Solitary skull metastasis as the first symptom of hepatocellular carcinoma: case report and literature review

Xieli Guo1,2
Jiangliu Yin3
Yugang Jiang4

1Department of Neurosurgery, Second Xiangya Hospital of Central South University, Changsha, Hunan, People’s Republic of China; 2Department of Neurosurgery, Jinjiang Hospital of Quanzhou Medical College, Jinjiang, Fujian, People’s Republic of China; 3Department of Neurosurgery, Changsha Central Hospital, Changsha, Hunan, People’s Republic of China

Abstract: Skull metastasis from hepatocellular carcinoma (HCC) is reported rarely. In addition, solitary skull metastasis as the first symptom of HCC is reported even less. Here, we reported a case of solitary skull metastasis as the first symptom of HCC and reviewed the literature on skull metastasis. A 49-year-old male patient was admitted to Jinjiang Hospital of Quanzhou Medical College with a painless parietal-occipital scalp mass, and he denied any history of hepatic disease. A cranial computed tomography demonstrated a hypervascular enhancement with osteolytic change in the right parietal-occipital region, cranial magnetic resonance imaging indicated a highly enhanced and osteolytic skull tumor, and abdominal computed tomography showed a huge tumor in the liver. The other examinations showed no other metastases. Laboratory data showed no liver dysfunction while hepatitis B surface antigen was positive, and alpha fetal protein level was high. A craniectomy was performed and the mass was totally removed. The histological diagnosis was skull metastasis from HCC. The patient was subsequently treated by transcatheter arterial chemoembolization. In a review of published literature, the incidence of skull metastasis from HCC in the period between 1990 and 2011 has significantly increased. The misdiagnosis rate of skull metastases as the first symptom from HCC was high. Therefore, it is necessary to give each patient with a scalp mass that has invaded the skull a liver ultrasound or computed tomography scan. On the other hand, we found that metastases that occurred in the calvaria site were more frequent than those that occurred in the skull base and facial skeleton. This may be worthy of further investigation in the future.

Keywords: hepatocellular carcinoma, skull metastasis, bone metastasis, positron emission tomography

Case report

A 49-year-old male visited Jinjiang Hospital of Quanzhou Medical College with the complaint of a painless mass in the right parietal-occipital region of the skull. The mass was found incidentally 1 month earlier by the patient himself and it had grown rapidly. He denied any head traumas or any significant medical problems, including prior history of hepatic disease or chronic alcoholism. Bony window of cranial nonenhanced computed tomography (CT) scan showed a 5 × 5 cm2 soft tissue mass with irregular destruction (Figure 1A), and contrast-enhanced CT scan showed a hypervascular enhancement with osteolytic pathological change in the parietal-occipital region of the skull (Figure 1B). On admission, neurological and physical examinations revealed no neurological deficits, hepatomegaly, or obvious abnormalities except a painless nonmovable mass about 5 × 5 cm2 in size over the right parietal-occipital region. Laboratory data showed no liver dysfunction while HBsAg (hepatitis B surface antigen) was...
positive, and AFP (alpha fetal protein) level was high (Table 1). On cranial magnetic resonance imaging, the tumor was a homogeneous well-defined mass with involvement of the inner and outer skull table. It revealed isosignal intensity on T2-weighted (Figure 2A) and T1-weighted imaging (Figure 2B), with significant enhancement by gadolinium (Figure 2C). Abdominal B ultrasound showed a large mass in the right lobe of the liver (Figure 3); therefore, a contrast-enhanced CT of the abdomen and a nonenhanced CT of the breast were taken. Contrast-enhanced CT of the abdomen showed a huge enhanced carcinoma in the right lobe of the liver (Figure 4A–C). Nonenhanced CT of the breast showed no lung metastases (Figure 5). A single-photon emission computed tomography of total skeletal bones showed no metastases (Figure 6). Our diagnosis was...
Solitary skull metastasis as first symptom of hepatocellular carcinoma

Hepatocellular carcinoma (HCC) with skull metastasis and chronic hepatitis B.

The carcinoma was radically resected with surrounding normal bone via right parietal-occipital craniectomy under general anesthesia. During the operation, a large and well-demarcated reddish-brown mass was found to have penetrated both tables of the skull through the diploic space. The carcinoma looked like cauliflower, and the underlying dura was intact and did not show any evidence of gross carcinoma invasion. The dural surface attached to the carcinoma was curedtted and the rough surface of the dura was cauterized by bipolar forceps. The carcinoma was totally removed. Histopathological examination of the carcinoma revealed pleomorphic tumor cells with eosinophilic cytoplasm, and prominent nucleoli and mitosis arranged in trabecular and solid pattern. The pathological findings confirmed the diagnosis of metastatic HCC (Figure 7A and B). Postoperative recovery was satisfactory. To treat the primary carcinoma, transcatheter arterial chemoembolization with pirarubicin (40 mg), carboplatin (200 mg), floxuridine (250 mg), Lipiodol, and Gelatin sponge particles was performed after selecting a feeding artery of the tumor on aortography. The patient was discharged 1 month later. The patient survived after half a year of follow up and did not show any evidence of recurrence in the skull. However, because of the recurrence of hepatocellular carcinomas, the patient died from liver failure in the 18 months since he received transcatheter arterial chemoembolization.

Discussion

Hepatocellular carcinoma is the fifth most common cancer in the world and is especially prevalent in Africa and East Asia. The incidence of HCC in developing countries is
third most common of the various types of cancer. Intrahepatic metastasis is the most common metastasis of HCC. Extrahepatic metastases of HCC usually occurs in the regional lymph nodes (16%-40%) and lungs (34%-70%), but less commonly in the skeleton (1.6%-16%). In skeleton metastasis, HCC usually metastasizes preferentially to the vertebral column, pelvis, femora, and ribs, but rarely to the skull. The incidence of skull metastases from HCC is 0.4%-1.6%, and 9% of patients with calvarial metastases have other skeletal deposits.

After a thorough search of the literature, we found 48 articles in total describing patients who were identified with calvaria, skull base, or facial skeleton metastasis from HCC, which formed the basis of this review. In our review of published literature, a total of 59 patients with skull metastasis from HCC were found. The incidence of skull metastases from HCC is 0.4%-1.6%, and 9% of patients with calvarial metastases have other skeletal deposits.

Figure 7 The histopathological characteristics of carcinoma and the immunohistochemical finding.

Notes: (A) Histopathological characteristics of carcinoma. The carcinoma showed thick trabecular growth pattern with intercellular canaliculi resembling liver cell plates and sinusoids. The carcinoma cells maintain a polygonal shape and have abundant granular eosinophilic cytoplasm, round vesicular nuclei, and prominent nucleoli (He ×200).

(B) The immunohistochemical finding. The carcinoma cells show glypican-3 (+), AFP (−), villin (+), CK7 (−), CK20 (−), vimentin (−), CD10 (−), and Ki67 (+) of about 30%.

Abbreviations: HE, hematoxylin-eosin staining; AFP, alpha fetal protein; CK, creatine kinase; CD, cluster of differentiation or leukocyte differentiation antigen; Ki67, nuclear-associated antigen Ki67.

Table 2 Summary of reported cases in the literature with skull metastases from HCC (n=59)*

<table>
<thead>
<tr>
<th>Period</th>
<th>Calvarial metastases</th>
<th>Skull base metastases</th>
<th>Facial skeleton metastases</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966–1989</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>1990–2011</td>
<td>25</td>
<td>12</td>
<td>8</td>
<td>45</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>16</td>
<td>12</td>
<td>59</td>
</tr>
</tbody>
</table>

Note: *Fourteen cases in the literature with solitary skull metastases from HCC were reported.

Abbreviation: HCC, hepatocellular carcinoma.

Table 3 Summary of reported cases in the literature with skull metastases as the first symptom from HCC (n=33)

<table>
<thead>
<tr>
<th>Period</th>
<th>Misdiagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calvarial metastases</td>
</tr>
<tr>
<td>1966–1989</td>
<td>4 (4)</td>
</tr>
<tr>
<td>1990–2011</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
</tbody>
</table>

Note: *The data in parentheses is the number of patients who were misdiagnosed.

Abbreviation: HCC, hepatocellular carcinoma.
life. Molecular imaging by positron emission tomography is, therefore, set to probe the molecular abnormalities that are the basis of disease and provide additional biochemical or molecular information about primary brain tumors. In all, it is necessary to give each patient with a scalp mass that has invaded the skull molecular neuroimaging, such as positron emission tomography, to reduce the misdiagnosis rate and to rule out the possibility of skull metastasis from HCC.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**