CASE REPORT

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Diffuse Intrasinusoidal Liver Metastasis of Small Cell Lung Cancer Causing Fulminant Hepatic Failure: CT Findings –A Case Report

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A 65-year-old man with small cell lung cancer treated with two courses of chemotherapy manifested appetite loss and abdominal distention 10 days before admission. Helical CT scanning of the abdomen and pelvis disclosed marked hepatomegaly without any visible nodular lesion in the hepatic parenchyma. He died of severe liver dysfunction with multiorgan failure on the 20th hospital day. Autopsy revealed diffuse invasion of tumor cells into the sinusoid throughout the liver.

Key words: liver, neoplasm, metastasis, diffuse intrasinusoidal liver metastasis, CT

Introduction

Fulminant hepatic failure due to diffuse intrasinusoidal liver metastasis is uncommon. It is known that primary liver neoplasms such as hepatocellular carcinoma and/or secondary malignancies of the liver can cause fulminant hepatic failure when cancer cells diffusely spread into the hepatic sinusoid.[1-7] We report a patient with small cell lung cancer with diffuse intrasinusoidal liver metastasis that caused fulminant hepatic failure and in whom CT showed only diffuse liver enlargement without any visible nodular lesion.

Case Report

A 65-year-old man with small cell lung cancer had been treated with two courses of chemotherapy. He was admitted to our hospital because of appetite loss and abdominal distention that started 10 days before. He also complained of dark yellowish urine and dyspnea that began seven days before. Physical examination revealed hepatomegaly and bilateral pretibial edema. Consciousness was clear. Tumor markers for small cell lung cancer obtained on the 10th hospital day were as follows: neuron specific enolase 410 ng/ml (<10), Pro-gastrin-releasing peptide (Pro-GRP) 218,000.0 U/ml (<46.0).

Tests for hepatitis A, B, and C, autoantibodies, cytomegalovirus, and Epstein-Barr virus serology were negative.

On his first hospital day, we performed helical CT scanning of the abdomen and pelvis. The arterial dominant phase was not obtained. CT revealed marked hepatomegaly without any visible nodular lesion in the hepatic parenchyma (Fig. a). A small amount of ascites in the right subphrenic space was also disclosed. Abdominal ultrasonography obtained on the second hospital day revealed hepatomegaly associated with compression of the portal vein and hepatic vein. CT obtained about 70 days earlier had revealed a small cyst in the lateral segment of the left lobe of the liver and left renal stone. Otherwise it was unremarkable (Fig. b). Magnetic resonance imaging was not performed.

The patient's clinical course continued to deteriorate after admission, and he died of severe liver dysfunction with multiorgan failure on the 20th hospital day.

Metastatic liver disease was suspected as the cause of fulminant hepatic failure, before his death but was not confirmed. Autopsy revealed that the liver was diffusely enlarged, and the surface of the liver was diffusely scattered with tumor nodules. On the cut surface of the liver, widely distributed tumor nodules of varying sizes were present (Fig. c). Microscopically, diffuse invasion of tumor cells into the sinusoid was evident throughout the liver. Massive replacement of hepatocytes by tumor cells was noted (Fig. d).

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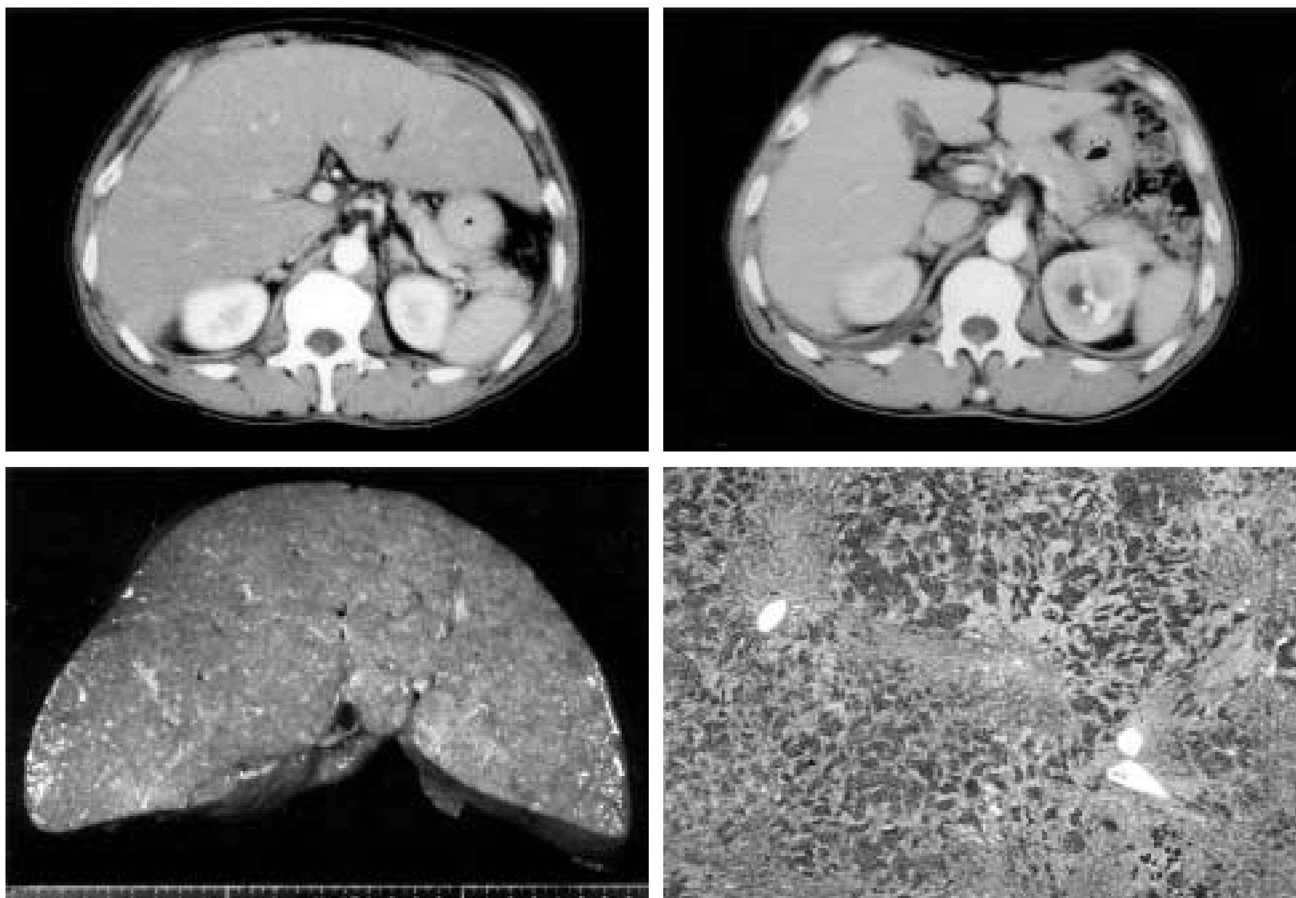

Fig. A 65-year-old man with diffuse intrasinusoidal liver metastasis of small cell lung cancer.
a: CT scan of the abdomen at the level of the origin of the superior mesenteric artery reveals marked hepatomegaly, which is apparent in comparison with b. No obvious nodular lesions are depicted in the liver.
b: CT at almost the same level obtained about 70 days before shows a normal-sized liver with a small cyst in the left lobe.
c: Macroscopy of the resected liver shows diffuse enlargement. On the cut surface of the liver, widely distributed tumor nodules of varying sizes are present.
d: Microscopy reveals tumor cells (darkly stained) diffusely invading into the sinusoid. Massive replacement of hepatocytes by tumor cells is noted. (hematoxylin & eosin stain, ×100)

Discussion

Metastatic cancer of the liver usually presents itself as multiple nodular lesions and may cause striking hepatomegaly. Hepatic metastases are found in 50% of patients who have died of cancer. Surprisingly, the liver metastases can be asymptomatic. Laboratory findings of hepatic functional insufficiency may not be evident.[1,2] However, it is known that primary liver neoplasms such as hepatocellular carcinoma and/or secondary malignancies of the liver can cause fulminant hepatic failure when cancer cells diffusely spread into the hepatic sinusoid.[1-7]

Although diffuse intrasinusoidal metastases to the liver are rare, Alcalde *et al*. reported nearly 50 cases.[3] The primary sites were breast cancer, gastric cancer, colon cancer, lung cancer, pancreatic cancer, lymphoma, leukemia, malignant melanoma, urothelial cancer, Merkel cell tumor, and uterine cancer.[1-5] Although the mortality rate is very high despite treatment, a few cases of survival after prompt initiation of chemotherapy have been reported in hematological malignancies.[4]

Fulminant hepatic failure is defined as liver failure with encephalopathy developing within eight weeks of the onset of symptoms in the absence of pre-existing liver disease. Most cases of fulminant hepatic failure are due to viral or drug-induced hepatitis.[7,8] In our case, neither viral hepatitis nor drug reaction was likely.

Previous reports have explained that fulminant hepatic failure in cases of diffuse intrasinudoidal liver metastases is due to massive parenchymal destruction by tumor infiltration or infarction and necrosis of the liver by vascular involvement of the tumor.[2,6] In our case, tumor cells invaded diffusely into the hepatic sinusoid with

diffuse destruction of the liver parenchyma. Vascular involvement of the liver was not prominent.

Alcalde *et al*. mentioned that CT showed hepatomegaly but no visible nodular lesions in a case of diffuse intrasinusoidal metastases of urothelial carcinoma. A percutaneous postmortem liver biopsy revealed that carcinoma cells replaced much of the liver tissue.[3] These findings are similar to our case. We concluded that the liver of our patient showed homogeneous density on CT because of diffuse invasion of tumor cells into the sinusoid.

When diffuse liver enlargement is seen on CT and hepatic individual nodular lesion is not visualized with CT in cases of malignant neoplasm, it can be difficult to differentiate diffuse intrasinusoidal liver metastasis from other diseases that present diffuse liver enlargement, such as fatty infiltration, hepatitis, diffuse hepatocellular carcinoma, lymphoma, some kinds of glycogen storage disease, amyloidosis, diffuse granulomatosis, or passive congestion, so the cause of fulminant hepatic failure may remain obscure unless biopsy or autopsy is performed.

We did not study the patient with magnetic resonance imaging. Considering the spatial resolution of current MR imagers, it would not have been possible to detect the small nodules. However, MRI with SPIO (superparamagnetic iron oxide) might have been helpful.

In conclusion, although fulminant hepatic failure due to diffuse intrasinusoidal liver metastasis is uncommon, it must be considered in the differential diagnosis when CT shows diffuse liver enlargement in a patient with malignant neoplasm, especially when viral hepatitis and drug reaction are excluded.

References

1) Myszor MF, Record CO. Primary and secondary malignant disease of the liver and hepatic failure. *J Clin Gastroenterol*, 12: 441–446, 1990.
2) Sawabe M, Kato Y, Ohashi I, Kitagawa T. Diffuse intrasinusoidal metastasis of gastric carcinoma to the liver leading to fulminant hepatic failure. *Cancer*, 65: 169–173, 1990.
3) Alcalde M, Garcia-Diaz M, Pecllin J, *et al*. Acute liver failure due to diffuse intrasinusoidal metastases of urothelial carcinoma. *Acta Gastroenterol Belg*, 59: 163–165, 1996.
4) Te HS, Schiano TD, Kahaleh M, *et al*. Fulminant hepatic failure secondary to malignant melanoma: case report and review of the literature. *Am J Gastroenterol*, 94: 262–266, 1999.
5) Wang M, McGrew W, Wofford B, Patel J, Dunn GD. Merkel cell tumor with liver metastases: presentation as fulminant hepatic failure. *Am J Gastroenterol*, 80: 376–380, 1985.
6) Harrison HB, Middleton HM III, Crosby JH, Dasher MN Jr. Fulminant hepatic failure: an unusual presentation of metastatic liver disease. *Gastroenterology*, 80: 820–825, 1981.
7) Mas MR, Simsek I, Can C, Ateskan U, Erdem H, Kocabalkan F. Fulminant hepatic failure as the initial manifestation of primary hepatocellular carcinoma. *Eur J Gastroenterol Hepatol*, 12: 575–578, 2000.
8) O'Grady JG, Portmann B, Williams R. Fulminant hepatic failure. In *Disease of the Liver, 7th ed*. (Schiff L, Shiff ER eds.; J. B. Lippincott Company, Philadelphia), pp. 1077–1090, 1993.