Hepatoma presenting as craniospinal metastasis: analysis of sixteen cases

Jen-Pei Lee

Abstract

Sixteen cases of hepatoma presenting as craniospinal metastasis without obvious hepatic involvement were reviewed. Metastatic spread of hepatoma to the cerebrum was found in one case, to the cranium in six cases, and to the vertebral bone in nine cases. All of these cases had mildly abnormal liver function when first evaluated. Of those patients with hepatoma, 56% had evidence of hepatomegaly. Alpha fetoprotein was present, at levels greater than 320 ng/ml, in 69%. Ninety four per cent died of the primary liver disease within one year. For any patient who develops craniospinal metastasis of unknown origin in a geographical area where hepatoma is a common disease, hepatoma should be considered in the differential diagnosis.

(J Neurol Neurosurg Psychiatry 1992;55:1037–1039)

Hepatoma has a widely varying incidence in different parts of the world. It is at least 10 times higher in South African black groups and Southeast Chinese than in North Americans and Europeans.1 In Taiwan, hepatoma is one of the most common malignancies. In postmortem examinations, it represents 5-5% of the total and 21-8% of all malignancies. Most patients with hepatoma present with hepatomegaly, right upper quadrant pain, or an abdominal mass.2 On rare occasions, the patients may have initial symptoms related exclusively to the metastatic disease. In this paper, we describe our experience of 16 patients with hepatoma who presented primarily as craniospinal metastasis without obvious hepatic involvement.

Materials and methods

A retrospective review of the clinical records of 768 patients with primary hepatoma admitted to Chang Gung Memorial Hospital between July 1981 and June 1988 produced 16 patients who initially presented with neurological symptoms caused by craniospinal metastasis. None of these patients had any obvious hepatic symptoms suggestive of primary liver diseases. The final diagnosis was confirmed by histological examination of operative or biopsied specimens from the site of metastasis which caused the neurological complication. There were 13 men and three women, ranging in age from 26 to 60 (mean 44) years. On the basis of site of metastasis, three groups were found: cerebral, cranial, and vertebral, including one, six, and nine cases respectively. Routine liver function tests and a serological test for hepatitis B surface antigen were done on the first day of admission. Additional liver investigations, including serum alpha fetoprotein (AFP) measurements, liver-spleen CT, abdominal sonography, or coeliac angiogram, were performed after the tissue diagnosis had been made. AFP was classified as “positive” if the level was above 320 ng/ml.

Results

Clinical features

The clinical manifestations and the site of metastasis in each patient are listed in the table.

In the cerebral group, the patient presented with progressive weakness and numbness in the left arm, followed by intracranial haemorrhage and disturbed consciousness. Tumour bleeding was confirmed by histological study.

In the cranial group, two different sites of metastasis were found, the calvarium and the base of the skull; there were three instances of each. Two of the three patients with metastasis to the calvarium had a progressively enlarging mass in the vertex. During the operation, no intradural invasion was found. The third patient had symptoms and signs suggestive of intracranial tumour, and intradural extension and parenchymal involvement of the brain were demonstrated. All three patients with metastasis to the base of the skull presented with symptoms of cranial nerve involvement. Those with retrobulbar or parasellar involvement developed diplopia, ptosis and limitation of eye movements. The patient with metastasis to the jugular fossa and hypoglossal canal manifested dysarthria and tongue atrophy.

In the vertebral group, one metastasis was in the cervical spine, two in the thoracic region, four in the lumbar vertebrae, and two in the sacrum. All of these patients experienced back pain or neck pain as the first symptom, followed by symptoms of spinal cord involvement. The patient with cervical involvement presented with arm weakness. The patients with lesions in the thoracic region had progressive paraparesis as the predominant symptom. With metastasis of the lumbar vertebrae, all except one patient presented with paraparesis or sphincter problems, or both. This patient’s symptoms mimicked a herniated intervertebral disc. With lesions in the sacral region, sphincter problems were the main complaint.

Hepatomegaly is an important symptom
<table>
<thead>
<tr>
<th>Case no</th>
<th>Age</th>
<th>Sex</th>
<th>Presenting symptoms</th>
<th>Site of metastasis</th>
<th>Hepatomegaly</th>
<th>Survival (from the onset of symptoms) (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>59</td>
<td>M</td>
<td>Left arm weakness and numbness for one week, sudden onset of headache with left hemiplegia and disturbed consciousness</td>
<td>Brain parenchyma (right frontotemporal parietal) with intracranial haemorrhage</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Cranial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>F</td>
<td>Progressive enlarging scalp mass over vertex for 4 months</td>
<td>Calvarium, dura, brain parenchyma</td>
<td>–</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>48</td>
<td>F</td>
<td>Progressive enlarging scalp mass over the left parietal and right frontal region for 6 months</td>
<td>Calvarium</td>
<td>+</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>M</td>
<td>Progressive enlarging scalp mass in right occipital region for 2 months</td>
<td>Calvarium</td>
<td>+</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>M</td>
<td>Diplopia and proptosis for 2 months. Ophthalmoplegia for 1 month</td>
<td>Skull base (retrobulbar)</td>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>M</td>
<td>Progressive dysarthria and atrophy of left tongue for 2 months</td>
<td>Skull base (jugular fossa hypoglossal canal)</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>47</td>
<td>M</td>
<td>Right hemiparesis for 3 months blurred vision with ptosis and limitation of eye movement (ODE) numbness on the right forehead for one month</td>
<td>Skull base (paraspina)</td>
<td>+</td>
<td>6</td>
</tr>
<tr>
<td>Vertebral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>M</td>
<td>Root pain over right C7. Right arm weakness for 2 weeks</td>
<td>C7</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>M</td>
<td>Back pain for 2 months. Progressive paraparesis for 2 months</td>
<td>T7</td>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>10</td>
<td>38</td>
<td>M</td>
<td>Lower back pain for 6 weeks. Paraparesis for 3 weeks</td>
<td>T8, 9</td>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>11</td>
<td>60</td>
<td>M</td>
<td>Low back pain for 4 months. Progressive paraparesis for 4 months, sphincter disturbance for 1 month</td>
<td>L1, 2</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>50</td>
<td>F</td>
<td>Lower back pain with progressive paraparesis for 2 months</td>
<td>L2, 3</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>13</td>
<td>46</td>
<td>M</td>
<td>Lower back pain with numbness over left leg for 2 months, left sciatica for 2 weeks</td>
<td>L4</td>
<td>–</td>
<td>7</td>
</tr>
<tr>
<td>14</td>
<td>31</td>
<td>M</td>
<td>Lower back pain with left sciatica for 3 months. Spinalg disturbance for 2 weeks</td>
<td>L5</td>
<td>+</td>
<td>4</td>
</tr>
<tr>
<td>15</td>
<td>26</td>
<td>M</td>
<td>Buttock pain radiating to right thigh for 2 months, sphincter disturbance for 1 month</td>
<td>Sacrum</td>
<td>+</td>
<td>13</td>
</tr>
<tr>
<td>16</td>
<td>50</td>
<td>M</td>
<td>Buttock pain with sphincter disturbance for 3 months</td>
<td>Sacrum</td>
<td>+</td>
<td>7</td>
</tr>
</tbody>
</table>

related to liver disease, but only 56% (9/16) of patients with hepatoma in this series had signs of hepatomegaly.

**Laboratory data**

In none of these 16 patients were liver function tests (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase) entirely normal. Hepatitis B surface antigen was checked on the first day of admission but only 75% (12/16) of specimens were positive. Of all the patients in which AFP was examined after tissue diagnosis, 69% (11/16) were positive.

Abdominal sonography was performed in all cases after establishment of the pathological diagnosis. In all except two, mass lesions were found in the liver. Coeliac angiography was done in one of these two cases and showed multiple hypervascular nodules in the liver. Liver–spleen CT demonstrated a positive finding in the other case.

**Survival**

The length of survival was recorded from the onset of the first symptom. Fifteen of 16 (94%) patients died within one year. All died of hepatic failure, except one who succumbed to acute respiratory failure caused by lung metastasis with massive pleural effusion.

**Discussion**

Although necropsy examinations of patients dying of hepatocellular carcinoma have revealed evidence of metastasis in 50–75% of cases, it is distinctly unusual for the initial clinical presentation to be related primarily to the presence of metastasis, without overt evidence of hepatic involvement. Popper and Schaffner divided hepatocellular carcinoma into frank, febrile, acute abdominal, icteric, metastatic, and occult types. Patients with the metastatic type, presenting with symptoms and signs related to distant metastasis without abdominal discomfort or palpable liver mass, are quite uncommon, comprising 1.5–5.3% in different series.

Earlier reports have stated that extraphepatic metastasis of primary carcinoma of the liver is uncommon. The lung and regional lymph node are the most common sites of metastasis. The central nervous system is an unusual site.

The most common sites of metastasis causing CNS complications are the vertebrae and spinal epidural space. Of 19 such cases described by Collomb et al., 13 patients had metastasis to the vertebrae and epidural space, one to the cranium, and five to the cerebrum. In Chang and Chen's series, vertebrae and the epidural space were involved in four cases, the cranium in two, and the cerebrum in one. A similar distribution was noted in our series.

The metastatic spread of primary hepatoma might initially result from invasion of the hepatic and portal veins. The regional lymph nodes, including periportal and peripancreatic nodes, were extensively involved. Pulmonary vascular metastasis then develops after the venous structures have been invaded and may be followed by widespread hematogenous spread with metastasis to the bone and brain.

Some explanations offered for the rarity of brain metastasis in patients with hepatoma include a rapidly fatal course, most patients having died within six months of the onset of symptoms. It is also possible that there have been more cases of metastasis to the nervous...
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*J Neural Neurosurg Psychiatry* 1992 55: 1037-1039
doi: 10.1136/jnnp.55.11.1037

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