Case Report of Skull Metastasis From Hepatocellular Carcinoma After a Liver Transplant

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Abstract
A solitary skull metastasis from hepatocellular carcinoma is rare. A 38-year-old man with hepatocellular carcinoma presented to our institution with a palpable temporal scalp mass. We took a magnetic resonance image, and discovered an enhanced and osteolytic skull tumor. The tumor was removed by an occipital craniectomy, and the histologic diagnosis was a cranial metastasis owing to hepatocellular carcinoma.

A skull metastasis owing to hepatocellular carcinoma should be considered in the differential diagnosis in patients with a subcutaneous scalp mass. Although a distant metastasis can affect the prognosis of the patient, early treatment may improve survival.

Key words: Hepatoma, Scalp, Transplant

Introduction
Hepatocellular carcinoma (HCC) constitutes approximately 3% of all cancers and is considered one of the most common causes of death from cancer. The incidence varies widely in different areas of the world. Many cases occur in countries where there are high rates of chronic hepatitis B virus (HBV) infection. The highest incidences are found in Asian (China, Taiwan) and African countries. Many of these people are exposed to dietary aflatoxins, derived from the fungus Aspergillus flavus, that when combined with HBV infection, increase the risk of HCC.1,2 In Western countries, the incidence is increasing, but at a much lower rate than it is in Asian countries. The major causative factors are infections with HBV or hepatitis C virus (HCV), chronic alcoholism, and exposure to aflatoxin. Hemochromatosis and hereditary tyrosinemia less commonly give rise to HCC; the tumor usually develops in persons with cirrhosis.1,2

In Western countries, the tremendous rise in obesity, the metabolic syndrome, and diabetes also are thought to affect the incidence of HCC. Fatty liver and nonalcoholic steatohepatitis may lead to cirrhosis, and eventually, to HCC.3 Owing to the current vaccination strategies for HBV infection, screening, and treatment for HCV infections, future incidences and the common causes of HCC may change.2,3

Hepatocellular carcinoma usually metastasizes to regional lymph nodes and the lungs. The incidence of bone metastases is low.3,4 Multiple extrahepatic metastases usually develop after resection of the primary liver mass that receives palliative chemotherapy. Only a solitary metastasis, such as our case, should be considered for surgical resection. We report a 38-year-old man with a solitary skull metastasis owing to HCC, who presented to us with a painless scalp mass.

Case Report
At the time of this writing, a 38-year-old man presented at our institution with a scalp mass of 1 month’s duration. He had no recent history of a head trauma. On local physical examination, there was a well-defined localized mass over right temporal side of his scalp. We detected no head or neck lymphadenopathy.
The patient had an operation 4 months earlier to remove a liver mass that was diagnosed as HCC. Because the mass was small and the patient was in good condition, he received a liver transplant from a diseased donor. After the transplant, the patient received tacrolimus and mycophenolate mofetil, with no signs of rejection on routine clinical follow-up.

At a recent hospital admission to the neurosurgery ward, results of his laboratory tests showed normal liver function. The results of an assay for hepatitis B surface antigen were positive (because of the vaccination) and so were the results for hepatitis B core antibody; the results of a hepatitis B envelope antigen and a hepatitis B envelope antibody were negative. Results for HCV antibody and hepatitis D antibody were negative. We evaluated his alpha-fetoprotein level and found that it was elevated. No remarkable intrahepatic or extrahepatic recurrence was documented in the chest or on an abdominal computed tomography scan.

On brain magnetic resonance imaging, we saw a homogeneous, well-defined mass in right temporal area, on T1- and T2-weighted images, with gadolinium enhancement (Figures 1A, B, and C). The mass involved the inner and outer skull tables. We performed a right temporal craniectomy and removed the tumor. During the operation, we saw that the tumor was attached to the dural surface, showing evidence of gross tumor invasion. Therefore, the underlying dura was curetted and cauterized by bipolar forceps. We saw no brain parenchymal involvement. During the operation, we notice no significant bleeding.

We sent the specimen for a histopathologic evaluation. Microscopically, the tumor had invaded between the trabecular bones (Figure 2). There also was an area of vascular invasion in dura matter. Tumoral hepatocytes revealed the trabecular pattern of growth (arranged in plates of various thicknesses), and separated by sinusoid vascular spaces. The malignant cells were polygonal, with an eosinophilic granular cytoplasm, rounded nuclei, and prominent nucleoli (Figure 2). When the tumor cells were stained immunohistochemically, there was strong immunoreactivity for HepPar 1, anti-hepatocyte antibody (Dako A/S, Glostrup, Denmark) (Figure 3). Postoperatively, the patient’s serum alpha-fetoprotein levels decreased.

These findings are compatible with a diagnosis of metastatic HCC. We discharged the patient from the hospital with no neurologic deficits. We administered radiotherapy and chemotherapy, and he was alive at 3 months’ follow-up.

Figure 1. Magnetic Resonance Imaging Findings

(A) Magnetic resonance imaging of the brain. (B) T1-weighted magnetic resonance image demonstrates a homogeneous, well-defined mass in right temporal lobe, before and after gadolinium infusion. (C) We detected strong enhancement of the tumor.

Figure 2. Pathologic Findings

Malignant tumor cells infiltrate between the bone trabeculae (purple arrow) (present in vessels in favor of vascular metastasis [yellow arrow]) and individual tumor cells with eosinophilic cytoplasm arranged in solid pattern, which is consistent with metastases of hepatocellular carcinoma (red arrow; H&E ×400).
**Discussion**

Hepatocellular carcinoma is found most commonly in Asian countries because of infections with HBV and HCV. However, because many countries including Iran implemented a childhood hepatitis B vaccination program, we expected to see a noticeable decrease in the incidence of HBV infection.\(^1,2\) However, HCV replaced HBV as a major risk factor of HCC in Iran and worldwide.\(^5,6\) The most common sites of distant metastases are the lungs, the adrenal glands, and the bones.\(^4,7\)

The incidence of bone metastases from HCC is approximately 2% to 16%; that preferentially metastasizes to the axial skeleton including the vertebrae, the pelvic bones, and the ribs. Rarely, do the skull bones metastasize, and they usually affect men in their 60s.\(^4,7\)

Central nervous system dissemination of malignant cells occurs by 2 different routes.\(^8-10\) The first route is the hematogenous and lymphatic spread of cancer cells to the lungs, and after that, to the brain parenchyma. The second means of dissemination is via the Batson venous plexus, propagation through diploic venous channels, and because of expansion of the inner and the outer skull bones.\(^10,11\) In our case, pathological examination of the resected mass showed vascular cancer cell emboli; therefore, we thought that the tumor cells disseminated and reached the brain hematogenously.\(^4,7\)

Hsieh and associates\(^11\) summarized 68 patients with a cranial metastasis because of HCC. They mentioned that the incidence of skull metastases was 8.8%, which involved the caldarium, and skull base.\(^4,7\)

According to the literature, the most common clinical presentation of a skull metastasis from HCC is a painful subcutaneous mass, followed by neurologic deficits (ie, facial palsy, deafness, and visual defect), headache, and less commonly, seizure.\(^12\) Intracranial hemorrhage, epidural, or subdural hematomas are rare clinical presentations of skull metastasis.\(^13,14\) The most-common radiologic finding of a skull bone metastasis is the destructive or the osteolytic-type lesion, as was true with our patient.\(^12\)

Our patient was known to have HCC, with no definite risk factors, when he presented at our institution with a scalp mass. At that time, a bone metastasis was found in his skull without brain invasion. Overall, a distant metastasis is a poor prognosis. Although surgical resection of the metastatic lesion prolongs the patient’s life, it prevents intracranial hemorrhage and neurologic deterioration.\(^15\) Yen and associates suggest that in patients with an intracranial metastasis, surgical or radiologic treatment are associated with significantly longer survival.\(^8\)

Radiotherapy, chemotherapy, surgery, and palliative care have been performed for a skull metastasis to relieve pain and reduce the risks of neurologic sequelae.\(^15,16\) Transarterial embolization before a surgical intervention also has been performed.\(^15\) Finally, a skull metastasis from HCC is rare, and it negatively affects a patient prognosis. Still, it is important to diagnose early and use proper management to treat the metastasis.

**References**


*Figure 3. IHC Findings*

Tumor cells were positive for Hep Par1 (IHC ×400).


