CASE REPORT

Diffuse Liver Metastasis of Small Cell Lung Cancer Causing Marked Hepatomegaly and Fulminant Hepatic Failure

Hisamitsu Miyaaki¹, Tatsuki Ichikawa¹, Naota Taura¹, Mio Yamashima¹, Hideyuki Arai², Yoko Obata², Akira Furusu², Hiroko Hayashi³, Shigeru Kohno² and Kazuhiko Nakao¹

Abstract

A 62-year-old female was admitted for examination of an abnormal liver function. Plain CT and MRI of the abdomen showed marked hepatomegaly but no visible nodular lesion in the liver. On the 3rd hospital day she had hepatic encephalopathy and was treated with a course of high-dose steroids, but ultimately died of disease progression on the 7th hospital day. An autopsy revealed a small pulmonary nodule with the histological findings showing small cell carcinoma. There was almost complete parenchymal replacement with metastatic tumor in the liver. Neoplastic involvement of the liver should be considered in the differential diagnosis of fulminant hepatic failure of unknown etiology.

Key words: small cell carcinoma, fulminant hepatic failure, hepatomegaly


Introduction

Fulminant hepatic failure (FHF) is defined as liver disease that causes encephalopathy within 8 weeks of the onset of symptoms in a patient with no prior evidence of liver disease. The most common causes of FHF are viral hepatitis and drug toxicity (1). FHF due to primary and metastatic carcinoma is rare. This generally occurs as a result of diffuse neoplastic infiltration or vascular involvement. The most common cause of FHF secondary to the infiltration of the liver is hematologic malignancies (2-4). Small cell lung cancer manifesting as acute hepatic failure resulting from diffuse parenchymal infiltration by a metastatic tumor is rare. This report presents a patient with FHF due to massive metastatic small cell lung cancer that was unrecognized until autopsy.

Case Report

A 62-year-old female was admitted to the nephrology department because of hyponatremia (Na 117 mEq/L). Though it was improved by mineral corticoid, she showed marked hepatomegaly with spontaneous pain and abnormal liver function. She was transferred to the department of gastroenterology and hepatology for an examination of her liver function. She had a history of aortitis syndrome. She had no history of blood transfusion, hepatitis, or alcohol abuse, but she smoked an average of one pack of cigarettes a day for 40 years. A physical examination revealed jaundice, massive ascites and hepatomegaly. Her consciousness level was clear. Relevant laboratory test results were: hemoglobin 11.1 g/dL; leukocyte count 14,200/mm³; platelet count 70,000/mm³; prothrombin time 54%; serum albumin 2.8 g/dL; total bilirubin 8.1 mg/dL; serum aspartate transaminase (AST) 266 IU/L; serum alanine transferase (ALT) 126 IU/L; alkaline phosphatases 1,672 IU/L; lactate dehydrogenase (LDH) 934 IU/L.
Abdominal ultrasound revealed hepatomegaly without dilated bile ducts or a focal mass. A computed tomography (CT) and magnetic resonance imaging (MRI) without contrast showed hepatomegaly and edema of a periportal lesion (Fig. 1). Contrasted CT and MRI were not performed because her renal function was not good. The patient’s clinical course continued to deteriorate after admission. On the 3rd hospital day she had hepatic encephalopathy and was treated with a course of high-dose steroids but ultimately died of the disease progress on the 7th hospital day. Metastatic liver disease was suspected to be the cause of fulminant hepatic failure, but this could not be confirmed, because imaging modalities did not show any tumor lesion. An autopsy revealed a small pulmonary nodule with histology showing a small cell carcinoma (Fig. 2a, 2b) that was not seen on chest radiographs (Fig. 3) and CT. The liver was enlarged, weighting 3,550 g. The cut surface of the liver showed widely distributed tumor nodules of varying sizes. Only a few hepatocytes could be identified microscopically, and the parenchyma was almost completely replaced with metastatic small cell carcinoma, identified as oat cells (Fig. 4a, 4b). These carcinomas showed marked lymph-vascular invasion. Immunohistochemical staining of these tumor cells was strongly and diffusely positive for CD56 and diffusely positive for TTF-1 and faintly positive for synaptophysin. These

**Figure 1.** a: CT scan of the abdomen at the liver shows marked hepatomegaly. No obvious nodular lesions are depicted in the liver. b: CT at almost the same level taken one year previously shows a normal-sized liver.

**Figure 2.** a: Macroscopically, the resected right upper lung lobe shows a small nodule lesion. b: Microscopically, the specimen shows the cytoplasm to be scant, while the nuclear chromatin is fine.

**Figure 3.** Chest radiograph shows no abnormal shadow in either lung field.
immunohistochemical findings indicated small cell carcinoma.

**Discussion**

The liver is the most common site for metastatic tumor deposits with evidence of hepatic metastases reported in 36% of all patients who died from cancer (4). Despite this, liver dysfunction may not be evident. FHF secondary to a metastatic tumor is rare. In some cases, tumors may replace up to 90% of the liver without any manifestation of jaundice. Only 7.2% of 292 patients with metastatic liver disease developed a coma, and it occurred mostly in patients with breast, gastric cancer, colon cancer, and lymphoma (5). Small cell lung cancer is so highly invasive that hepatic metastasis is common, but a rapid progression to FHF is extremely rare. The cause of the present admission was hyponatremia. Patients with small cell carcinoma, which produces AVP, sometimes also demonstrate hyponatremia. In the present patient, the cause of hyponatremia could have been the presence of the AVP producing tumor, because the plasma AVP concentration increased to 46.3 pg/mL. The incidence as defined by clinical and biochemical findings ranges from 7-16% (6, 7). Four of 40 patients who showed clinically significant hyponatremia were identified from 1 to 4 months before the malignancy was clinically detected (7). Although the presence of hyponatemia as a first sign of small cell carcinoma is not rare, it remains difficult to detect an AVP-producing tumor at an early stage.

Previous reports have explained that FHF in cases of diffuse intrasinusoidal liver metastases is due to destruction of the liver cell by spreading diffuse carcinoma cells, ischemia by vascular occlusion of the portal vein by of the tumor or nonocclusive infarction of liver due to shock from other causes such as sepsis or cardiac dysfunction (8, 9). The tumor cells spread diffusely in the liver of the current patient and only a few hepatocytes could be identified. Moreover, there was significant vascular involvement of the portal vein. A previous report discussed that CT showed hepatomegaly but it was not visible in a case of diffuse metastases of small cell lung cancer (10). US, CT and MRI also showed marked hepatomegaly in that case but did not visualize a nodular liver lesion. These findings are similar to the present case.

The sensitivity of plain CT scan in the detection of liver tumors larger than 2 cm is 92%, but the sensitivity in detection of a liver tumor smaller than 2 cm is only 8%. The sensitivity of MRI in detection of the liver tumor smaller than 2 cm is 33% (11). These patients cannot undergo contrast CT because of poor renal function. The sensitivity of contrast CT for a liver tumor smaller than 2 cm is 20% (11). The hepatic tumor in the current patient had invaded diffusely and each tumor was too small to be visualized.

It can be difficult to differentiate other disease associated with hepatomegaly when marked hepatomegaly is seen on CT and MRI and no hepatic nodular lesion is visualized. Likewise, in most previous cases, appropriate chemotherapy was not performed, and no diagnosis was made before death, because FHF develops secondary to diffuse liver metastasis, grows rapidly and no effective treatment has yet been established, except for chemotherapy (10, 12, 13). In conclusion, diffuse liver metastasis must be considered when imaging modalities show hepatomegaly in patients with fulminant hepatic failure, especially when viral hepatitis and drug reactions are excluded.

**References**


© 2010 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imindex.html