CASE REPORT

Multiple Skull Metastases from Hepatocellular Carcinoma Successfully Treated with Radiotherapy

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Abstract

We report a Japanese man who presented with multiple cranial nerve palsies with hepatitis B virus-related multiple hepatocellular carcinoma (HCC). He presented with right III, IV, VI, IX, X, and XII cranial nerve palsies. Metastases involving the clivus and the right occipital bone from HCC were diagnosed by the findings of magnetic resonance imaging of the head, cerebral angiography, and 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography/computed tomography. In this case, over one-year survival and improvement of neurological signs were achieved by radiotherapy in spite of multiple skull metastases, which are extremely rare.

Key words: hepatocellular carcinoma, cranial nerve palsy, clivus, skull, radiotherapy

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Introduction

Hepatocellular carcinoma (HCC) is the third most common cause of cancer death in Japan, and it frequently metastasizes to the lung, regional lymph nodes, and the skeletal system (1). In the skeletal system, metastasis occurs commonly in the spine, ribs, pelvis, and long bones, but skull metastasis has been rarely reported (2, 3). When extrahepatic metastasis from HCC occurred, the prognosis was reported to be poor (1). We describe a patient presenting with multiple cranial nerve palsies with skull metastases from HCC, who was successfully treated with radiotherapy.

Case Report

A 65-year-old Japanese man had been treated for chronic hepatitis B virus infection for 12 years, and multiple HCC in S3, S5, and S7 with cirrhosis were identified, and treated with transcatheter embolization (TAE) seven months before the onset of neurological symptoms. He presented with difficulty of speech and swallowing, and right occipitalgia for one month, followed by double vision. Neurological examination revealed restriction of right eyeball movement and right-side soft palatal movement, diplopia, dysarthria, dysphagia, hoarseness, and deviation of the tongue to the right side, which suggested right VI, IX, X, and XII cranial nerve palsies.

Laboratory studies on admission revealed the following abnormal values: platelets 7.3×10^4/μL, aspartate aminotransferase 54 IU/L (normal limit <40), alanine aminotransferase 54 IU/L (normal limit <45), lactate dehydrogenase 234 IU/L (normal limit <220), alkaline phosphatase 525 IU/L (normal limit <360), alfa-fetoprotein (AFP) 14,000 ng/mL (normal limit <10), and protein induced by vitamin K absence (PIVKA-II) 7,688 MAU/mL (normal limit <39). Examination of cerebrospinal fluid showed no remarkable findings, and the cytology was negative. Magnetic resonance imaging (MRI) of the head revealed a mass involving the clivus with isointensity on T1-weighted images (T1WI) (Fig. 1A), which was immediately enhanced on contrast-enhanced T1 WI (Fig. 1B, 1C). Computed tomography (CT) of the head showed osteolytic change of the clivus, and abdominal CT showed two HCC in the liver (S2 and S5). Cerebral angio-
treated with TAE, 2-deoxy-2-\[^{18}\text{F}\]fluoro-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) showed increased uptake in the clivus without any other site of abnormal uptake (Fig. 1E).

Skull base metastasis from HCC was diagnosed on the basis of these findings. About 50 days after the initial symptoms, radiotherapy was delivered using laterally opposed 10 MV X-rays to the skull base, which is shown as a gray field (F) (black arrowheads). The dose distribution of radiotherapy to the skull base is illustrated (G).

Dysarthria and dysphasia gradually improved six months after the onset of neurological symptoms, and oral intake became possible. Improvement of right ptosis and horizontal eyeball movement were identified eight months after the initial symptoms with a decrease in tumor markers (AFP 224 IU/L; PIVKA-II 241 MAU/mL). The lesion in the clivus was heterogeneously enhanced, and the right occipital lesion disappeared on contrast-enhanced T1WI of MRI (Fig. 2C); FDG-PET/CT revealed no abnormal uptake in the head (Fig. 2D), but it was unknown whether or not abnormal uptake in the right occipital bone was improved by the second radiotherapy because FDG-PET/CT was not performed before the second radiotherapy. At fifteen months after the initial symptoms, he demonstrated no adverse effects of radiotherapy.

**Discussion**

Skull metastasis frequently occurs in lung and breast cancers. In the previous report, bone metastasis from HCC was 4-20% (1); however, the incidence of skull metastasis from HCC has been reported to be 0.4-1.6% (4). Only 25 cases of skull base metastasis of HCC have been reported (3). Cranial nerve deficits were found in 41% of cases of skull metastasis (4), and in 96% of cases of skull base metastasis (3). Survival time of the 42 patients with skull metastasis from HCC ranged from 6 days to 108 months (mean 8.9 months) (4), but the 17 patients with skull base metastasis...
The right occipital bone mass was intermediately enhanced on contrast-enhanced axial T1WI (A) (white arrowhead). Radiotherapy was delivered to the right occipital bone, illustrated as a gray field (B) (black arrowheads). The lesion in the clivus was heterogeneously enhanced, and the right occipital lesion disappeared on contrast-enhanced axial T1WI after the second radiotherapy (C). FDG-PET/CT revealed no abnormal uptake after the second radiotherapy (D).
case could be successfully treated with radiotherapy in spite of skull base metastasis, which is commonly associated with a poor prognosis. It was considered that the prolonged survival time with improved neurological manifestation in our case was associated with good control of the primary lesions and no metastasis to any other site.

In the present case, although histological examination was not performed, the diagnosis was considered to be skull metastases from HCC from the following findings: extremely elevated levels of tumor markers, and the findings of some imaging modalities. When skull metastasis from HCC is diagnosed, radiotherapy may be an option for the metastatic lesions. Although our patient presented with no adverse effects of radiotherapy at the last follow-up, a system using intensity-modulated radiation therapy should be established to reduce the radiation dose to the brainstem for skull base metastasis.

References


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