

Vertebral Metastasis from Hepatocellular Carcinoma of Unknown Origin

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This 51-year-old man suffered from paraparesis of 1-week history. On preoperative images, spinal cord compression by infiltrative vertebral mass was shown at T3 and T4 level. Several months earlier, he underwent surgical resection of left 2nd to 4th ribs, due to painful growing chest wall mass, which was proved to be hepatocellular carcinoma. All available diagnostic procedure failed to uncover origin of malignancy. Operation was followed by adjuvant irradiation and chemotherapy to the vertebral mass, however he only to die in 3 months after operation. This is an extremely rare case of ectopic hepatocellular carcinoma at thoracic vertebrae which showed very aggressive clinical course. Possible pathogenic process is presented and discussed.

KEY WORDS : Ectopic hepatocellular carcinoma · Metastasis · Vertebrae.

Introduction

Hepatocellular carcinoma (HCC), one of the most prevalent malignancies in the world, commonly metastasizes to the extrahepatic organs, even into the intracranial space⁷. Symptomatic skeletal metastasis, however does not show up frequently and this is particularly true if the HCC initially presents as a symptomatic skeletal involvement^{4,9-13}. Ectopic liver tissue, occurring outside the mother liver parenchyma, seems to suffer more susceptible carcinogenic insults than the mother liver because of its structural impairment. And therefore, ectopic HCC can be defined as the HCC arising from liver parenchyma in an extrahepatic organ or tissue^{1,3,14}. Among the skeletal metastases from ectopic HCC, presentation of chest wall mass is very extraordinary^{2,6}, and furthermore, its vertebral involvement presenting as spinal cord compression with subsequent paralysis has not been reported yet.

To our knowledge, this is the first case report of vertebral metastasis from the ectopic HCC. A male patient who presented with paraparesis due to thoracic cord compression by the HCC metastasis is described. Full diagnostic work-up was conducted for disclosure of the primary site of HCC, but we could not find any culprit. Metastasis from the ectopic HCC or HCC of unknown origin, which initially found at the chest wall, was the final diagnosis. We briefly summarized our case and tried to figure out possible pathogenic mechanisms.

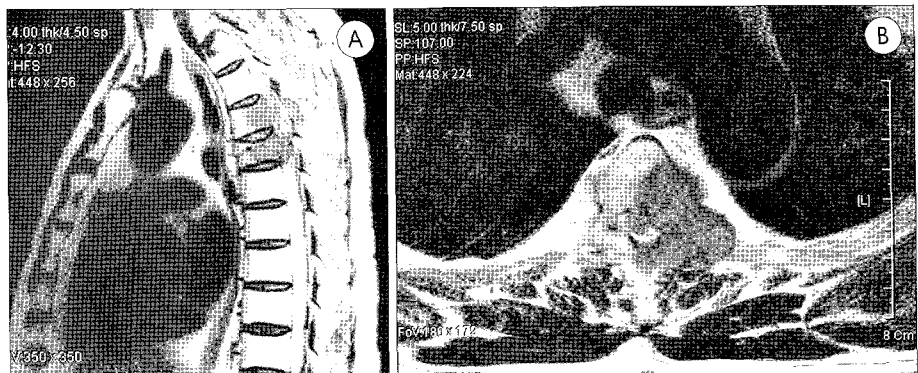


Fig. 1. Preoperative magnetic resonance images. (A) Sagittal T2-weighted left paramedian image shows infiltrating compressing mass at T3 and T4 vertebrae. Note signal changes within vertebrae and spinal cord. (B) Axial T2-weighted image depicts spinal cord compression by the mass located at the left side of vertebral bodies, pedicles, lamina and costochondral junction.

• Received : August 5, 2005 • Accepted : February 8, 2006

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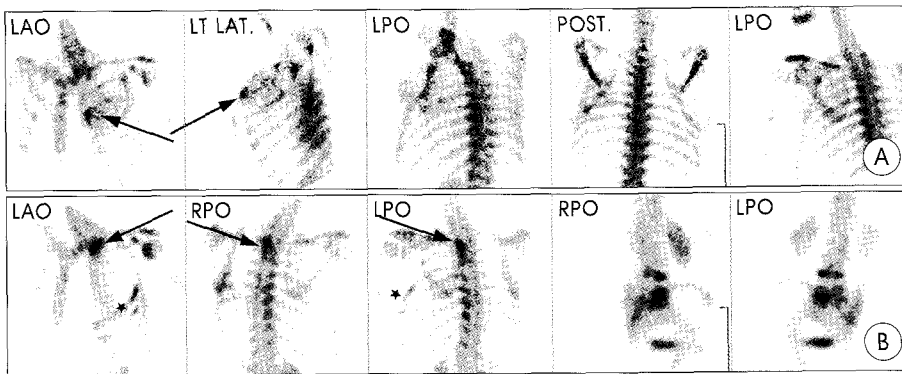


Fig. 2. Radionuclide bone scans. (A) Tc^{99m} -Bone scan, obtained 3.5 months prior to the admission, shows hot uptake spots of radionuclide at the left anterior chest wall of the 2nd to 4th ribs (arrows). (B) Bone scan at admission shows newly developed hot uptake foci mainly located at the left side of T3 and T4 vertebrae (arrows) and 5th to 6th ribs (asterisks).

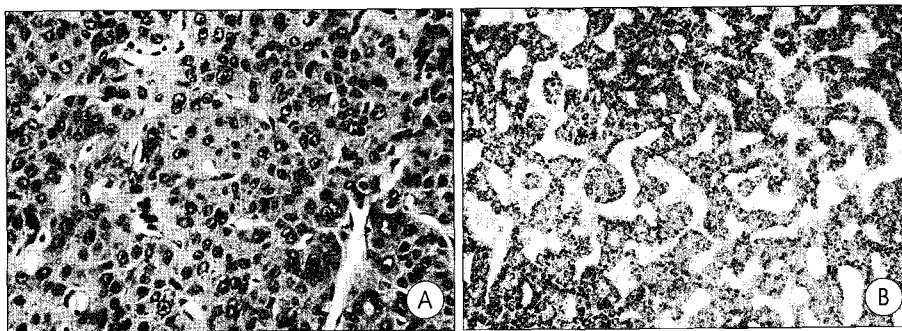


Fig. 3. Photomicrographs in the surgical decompression of left anterior chest wall. (A) The section from the soft tissue of chest wall showing metastatic hepatocellular carcinoma (H&E, $\times 100$). (B) On immunohistochemical staining for anti-hepatocyte antigen, the tumor cells show immunoreactivity in their cytoplasm (IHC, $\times 100$).

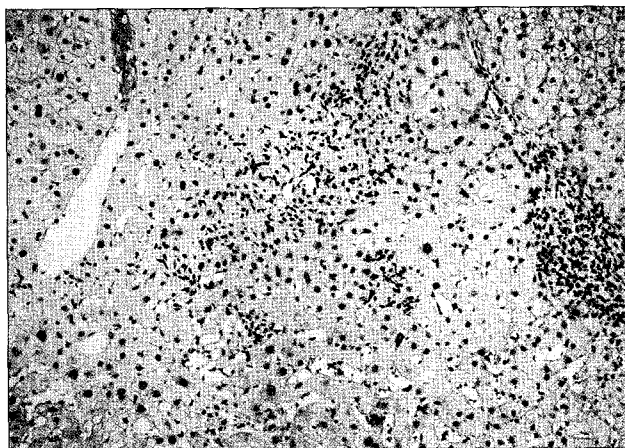


Fig. 4. Photomicrograph in the liver biopsy shows chronic hepatitis with mild liver cirrhosis (Child A), but no malignancy (H&E, $\times 50$).

Case Report

A 51-year-old male patient was brought to our institute for lower limb paralysis of 1-week duration. On neurological examination, he showed spastic paraparesis (Gr. 2), paresthesia below T-4 cord level, hyperactive deep tendon reflexes, reduced anal tone and overflow voiding incontinence. He also felt

tenderness when palpating upper dorsal area. Serological tests for hepatitis B showed positive antigen and antibody, and -fetoprotein (AFP) of 45ng/ml (normal: <20 ng/ml). He showed mild trophic changes of the skin texture, but did not exhibit icteric changes in the skin or ascites in the abdomen. Magnetic resonance (MR) imaging of the thoracic spine showed spinal cord compression by the metastatic mass that infiltrated the bodies and pedicles, mainly left side of the T3 and T4 vertebrae (Fig. 1).

He had been diagnosed as hepatitis B carrier 8 years ago, and continued outpatient visit to hepatology specialty. Three and a half months prior to the present admission, he underwent resection of the left 2nd to 4th ribs and parietal pleura in addition to reinforcement with Teflon, due to painful anterior chest wall mass (3 \times 5cm) (Fig. 2). Histopathological examination revealed HCC (Fig. 3), and various diagnostic attempts including celiac angiography, peritoneoscopy, gastrofiberscopy and abdominal ultrasonography/MRI had been applied to uncover the primary focus of the HCC, but only to fail. Liver biopsy showed chronic hepatitis with mild liver cirrhosis (Child A) (Fig. 4). Postoperatively, corresponding area including sternum and vertebrae was externally irradiated (5000 rad / 6 weeks).

At the present visit, we urgently conducted radioisotope bone scan to detect another foci of skeletal metastasis because we consider this to be another metastatic vertebral involvement, but additional hot uptake lesions were not found except those at T3 and T4 vertebrae, the same as shown on MRI. Because of previous operative scarring on the left anterior chest wall, we planned to decompress the lesion via a posterior approach. Following laminectomy T3-T5, highly vascular tumor was encountered at the left side of pedicle and posterior surface of bodies, and this fragile mass was removed in piecemeal fashion by using bipolar coagulator, hemostatic sponge and bone wax. HCC with unknown primary site was also confirmed in histopathological examination (Fig. 5). Despite booster external irradiation (3000 rad) and 3 cycles of chemotherapy (cisplatin 20mg/m², adriamycin 40mg/m²), his neurological condition remained unchanged and even deteriorated progressively.

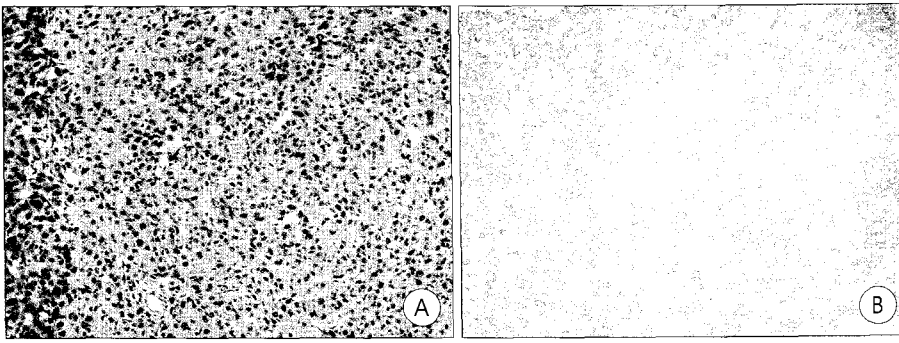


Fig. 5. Photomicrographs in the surgical decompression of pedicle and posterior surface of bodies of T3–4. The metastatic hepatocellular carcinoma invades the bone and marrow tissue.

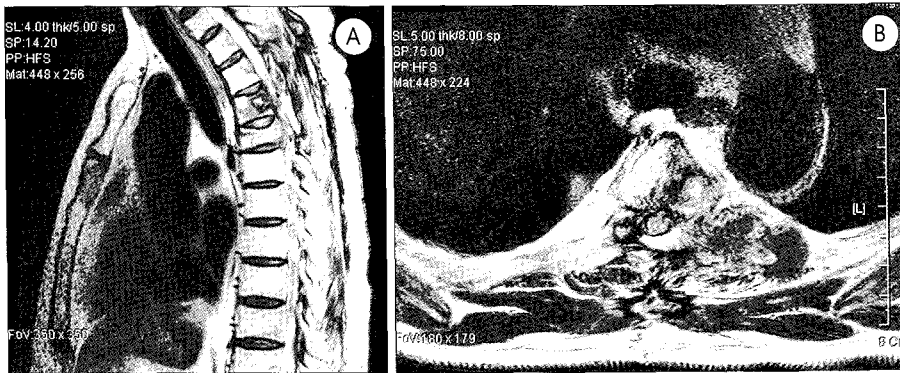


Fig. 6. Magnetic resonance images taken one month after the operation. (A) Sagittal T2-weighted left paramedian image shows more progressive compression fracture at T3 and T4 with consequent aggravation of kyphotic deformity. (B) Axial T2-weighted image demonstrates restoration of the compressed cord, but also shows regrowth of the mass at the left side of costochondral junction.

Consecutive MR images also showed progression of the lesion (Fig. 6). He died 3 months postoperatively due to the adult respiratory distress syndrome and sepsis caused by infection of pressure sore at sacrum.

Discussion

Metastasis is a fairly common sequel in HCC, eventually occurring in more than half of patients and chiefly affecting the lungs, abdominal lymph nodes, and diaphragm¹¹. Skeletal metastasis from the HCC is a relatively well-documented condition with the incidence of 2 to 16%, and mostly to the vertebra, rib, sternum, skull and long bones. However, the initial clinical manifestation of symptomatic skeletal metastasis without accompanying hepatopathy is uncommon, in patients with HCC⁹⁻¹³.

An ectopic liver is a very rare developmental anomaly that is most often detected incidentally by peritoneoscopy, laparotomy, and autopsy. It occurs in various sites adjacent to the liver, including gallbladder, hepatic ligaments, spleen, omentum, retroperitoneum, and thorax. Ectopic liver has an incomplete vascular and ductal system, is functionally impaired compared to the normal liver, and therefore, it is more prone to hepatocarcinogenesis. This is also proved by the fact that the mother

liver had no HCC in almost all cases with ectopic HCC^{1-3,6,14}. The origin and definition of the ectopic liver, however, are still inconclusive. Some asserted “ectopic” liver as liver tissue connected to the mother liver by vascular stalk (accessory lobe). Others insisted that “ectopic” HCC originate from liver tissue exclusively outside the liver proper without any connection with the mother liver, although the distinction between two is not always possible^{1,14}. The respective incidence of accessory lobe was 0.09%, and ectopic liver was 0.47%, according to the laparoscopic series¹¹. The latter seems to be more suitable explanation for the current situation, because we could not find any cancerous changes of mother liver or any connection of ectopic HCC with the mother liver. In overall, the development of HCC originating from an ectopic liver, without evidence of HCC in mother liver, is an

unusual phenomenon. Hepatoid adenocarcinoma, a variant of adenocarcinoma producing AFP and morphologically mimicking HCC, arises most frequently from the mucosa of stomach. And, this lesion must be differentiated from the HCC by numerous liver-specific proteins and immunohistochemistry^{4,10}. Near-normal level of AFP, absence of gastric malignancy on gastrofiberoscopy and peritoneoscopy, and strong staining for anti-hepatocyte antibody in immunohistochemistry, this case exhibited, are the main distinguishing points from the hepatoid adenocarcinoma.

As for the pathogenesis involved, we initially suspected that HCC on mother liver regressed spontaneously at the time when the patient paid a clinical attention for skeletal metastasis. However, this assumption is very unlikely to occur if we consider absence of cancerous liver tissue in this patient (chronic hepatitis with mild cirrhosis). Spontaneous regression of HCC is an extremely rare condition⁵. We suggest that the ectopic HCC initially arose *de novo* outside the liver in the vicinity of the chest wall and then, extended to the vertebrae by contagious spread for the following reasons: First, ectopic liver tissue is already well known for its tendency of hepatocarcinogenesis than the mother liver is, whether it is accessory or ectopic¹¹. Second, we could not find any evidence of HCC elsewhere in the body, except ribs and vertebrae. Third, there has been

a report concerning HCC metastasis to the ribs⁶), and spatial distribution of this primary ectopic HCC to the vertebrae could be sufficiently recognized, although the patient underwent wide resection including ribs and pleura was followed by irradiation. And fourth, we failed to verify the presence of non-cancerous liver parenchyma within the HCC in the specimen of vertebrae on histopathological examination. This is suggestive of the expansive growth of the HCC, and total cancerous replacement of liver tissue with the HCC. We therefore, suppose that primary ectopic HCC originally arose from the ribs or pleura in the chest wall, and spread to the vertebrae, although wide surgical resection of ribs including pleura and external irradiation was conducted. This is in contrast to the relatively benign nature of the previously reported cases^{2,6}), this patient showed very rapid clinical course. We are not sure that specific histopathological subtypes peculiar to this malignant nature would ever be existed.

Conclusion

There are some interesting points with regard to this case. First, a certain type of HCC shows skeletal metastasis as an initial clinical manifestation. Second, although the majority of ectopic HCCs that arise in the chest wall have been reported to show relatively benign clinical course, there are other variant that shows resistance to all treatment modalities. And last, clinicians should pay attention to this kind of unusual clinical course of ectopic HCC or HCC of unknown origin.

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