INTERNAL MEDICINE

□ CASE REPORT □

Brain Metastasis from Hepatocellular Carcinoma Treated with a Cyber-Knife

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Abstract

A 70-year-old right-handed Japanese man who had undergone surgical resection for hepatocellular carcinoma (HCC) 2 years earlier was diagnosed with lung metastasis 3 months before consulting our hospital with a headache and visual field disturbance. Head computed tomography revealed a brain tumor with an intracerebral hemorrhage. Using ^{99m}Tc-PMT (pyridoxal-5-methly-triptophan) scintigraphy, we determined that the brain tumor was metastasis from the HCC and utilized the cyber-knife for treatment. The prognosis of patients with brain metastasis from HCC has been reported to be poor. Use of the cyber-knife was non-invasive, and proved to be effective for improving prognosis and quality of life.

Key words: brain metastasis, hepatocellular carcinoma, cyber-knife

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Introduction

Brain metastasis from hepatocellular carcinoma (HCC) is rare (1) and the prognosis of affected patients is poor (2-4). Therapy for the condition is difficult, because of the poor prognosis, as the short life expectancy at the time diagnosis of brain metastasis makes it difficult to perform aggressive treatment such as surgery, which is invasive, or radiation therapy, which requires time.

Recently, the cyber-knife, a new type of device used for stereotactic irradiation that combines a robot manipulator with a linear accelerator, has become available for the treatment of metastatic brain tumors (5). The non-invasive characteristics of the device are thought to improve the quality of life (QOL) of affected patients and prevent re-hemorrhaging. This is the first known report of the use of the cyber-knife for brain metastasis from HCC.

Case Report

A 70-year-old right-handed Japanese man came to our hospital in August 2007, complaining of a headache and visual field disturbance. He had a past history of surgical resection of an HCC in May 2005 at another hospital and recurrence of lung metastasis without intrahepatic tumors was diagnosed in May 2007 (Fig. 1A). Multiple lung metastases progressed in spite of systemic chemotherapy with 5-fuluorouracil (5-FU: 350 mg/m^2/day at 5 days/week) and fluorodeoxyglucose-positron emission tomography (FDG-PET) and computed tomography (CT) scans, performed in June 2007, did not reveal an abnormal up-take of FDG, except for the areas of lung metastasis.

Upon admission to our institution, an intracranial hemorrhage was revealed by head CT (Fig. 2A), which was treated conservatively and did not show progression. In ^{99m}Tc-PMT (pyridoxal-5-methly-triptophan) scintigraphy, all

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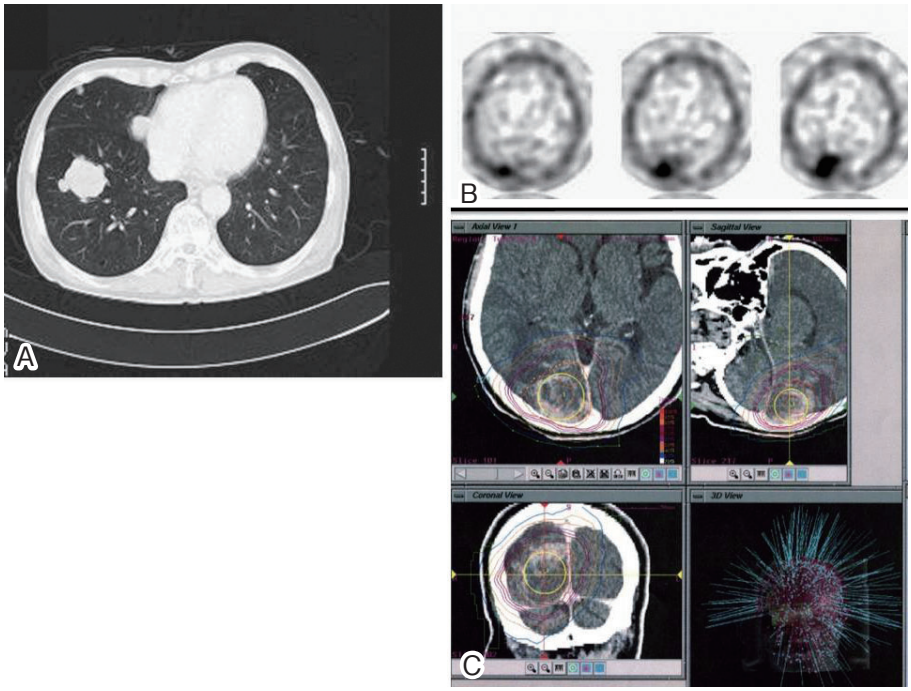

Figure 1. **A: Chest CT image showing progression of lung metastasis (August 2007). B: The brain tumor was diagnosed as metastasis from HCC using ^{99m}Tc-PMT (pyridoxal-5-methly-triptophan) scintigraphy. C. Brain metastasis was treated using a cyber-knife (Cyberknife II).**

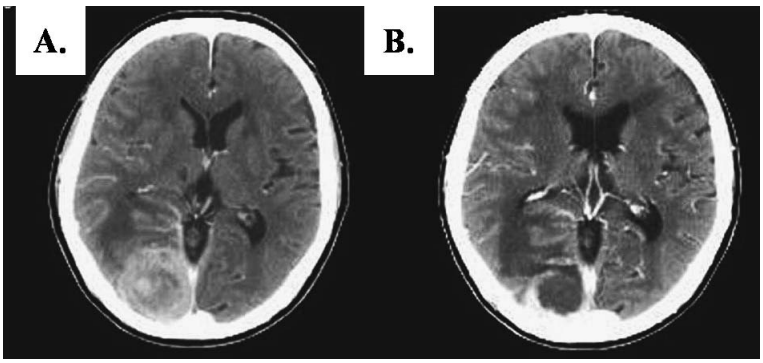

Figure 2. **A: Enhanced head CT image obtained at admission showing a brain tumor with intracranial hemorrhage. B: Enhanced head CT image obtained 3 weeks after treatment with cyber-knife.**

tumors in the brain and lung showed an accumulation of ^{99m}Tc-PMT (Fig. 1B), and were diagnosed as metastases from HCC. The laboratory data are shown in Table 1. The tumor size was greater than 3 cm and progressive lung metastasis was diagnosed in spite of systemic chemotherapy. Therefore, we did not select surgical resection, because of the invasiveness of surgery and the poor prognosis of brain metastasis, and rather chose treatment with the cyber-knife to maintain QOL and avoid re-hemorrhaging. The treatment (marginal dose 35 Gy and central dose 43.75 Gy/5 fractions/a week) was performed 2 weeks later (Fig. 1C), and the headache and partial blindness were improved a few days later. Furthermore, brain CT at 3 weeks after treatment revealed no progression of metastasis or re-hemorrhaging (Fig. 2B). At 8 months after therapy, the patient was ambulant and follow-up examinations were continuing.

Discussion

Brain metastasis from HCC is rare, with the condition is reported to occur in only 0.2% of HCC patients (1). As for the reason for the rarity of brain metastasis from HCC, it has been noted that there is little affinity between HCC cells and the brain (6). However, with improvements in the prognosis of patients with HCC, due to the development of surgical resection, radiofrequency ablation, transcatheter arterial chemoembolization, and liver transplantation techniques, the number of cases with extra-hepatic metastasis following curative treatment is expected to increase as well as cases with characteristics similar to the present case. Thus, attention must be paid to not only lung and bone metastases, but also asymptomatic brain metastasis after curative therapy,

Table 1. Laboratory Data Obtained at Admission

Total protein	7.1	g/dL	Glu	127	mg/dL
Albumin	3.2	g/dL	HbA1c	5.5	%
Total bilirubin	1.8	g/dL			
AST	129	IU/L	WBC	4700	/μL
ALT	106	IU/L	RBC	356	10^4/μL
ALP	430	IU/L	HGB	11.8	g/dL
LDH	266	IU/L	MCV	94.7	fL
ChE	106	IU/L	MCH	33.1	pg
r-GTP	202	IU/L	MCHC	35.0	%
T-Chol	141	mg/dL	Plt	13.6	10^4/μL
TG	54	mg/dL	PT	63.8	%
BUN	9.3	mg/dL	PT(INR)	1.41	
Creatinine	0.49	mg/dL			
Na	134	mEq/L	AFP	407.5	ng/mL
K	4.0	mEq/L	AFP-L3	79.3	%
Cl	101	mEq/L	PIVKA-II	16577	mAU/mL
Ca	7.9	mg/dL	HBs-Ag	negative	
IP	2.4	mg/dL	Anti-HCV Ab	positive	

WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; Plt, platelet count, PT, prothrombin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; ChE, cholinesterase; γ-GTP, γ-glutamyltransferase; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; AFP, alpha-fetoprotein; AFP-L3; fucosylated AFP, PIVKA-II, protein induced by vitamin K absence/antagonist-II; HBsAg, hepatitis B surface antigen; anti-HCVAb, anti-hepatitis C virus antibody

because the major initial symptom is an intracranial hemorrhage.

Patients with brain metastasis from HCC have a poor prognosis, with some authors reporting that the survival period after diagnosis is less than 3 months (2-4). Intracranial hemorrhage was found to be the first manifestation in 33% of patients with brain metastasis from HCC (4) and these tumors are known to easily rupture.

Patchell et al reported that the characteristics of potential candidates for surgical resection are a single surgically acceptable symptomatic tumor and those with brain metastasis have a life expectancy of at least 2 months (7). The present patient did not hope for surgical resection. In addition, Chang et al (4) and Yen et al (8) found that patients who underwent surgery and/or radiation therapy had a survival time of more than 4 months, while most who received only supportive care died within 1 month. The reason why the prognosis for patients who receive supportive care is so poor is based not only on the spread of HCC to multiple organs, but also repeated intracranial hemorrhaging.

Natsuizaka et al noted that the median survival time of all extra-hepatic metastasis cases in HCC is 7 months (9), while in our institution, the median survival period for those patients is similar at 6 months. In the present case, 3 months had passed since the diagnosis of multiple lung metastases and cancer had progressed in spite of chemotherapy performed at another hospital, thus we considered that the disease was aggressively progressing.

Recently, the cyber-knife, a new type of device used for stereotactic irradiation that combines a robotic manipulator and linear accelerator, has become useful for the treatment of brain metastasis (10). For the present patient, we did not choose surgical resection but rather the cyber-knife, because the former requires a longer hospital stay and is more invasive. Another device is the gamma-knife, however, it requires fixing of a frame, which is invasive, and it is not suitable for large tumors (11). A few days after treatment with the cyber-knife, the headache and partial blindness symptoms were improved in our patient. The cyber-knife was thought to be effective for brain metastasis from HCC, especially in those patients with good hepatic reserve function and having no other risk factors for early death.

The major organ most commonly associated with metastasis from HCC is the lung and 78% of cases of brain metastasis from HCC also develop lung metastasis (8). In a number of patients with brain metastasis from HCC, the main problems encountered are metastasis to other organs and intrahepatic tumors that remain after treatment for brain metastasis, which explain the poor prognosis. Although intrahepatic tumors are not revealed in dynamic CT imaging, pro-

gressive lung metastasis resistant to systemic chemotherapy was found in the present case. Therefore, we selected the best available supportive care following treatment with the cyber-knife.

Moriya et al stated that the goal of therapy for brain metastasis is at most symptomatic improvement (12). Needless to say, in cases with good hepatic reserve function in which the primary HCC and metastasis are well controlled, the cyber-knife is thought to be useful, because of the shorter therapeutic period required and improvements in QOL, such as headaches and visual field disturbances. In the present patient, prevention of re-hemorrhaging by use of the cyber-knife improved the prognosis. This is the first report of use of the cyber-knife for brain metastasis from HCC. Although the accumulation of case reports is needed, we found the cyber-knife to be effective for improving QOL and preventing re-hemorrhage in the case of brain metastasis from HCC.

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