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Case report

Fulminant hepatic failure and hepatomegaly caused by diffuse liver metastases from small cell lung carcinoma: 2 autopsy cases

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ABSTRACT

Fulminant hepatic failure (FHF) is defined as a liver disease that causes encephalopathy within 8 weeks of onset in the absence of pre-existing liver disease. Although liver metastases are commonly found in cancer patients, FHF secondary to diffuse liver infiltration is rare. Here, we report the rare autopsy cases of patients with small cell lung carcinoma (SCLC) and secondary FHF. These patients presented with remarkable hepatomegaly and a near complete replacement of the liver parenchyma with metastatic tumor. Neoplastic involvement of the liver should be considered in the differential diagnosis of FHF.

1. Introduction

Globally, lung cancer is the most common human malignancy and the leading cause of cancer deaths, with 1.6 million newly diagnosed cases and 1.378 million deaths annually (International Agency for Research on Cancer). Small cell lung carcinomas (SCLCs) account for 25% of diagnosed lung carcinomas. Approximately 70% of newly diagnosed SCLC patients initially present with an advanced disease stage [1,2].

Fulminant hepatic failure (FHF) is a liver disease that causes encephalopathy within 8 weeks of symptom onset in patients without prior liver disease. FHFs most commonly result from viral hepatitis or drug toxicity and not from primary or metastatic carcinomas [3–6].

Although the liver is one of the most common metastatic sites for SCLC, mild to moderate liver disorder is often the only outcome. Liver disorders ranging from acute hepatic failure to FHF are rarely caused by diffuse parenchymal infiltration of SCLC [1,7–9]. Because of highly progressed disease states, clinical courses are usually too short to identify the causes, resulting in multi-organ failure. Diagnosis of hepatic infiltration in such patients presenting with FHF is difficult. High degrees of suspicion are required if there is no evidence of the primary disease.

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We describe 2 autopsy cases of rapid FHF secondary to SCLC: one of an acute recurrence of SCLC and the other with unknown initial etiology. These 2 rare cases had contrasting clinical courses and very intriguing imaging findings that provide new insights.

2. Case presentation

2.1. *Case 1*

A 69-year-old Japanese male SLCL patient received 4 courses of chemotherapy (60 mg/m^2 CPT-11, days 1, 8, and 15 and 80 mg/m^2 CDDP, day 1). He showed good partial response (PR) to chemotherapy. No history of hepatitis, alcohol abuse, or drug allergy was noted. He was admitted for prophylactic cranial irradiation. During the irradiation, he complained of sudden epigastralgia and chest pain. Physical examination revealed arrhythmia, hepatomegaly, and bilateral pretibial edema, although he maintained alert consciousness. Follow-up examination showed elevated WBC, cardiac enzyme, and liver enzyme levels (Table 1, Case 1—Day 1). Serological tests for hepatitis virus, Epstein–Barr virus, (EBV) and cytomegalovirus (CMV) were negative. Abdominal ultrasonography showed only hepatomegaly (Fig. 1A). CT revealed marked hepatomegaly, although no space-occupying lesion (SOL) was apparent (Fig. 1B). Contrast-enhanced CT revealed diffuse multiple low-density areas (LDAs) in the liver (Fig. 1C). T2-weighted (Fig. 1D) and diffusion-weighted (DW; Fig. 1E) MRI showed hepatomegaly with diffuse small high-intensity areas (HIAs) that were contrasted in the dynamic phase and washed-out in the late phase with gadolinium-based contrast media (Fig. 1F), suggesting that hepatomegaly resulted from diffuse malignant parenchymal infiltration. Follow-up percutaneous liver biopsy (Fig. 2A) and bone marrow puncture showed SCLC metastasis to the bone marrow and liver. Serum levels of NSE and ProGRP (SCLC tumor markers) were highly elevated (Table 1, Case 1—Day 2). On Day 3, the patient became drowsy and exhibited abnormal behavior, indicating the onset of encephalopathy due to FHF (Table 1, Case 1—Day 3). He died of severe liver dysfunction and multi-organ failure on Day 7 after the initial complaint (Table 1, Case 1—Day 7). Postmortem examination showed a markedly enlarged liver (3570 g), with multiple coarse micro-nodules (Fig. 2B). The cut surface had multiple tumor nodules of varying sizes (Fig. 2C). Microscopic analysis indicated SCLC metastasis. SCLC had extensively infiltrated the hepatic sinusoids and replaced the hepatic parenchyma (Fig. 2D). Within the bilateral lungs, kidneys, adrenal glands, spleen, and vertebrae, diffuse SCLC micro-metastases were observed.

2.2. *Case 2*

A 63-year-old Japanese male patient was referred to our hospital with jaundice. He was a very heavy smoker with no history of hepatitis, alcohol abuse, or drug allergy. Follow-up examination revealed elevated liver enzyme levels (Table 1, Case 2—Day 1). Serological tests for hepatitis virus, EBV, and

Table 1 – Serological data from Cases 1 and 2.

Case 1

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
AST (U/L)	272	469	453	337	242	397	8790
ALT (U/L)	412	640	626	596	441	538	3728
LDH (U/L)	1848	2105	2440	2697	1987	2012	11390
ALP (U/L)		514	765	920	852		933
γ-GTP (U/L)		554	721	816	723	849	745
T-BIL (mg/dL)	2.7	2.9	4.4	5.5	6.9	9.4	15.9
PT (%)	79			66.6	70		9.1
PT-INR	1.44			1.59	1.54		10.78
NH3 (μg/dL)			126		124		150
NSE (ng/mL)		1585.8					1265.7
ProGRP (pg/mL)		3870					7920

Case 2

	Day 1	Day 4	Day 5	Day 6
AST (U/L)	150	175	185	196
ALT (U/L)	251	232	233	235
LDH (U/L)	3040	3333	3421	4061
ALP (U/L)	1003	875	856	886
γ-GTP (U/L)	1585	1522	1543	1372
T-BIL (mg/dL)	4.1	5.9	6.4	6.1
PT (%)		63.5	60.2	58.6
PT-INR		1.44	1.5	1.53
NH3 (μg/dL)			113	167
NSE (ng/mL)				2738.2
ProGRP (pg/mL)				197000