancer; liver metastasis

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Received: 26 June 2017

Accepted: 22 January 2018

Published online: 23 April 2018

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Acta Medica (Hradec Králové) 2017; 60(4): 163–166

<https://doi.org/10.14712/18059694.2018.14>

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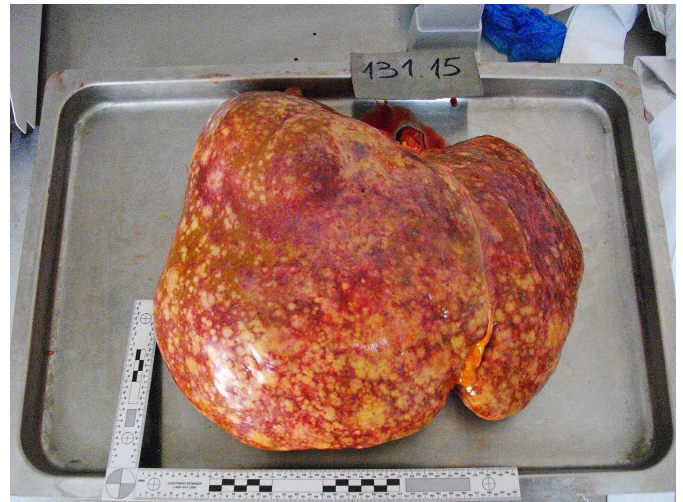
## INTRODUCTION

A pulmonary nodule is a well-circumscribed radiological opacity which diameter does not exceed 3 cm (1). Due to the recent advances in medical imaging, the incidental detection of pulmonary nodules has tremendously increased (2). Malignant nodules account for 1.1% to 12% of these nodules (3) and their early detection is a great challenge for the clinicians. The liver is one of the most frequent site of metastasis from primary malignant solid tumors. Small-cell lung cancer (SCLC) comprises 15% of all lung cancers (4) and is known for its aggressive biological behavior. Liver metastasis is seen in about 50% of patients with extensive-stage SCLC and is a poor prognostic indicator (5). SCLC metastases in the liver grow according to different metastatic patterns, yet the excessive hepatomegaly due to metastatic spread is quite uncommon.

We present an unusual case of a coin-like primary pulmonary lesion and a huge metastatic liver that was necrotomically proven to be a SCLC.

## CASE REPORT

A 59-year-old obese male was admitted to the Internal Medicine department for further investigation of metastatic liver disease of unknown primary origin. The patient had reported a history of coronary artery disease with percutaneous transluminal coronary angioplasty (PTCA) and was an active smoker. Since the patient died a few hours after admission, it was impossible to conduct further investigation and an autopsy was ordered. At autopsy, acute myocardial infarction was determined as the cause of death. Additionally, the macroscopic examination revealed a giant liver (8.2 kg) which parenchyma was almost completely replaced with metastatic tumor (Figure 1, Figure 2). A 25-mm white nodule was identified next to the right intermediate bronchus without peripheral nodules. An enlarged lymph node adjacent to the nodule was identified as well (Figure 3). No other lymph nodes were identified as enlarged or abnormal in the necrotomic examination. The other organs showed no modifications. Microscopic examination of the nodule revealed small round or oval cells. The nuclei were finely granular and hyperchromatic with unrecognizable cytoplasm, as well as absent or inconspicuous nucleoli. In some areas the cells had an elongated shape. There were areas of necrosis and vessel and lymphatic invasion (Figure 4). The same cells were also seen in the metastatic liver masses (Figure 5) and in the examined lymph node. Immunohistochemically, the cells were strongly positive for TTF-1 and CD56, moderately positive for chromogranin, synaptophysin and negative for CD45 and CD99. The proliferation index was 70–80% of the malignant cells (Figure 6). The macroscopic and microscopic features were consistent with SCLC presenting as a solitary pulmonary nodule with metastases in the liver and lymph nodes.



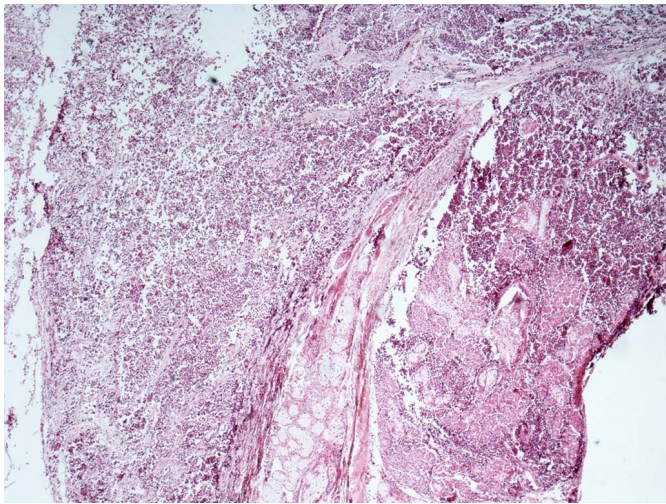
**Fig. 1** Diffuse hepatomegaly with varying sized metastatic nodules.



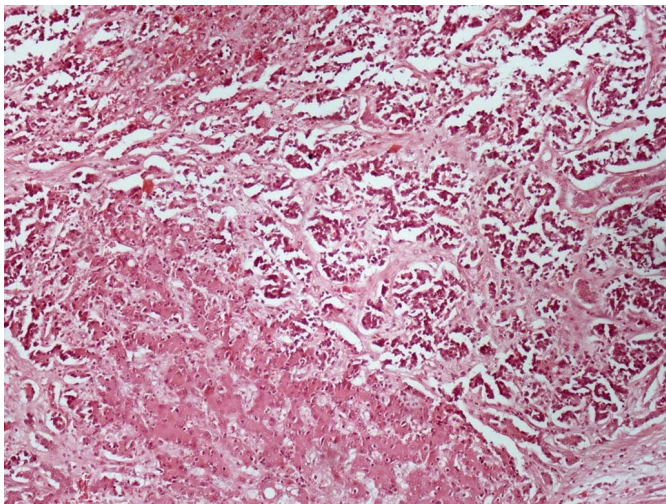
**Fig. 2** The liver contained multiple and variable nodules ranging from 0.5 cm to 3 cm in size.



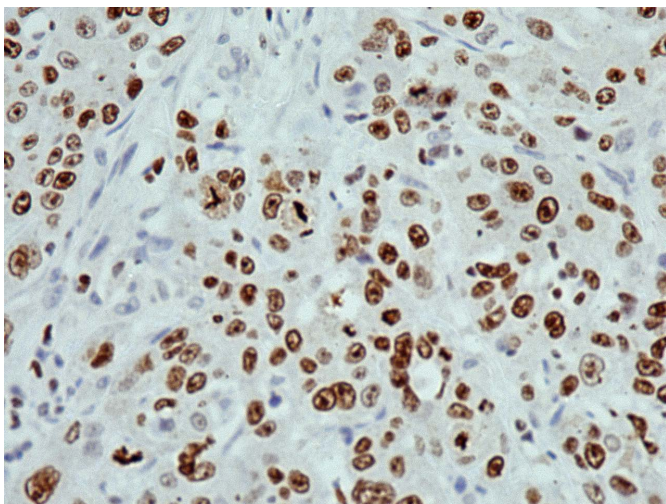
**Fig. 3** Macroscopic appearance of the 25-mm white-tan, soft, friable nodule with little areas of necrosis, was identified next to the right intermediate bronchus.



**Fig. 4** Small cell carcinoma showing cells with darkly staining nuclei and scanty cytoplasm (hematoxylin-eosin stain at 4×).



**Fig. 5** Microscopic findings from the same case demonstrate a diffuse pattern of small cells infiltrating through the hepatic parenchyma (hematoxylin-eosin stain at 4×).



**Fig. 6** TTF-1 positive staining in small cell lung cancer (immunohistochemical stain for thyroid transcription factor-1, 40×).

## DISCUSSION

Lung cancer is one of the most commonly diagnosed malignant tumor and one of the most common causes of cancer-related mortality, including the malignant mesothelioma (6, 7). SCLC accounts for approximately 15% of bronchogenic carcinomas and is strongly related to tobacco use (8). The likelihood of malignancy in solitary pulmonary nodules is generally related to the patient's characteristics – namely sex, age, family history of lung cancer and presence of emphysema – as well as the radiological characteristics of the nodule (9). Metastatic spread of cancer to distant organs is the main reason for the majority of malignancy-related deaths. Having studied 17,431 deceased lung cancer patients, Riihimaki et al. found out that the most usual metastatic sites of SCLC tumors are liver and central nervous system, yet liver and bone metastases signal poor survival, compared with nervous system metastases (10). Furthermore, in a retrospective study by Nakazawa et al. it was shown that liver metastasis was strongly correlated with poorer performance status of the patients (11). Additionally, Bremnes et al. have reported that liver metastasis was an independent prognostic factor in ED-SCLC (12). Hepatic metastases are present in about 50% of patients with extensive-stage SCLC (E-D SCLC) and they can be met either as nodular lesions or as diffuse malignant infiltration of the hepatic sinusoids (5). Excessive hepatomegaly with almost complete parenchymal replacement with metastatic tumor is rarely reported. Biliary tract obstruction due to metastases to lymph nodes in the *porta hepatis* or hepatic parenchyma is well described and regularly met in clinical practice (13) yet fulminant and subfulminant hepatic failure with encephalopathy resulting in hepatic coma is developed in only 7% of the patients (14).

## CONCLUSION

The aggressiveness of SCLC is well documented and, in many cases, metastatic lesions are diagnosed prior to the discovery of the primary tumor. It is therefore of paramount importance for the clinicians to take it into consideration in the investigation of distant metastases of unknown primary origin.

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