Metastatic Hepatocellular Carcinoma in the Nasal Septum: Report of a Case

Chia-Der Lin, Ken-Sheng Cheng, Chia-Hung Tsai, Chi-Long Chen, and Ming-Hsui Tsai

Abstract: Metastatic hepatocellular carcinoma (HCC) in the sinonasal region is rare. We report the case of a 45-year-old male hepatitis B carrier who had metastatic HCC 2 years after resection of the primary tumor. The patient died of terminal hepatic failure 6 weeks after the discovery of nasal septal metastasis. The clinical and histopathologic characteristics of the primary and metastatic hepatocellular tumors are described. This is the first reported case of nasal septal metastasis from HCC.

Key words: hepatocellular carcinoma metastasis nasal septum

Hepatocellular carcinoma (HCC) with sinonasal metastasis is a rare condition. There have been reports of sinonasal metastasis from HCC in the paranasal sinuses or nasal cavity [1–5], but nasal septal metastasis from HCC has not been previously reported. We report a case of HCC with nasal septal metastasis.

Case Report

This 45-year-old male hepatitis B carrier had a diagnosis of HCC in January 1997. He underwent left lobectomy and cholecystectomy in March 1997. The resected tumor was 7 x 6 x 6 cm in size. He was followed up regularly thereafter and liver sonography in June 1997 showed recurrence of HCC. Transcatheter arterial embolization was performed five times between July 1997 and January 1998. One course of chemotherapy with 5-fluorouracil, adriamycin and cisplatin was given between August 9 and August 20, 1998. Monthly follow-up sonography between October and December 1998 still revealed multiple solid masses in the liver parenchyma.

In April 1999, the patient was admitted with a 2-week history of dizziness and several episodes of tarry stool. Physical examination revealed pale conjunctiva, icteric skin and sclerae, and mild ascites. A bulging granular transseptal mass (1 x 1 cm) over the nose was noted (Fig. 1). Hemoglobin was 5.5 g/dL, platelet count was 406,000/µL and white blood cell count was 8,760/µL. Blood biochemistry demonstrated the following concentrations: glutamate pyruvate transaminase 88 IU/L, bilirubin 10.12 mg/dL, albumin/globulin 2.4/3.6 g/dL and blood urea nitrogen/creatinine 14.6/0.51 mg/dL. Abdominal sonography showed multiple nodules in the liver parenchyma with ascites, while an ulcerative lesion in the duodenum was found using panendoscopy. Biopsies from both the nasal septal mass and the duodenal lesion revealed metastatic HCC. Palliative radiotherapy to the nasal septum was given from April 27 to April 30, 1999, with a total dose of 800 cGy in four fractions. However, his condition progressively deteriorated and radiotherapy was discontinued. He died from hepatic failure on May 16, 1999, 6 weeks after the appearance of the nasal metastatic mass.

Fig. 1. Transseptal papillomatous lesion over the nasal septum.

Departments of Otolaryngology, Gastroenterology and Pathology, China Medical College Hospital, Taichung. Received: 12 April 2002. Revised: 14 May 2002. Accepted: 4 June 2002.
Reprint requests and correspondence to: Dr. Chia-Der Lin, Department of Otolaryngology, China Medical College Hospital, 2 Yuh-Der Road, Taichung 400, Taiwan.
Pathologic findings

Grossly, the resected liver tumor was a well-defined grayish and friable tumor mass. Microscopically, it was a moderately differentiated HCC with tumor cells arranged in a giant trabecular or acinar pattern. Tumor emboli in the hepatic veins were noted close to the main tumor (Fig. 2). The histopathologic features of the nasal septal mass were similar to those of the primary HCC (Fig. 3). Immunohistochemically, both primary tumor and metastatic lesion were negative for α-fetoprotein.

Discussion

HCC is a common primary hepatic malignancy with an incidence that varies greatly in different regions of the world. It is highly prevalent in Southeast Asia, Japan, Korea and sub-Saharan Africa [6]. The annual incidence of HCC reaches 10 to 25 cases per 100,000 population in Taiwan. Hepatitis B virus causes 80 to 90% of HCC in Taiwan, and hepatitis C virus is the second most common etiologic agent [7]. HCC has a high potential for metastasis, especially in recurrent cases [8]. The most frequent metastatic sites of HCC include lung, regional lymph nodes, adrenal gland and bone [8, 9]. Skeletal metastases of HCC usually occur in the vertebrae, ribs and long bones [9]. Reported sites of HCC metastasis to the head and neck region include the jaw [10, 11], orbital cavity [12] and skull [13] (Table 1). Metastasis of HCC to the sinonasal area is rare, with only five previous reports (Table 2) [1–5].

Metastatic tumors in the nose and paranasal sinuses arise most frequently from the kidney, followed by lung, breast, urogenital tract, gastrointestinal tract, thyroid and pancreas [14, 15]. Metastatic tumors to the paranasal sinuses have no distinctive clinical or radiologic features that may facilitate their early diagnosis. Epistaxis, facial deformity, pain and nasal obstruction are the common presenting symptoms, which are identical to those produced by primary tumors in the same area [14, 15].
Table 1. Summary of previous reports of hepatocellular carcinoma metastasis in the head and neck region, excluding the sinonasal region

<table>
<thead>
<tr>
<th>Source</th>
<th>Metastatic site</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshimura et al [10]</td>
<td>Mandible/maxilla</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Mandible</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Maxilla</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Mandible and maxilla</td>
<td>1</td>
</tr>
<tr>
<td>Font et al [12]</td>
<td>Orbital cavity</td>
<td>11</td>
</tr>
<tr>
<td>Chang and Howng [13]</td>
<td>Skull</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 2. Summary of the clinical presentations in previously reported cases of hepatocellular carcinoma metastatic to the sinonasal area

<table>
<thead>
<tr>
<th>Source</th>
<th>Age (yr)/ sex</th>
<th>Presenting signs/ symptoms</th>
<th>Anatomic site</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Izquierdo et al [1]</td>
<td>59/male</td>
<td>Epistaxis, nasal obstruction, facial</td>
<td>Left maxillary sinus with extension to nasal cavity</td>
<td>Died of terminal hepatic failure an unspecified interval after appearance of sinonasal metastasis</td>
</tr>
<tr>
<td>Patankar et al [2]</td>
<td>50/male</td>
<td>Nasal obstruction, epistaxis</td>
<td>Left nasal cavity</td>
<td>NS</td>
</tr>
<tr>
<td>Frigy [3]</td>
<td>61/male</td>
<td>Recurrent epistaxis</td>
<td>Left ethmoid sinus with extension to nasal cavity</td>
<td>Died of sudden respiratory failure 2 months after appearance of sinonasal metastasis</td>
</tr>
<tr>
<td>Knobber and Jahnke [4]</td>
<td>82/male</td>
<td>Recurrent epistaxis</td>
<td>Maxillary and ethmoid sinus with extension to nasal cavity</td>
<td>Died of hepatic failure an unspecified interval after appearance of sinonasal metastasis</td>
</tr>
<tr>
<td>Mochimatsu et al [5]</td>
<td>67/male</td>
<td>Proptosis</td>
<td>Sphenoid sinus</td>
<td>Died of terminal hepatic failure 21 months after appearance of sinonasal metastasis</td>
</tr>
<tr>
<td></td>
<td>40/male</td>
<td>Headache, left cheek pain</td>
<td>Left ethmoid sinus</td>
<td>Died of hepatic coma 1 month after appearance of sinonasal metastasis NS</td>
</tr>
<tr>
<td></td>
<td>67/male</td>
<td>Left exophthalmos</td>
<td>Left frontal sinus</td>
<td></td>
</tr>
<tr>
<td>Current report</td>
<td>45/male</td>
<td>Nasal septal granular mass</td>
<td>Isolated nasal septum</td>
<td>Died of terminal hepatic failure 6 weeks after appearance of nasal septal metastasis</td>
</tr>
</tbody>
</table>

NS = not stated.

The pathogenesis of metastatic paranasal/nasal tumors can be classified into lymphogenous or hematogenous spread. Once they have invaded the lymphatic system, malignant cells from most parts of the liver can spread along lymphatic channels to the hepatic lymph nodes in the porta hepatis, thence to the celiac nodes, and finally into the thoracic duct [16]. Therefore, regional lymph nodes such as hepatic, peripancreatic, celiac and paraaortic lymph nodes would be invaded before spreading into the head and neck region. This is not in accordance with the clinical presentation of an isolated metastatic paranasal/nasal tumor.

HCC is known to have a predilection for intrahepatic vascular invasion, particularly of the portal vein (Fig. 3). In autopsy studies of HCC, Nakashima et al [8] and Yuki et al [17] found tumor thrombosis of the portal vein and major hepatic vein in more than 60% of cases, which correlated with tumor size and macroscopic type of the primary tumor. A continuous tumor thrombus involving the inferior vena cava was found in some of these cases. In addition to conventional hematogenous spread via the caval venous system, Nahum and Bailey emphasized the role of the vertebral venous plexus in an unusual retrograde pattern of tumor spread [15]. The prevertebral and vertebral venous system consists of epidural and prevertebral veins with innumerable intertwining vessels that communicate at every somite level with either the intercostal veins, the venae cavae, the azygous system or the pelvic veins [18]. Inasmuch as there are no valves, an increase in intrathoracic or intraabdominal pressure could drive tumor cells into the vertebral venous plexus. Such retrograde flow may sometimes progress superiorly as...
far as the skull base. Emboli spread in this way reach the great venous sinuses of the skull base such as the pterygoid plexus, cavernous sinus, superior portion of the pharyngeal plexus and, by retrograde spread, enter the paranasal sinuses. This would explain the pathogenesis of metastatic renal, bronchogenic, breast and urogenital carcinomas in the paranasal sinuses [14], and suggest a possible mechanism of metastatic tumour spreading to the nasal cavity in this case.

Duodenal metastasis from HCC was also noted in this case. There are few previous reports of metastatic HCC to the duodenum, and these usually present with upper gastrointestinal bleeding [19, 20]. The pathogenesis of HCC metastasis to the duodenum may be via metastatic lymph nodes infiltrating into the adjacent duodenum [19], or direct extension of the bulging HCC into the lumen of the duodenum [20].

Our patient eventually died of terminal hepatic failure with marked hyperbilirubinemia. HCC with jaundice may be caused by hepatic insufficiency due to liver parenchymal disease or by obstructive jaundice due to the tumor [21]. Acute or fulminant hepatic failure may also result from massive intravascular metastatic carcinomatous embolization [22]. The prognosis of patients with HCC who present with jaundice due to hepatic insufficiency is dismal [21], and the prognosis of metastatic HCC is generally poor [10].

References