Hepatoma presenting as craniospinal metastasis: analysis of sixteen cases

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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 vertebrae 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.

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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 post-mortem examinations, it represents 5.5% of the total and 21.8% of all malignancies.¹

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

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Table Clinical features of 16 cases of metastatic hepatomas

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

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,³ it is distinctly unusual for the initial clinical presentation to be related primarily to the presence of metastasis, without overt evidence of hepatic involvement.⁴ Popper and

Schaffner⁵ 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.¹

Earlier reports have stated that extrahepatic metastasis of primary carcinoma of the liver is uncommon. The lung and regional lymph node are the most common sites of metastasis.² The central nervous system is an unusual site.^{4,6,7} 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*,⁷ 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,⁶ 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.⁸

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.⁴ It is also possible that there have been more cases of metastasis to the nervous

system, which perhaps have been overlooked or obscured by the symptoms of hepatic or other metabolic encephalopathy.⁹⁻¹⁰ When there is an absence of clinical manifestations, brain metastasis from primary hepatoma may be of little clinical significance. Most cases were found at necropsy,¹¹ so there is a discrepancy between the incidence of clinical neurological complications and incidence at necropsy.⁶

In rare instances, an apoplectic onset of symptoms from a cerebral metastasis has been reported.⁶ The first patient in our series presented this way, with a history of progressive left arm weakness and numbness followed by sudden onset of left hemiplegia and disturbed consciousness.

Metastasis to the skull may be found either in the calvarium or in the base. When in the calvarium, it may be either extradural only,⁶⁻¹² as in cases 3 and 4, or may exhibit intracerebral extension⁶ with raised intracranial pressure or focal symptoms, as in case 2 of our series. When metastasis to the base of the skull occurs, the cranial nerves may be involved, without associated increase of intracranial pressure, as in cases 5, 6 and 7 of this series.

Hepatoma is believed to be an unusual primary among cases of spinal cord compression by metastatic tumours. In different series among white groups, 1.2–3.0% were reported.¹³⁻¹⁶ This is in contrast to the much higher incidence of 17.1% among African cases.¹³ The nine cases reported here represent 15% of 59 cases of metastatic cancer to the spinal column (unpublished data) in our hospital series between 1981 and 1988, which is close to that described in the African cases.¹³ The vertebrae have been reported by Carnahan¹¹ and Green¹⁷ as the most common site of bone metastasis of hepatoma cells through the vertebral vein. From the overview of this series, the lumbar spine seems to be the most frequent site of vertebral metastasis, representing 44% (4/9) of cases. Clinically, all the patients with vertebral metastasis had a history of back pain or neck pain as the first symptom followed by symptoms of spinal cord compression. When the cervicothoracic spine was involved, myelopathy was the predominant symptom. When metastasis to the lumbar spine occurred, cauda equina syndrome was the main presentation. When sacrum metastasis developed, sphincter problems were the chief complaint.

Routine laboratory studies may provide little diagnostic help before biopsy. Although abnormal liver function may be detectable in the early stage, these findings do not differ from chronic liver disease. The most distinctive diagnostic laboratory test presently available for hepatoma is the immunoserological assay for AFP. The serologically positive percentage varied from 50% to 79.6% in different series.¹ In our series, 69% of patients with hepatoma were found to be positive. Serum AFP levels have been shown to be correlated with liver weight in AFP-producing hepatoma. Sometimes it is negative or low in patients with early hepatoma. However, the measurement of

serum AFP is useful in screening for early hepatoma. Even small hepatomas sometimes may present with elevated serum AFP level, which can be determined easily.

Liver ultrasound is a sensitive and easy method for the detection of hepatic tumours. Shen *et al.*¹⁸ reported a 93.9% (31/33) detection rate even with small hepatomas. Only a 54% detection rate was described by Kobayashi *et al.*¹⁹ In this series, 87.5% (14/16) of patients had a positive finding. Coeliac angiography is an established method for the diagnosis of hepatoma. A 77% detection rate was reported by Kobayashi *et al.*¹⁹ and the second case in our series was detected only by this method. Although it is sensitive and specific in detection of hepatoma, it is invasive and impractical for the follow up of high risk populations of patients.

It is well known that hepatoma runs a rapidly fatal course. In 83.5% of patients, death occurred within 6 months of the onset of symptoms.⁵ In our series, 93.8% of patients died within one year. The average survival is 6.3 months after the onset of symptoms. The ultimate prognosis of patients with metastasis to the central nervous system is dependent on the natural history of the primary lesion.

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