

**HEPATOCELLULAR CARCINOMA PRESENTING AS SPINAL METASTASIS**Majed Odeh<sup>1\*</sup>, Yana Kogan<sup>1</sup> and Jacob Bejar<sup>2</sup><sup>1</sup>Department of Internal Medicine A, Bnai Zion Medical Center, and Technion faculty of Medicine, Israel Institute of Technology, Haifa, Israel.<sup>2</sup>Institute of Pathology, Bnai Zion Medical Center, and Technion Faculty of Medicine, Israel Institute of Technology, Haifa, Israel.**\*Corresponding Author: Prof. Majed Odeh**Department of Internal Medicine A, Bnai Zion Medical Center, and Technion faculty of Medicine, Israel Institute of Technology, Haifa, Israel.  
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**ABSTRACT**

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world, and is the most common primary hepatic malignancy in adults. Bone metastasis as the initial manifestation of HCC is rare. However, it sometimes may be very serious with significant spinal cord compression. We report a patient with silent cirrhosis due to infection with hepatitis B virus, who presented with upper back pain of four weeks duration as the initial manifestation of HCC, with subsequent development of significant spinal cord compression due to vertebral metastasis. It is concluded that spinal metastasis from HCC should be considered in the differential diagnosis of un-resolving back pain in patients with underlying chronic liver disease, particularly cirrhosis, in order to prevent serious spinal cord compression with early intervention.

**KEYWORDS:** Hepatocellular Carcinoma, Cirrhosis, Bone Metastasis, Spinal Cord Compression.**INTRODUCTION**

Hepatocellular carcinoma (HCC) is the most common primary hepatic malignancy in adults, and one of the most prevalent cancers in the world, particularly in Asia and parts of Africa.<sup>[1,2]</sup> Although HCC occasionally arises in an otherwise apparently normal liver, it is usually associated with chronic underlying liver disease.<sup>[1,2]</sup> The most common presenting features are abdominal pain with detection of an abdominal mass in the right upper quadrant.<sup>[3]</sup> Extra-hepatic spread from HCC is not uncommon, and the lungs and regional lymph nodes are the most common sites of metastasis.<sup>[4]</sup> Bone metastasis as the initial manifestation of HCC is rare, and sometimes it may be very serious with significant spinal cord compression.<sup>[5-10]</sup> We describe a patient who presented with upper back pain of a four week duration as the initial manifestation of HCC with subsequent serious spinal cord compression due to vertebral metastasis.

**CASE PRESENTATION**

A 45-year-old previously healthy man was admitted with a four week history of upper back pain in the region between the scapulae. The pain was described as constant and dull, was exacerbated with movement, and was relieved only partially by analgesics. The patient denied fever, previous trauma to his back, and abdominal pain. His other medical history was unremarkable.

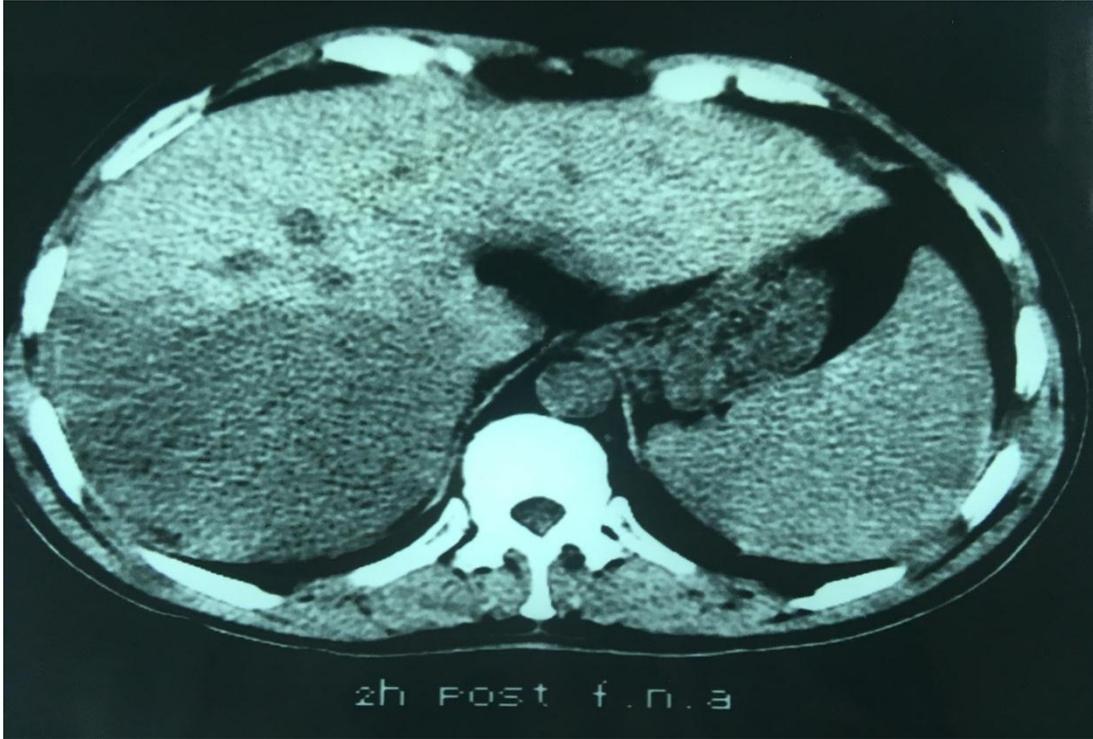
Physical examination revealed a heart rate of 76 beats per minute, blood pressure of 120/80 mm Hg, and a normal body temperature. There was a mild tenderness over the region of D<sub>2</sub> and D<sub>3</sub> thoracic vertebrae, no lymphadenopathy, and examination of the heart and lungs was normal. Abdominal examination was normal except of hepatomegaly with a 15 cm span of the liver which was tender. Neurologic examination was normal, and other physical findings were unremarkable.

Laboratory examination revealed the following results: hemoglobin was 15.2 g/dl, white blood cell count was 8000/mm<sup>3</sup> with 92% neutrophils, the platelet count and prothrombin time were normal. Serum aspartate aminotransferase was 203 IU/L (normal values ≤40 IU/L), serum alanine aminotransferase was 256 IU/L (normal values ≤40 IU/L), serum alkaline phosphatase was 296 IU/L (normal values ≤100 IU/L), serum gamma glutamyl transpeptidase was 750 IU/L (normal values ≤40 IU/L), and lactate dehydrogenase was 600 IU/L (normal values ≤480 IU/L). Other routine biochemical blood tests including bilirubin, calcium, albumin and globulin were within normal range. Serologic tests for hepatitis B surface antigen (HBsAg), HBeAg, and total anti-HB core antibody were positive.

Radiographs of the chest, and cervical and thoracic spine were normal, and radionuclide bone scan revealed no

abnormality. Abdominal CT scan demonstrated a heterogeneous enlarged liver containing a huge space occupying lesion in its right lobe (Fig. 1). The serum

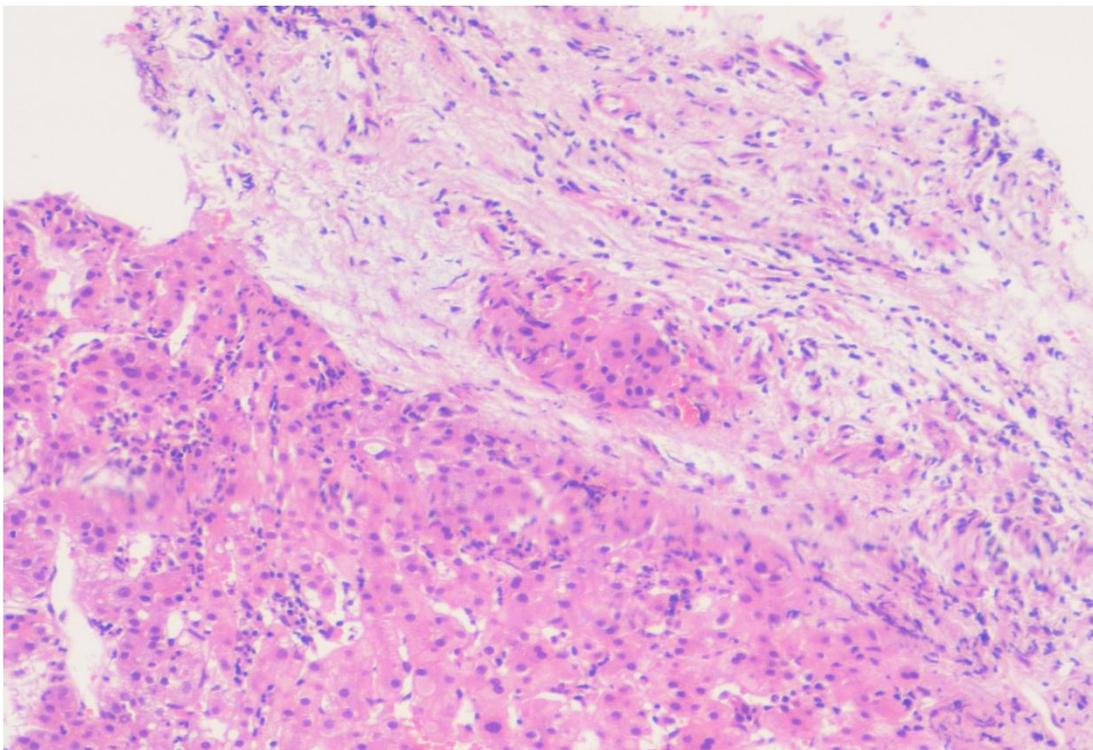
alpha fetoprotein was markedly elevated: 2083 ng/ml (normal values  $\leq 8$  ng/ml).



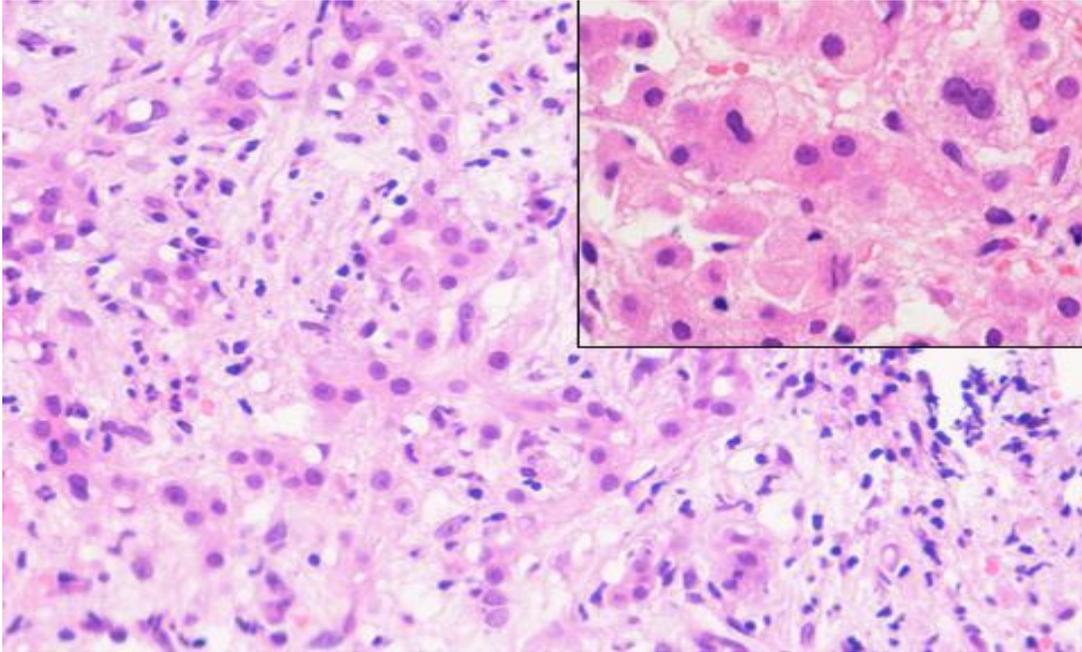
**Figure 1: Abdominal CT scan showing a heterogeneous enlarged liver containing a huge space occupying lesion in its right lobe.**

Liver needle biopsy was performed, and histologic examination of the biopsy specimen demonstrated irregular cirrhosis with active hepatitis component (Fig.

2), and macrotrabecular well differentiated hepatocellular carcinoma (Fig. 3).



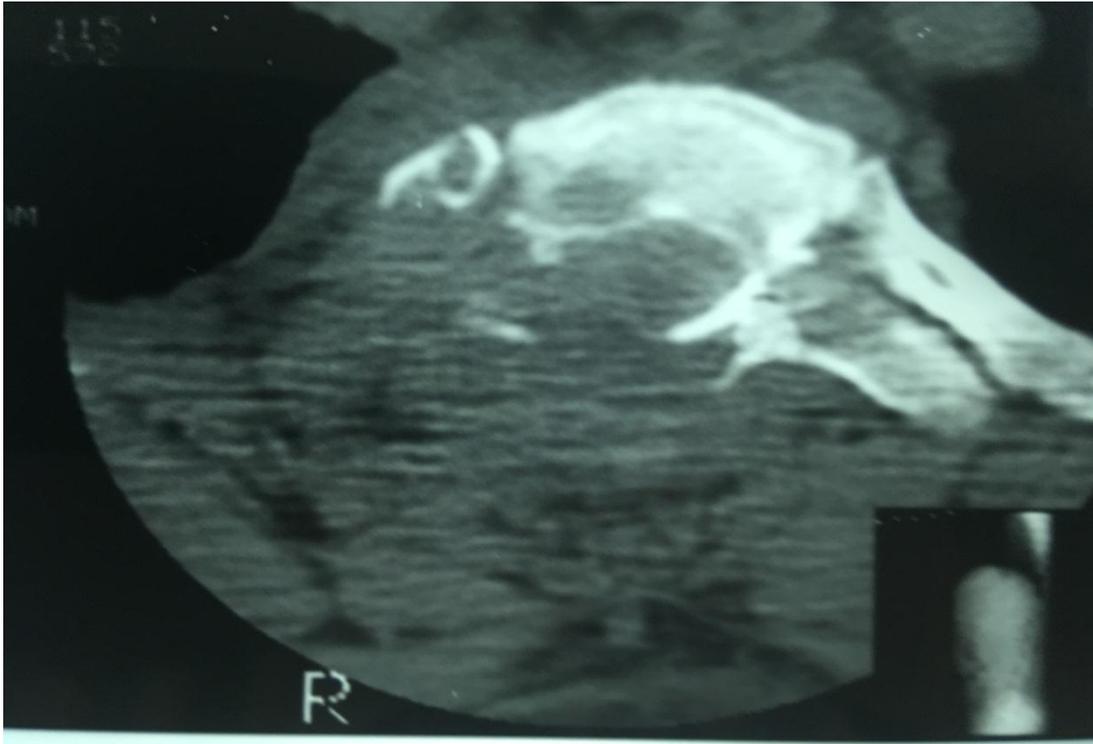
**Figure 2: Liver needle biopsy specimen showing cirrhotic remodeling of the parenchyma, low grade chronic lobular hepatitis, and complete septum formation. (x100). (H & E).**



**Figure 3: Hepatocellular carcinoma, well differentiated, macrotrabecular variant: The tumor is composed of large cells arranged in irregular formed 2 to 3 cell thick cords separated from each other by sinusoidal blood vessels lined by endothelial cells. (x200). [Insert]. The polyhedral tumor cells have abundant, finely granular, vacuolated, amphophilic cytoplasm, large nuclei with a prominent nucleolus. (x400). (H & E).**

Three days after admission, urinary retention, reduced anal sphincter tone, and paraplegia developed. Neurologic examination demonstrated neurologic deficits consistent with a lesion of the spinal cord in the level of D<sub>2</sub> and D<sub>3</sub> vertebrae. Brain CT scan was normal, and CT scan of the cervical and thoracic spine

demonstrated an osteolytic lesion in the body of D<sub>3</sub> vertebrae, and a soft tissue mass in the right aspect of D<sub>2</sub> vertebrae with bone destruction and involvement of the thecal sac (Fig. 4).



**Figure 4: Spinal CT scan showing a soft tissue mass in the right aspect of D2 vertebrae with severe bone destruction and involvement of the thecal sac.**

Treatment with dexamethasone intravenously and radiotherapy brought to a significant improvement of the patient's neurologic deficits. The urinary retention and reduction in anal sphincter tone almost completely resolved, and the paraplegia regressed to mild paraparesis. After that, the patient refused to get conventional therapy for his cancer preferring unconventional therapeutic modalities, and he died three months later at home in severe liver failure.

## DISCUSSION

HCC is one of the most common cancers in the world with an estimated one million new cases annually.<sup>[1,2,11]</sup> Cirrhosis, chronic HB virus (HBV) and hepatitis C virus (HCV) infection, male gender, and increasing age have all been identified as risk factors for development of HCC.<sup>[1,2,11]</sup> HCC is almost always associated with cirrhosis, and chronic viral hepatitis is recognized as the major etiologic factor in the development of this cancer worldwide.<sup>[1,2,11]</sup> Prognosis is generally poor, with mean survival being several months. The pathology, natural history, and prognosis of HCC is significantly influenced by the presence or absence of cirrhosis in the non-neoplastic liver, where presence of cirrhosis portends a poorer prognosis.<sup>[12,13]</sup>

Extrahepatic metastasis of HCC is not rare, and the lungs and regional lymph nodes are the most common sites of metastasis.<sup>[4]</sup> However, metastasis usually occurs late in the clinical course, and it is distinctly unusual for the initial clinical presentation of HCC to be related primarily to the presence of metastasis, without overt evidence of hepatic involvement.<sup>[3,14]</sup> Involvement of the

bone by metastasis from HCC is not uncommon, with the incidence during autopsy varying from 1% to 20% (median, 8%),<sup>[15,16]</sup> and HCC presenting as symptomatic bone metastasis, as was in the present case, is rare.<sup>[5-10,17]</sup> The most common sites of bone metastasis are the spine and ribs.<sup>[16-18]</sup> Metastatic spread to bone from HCC occurs through the pulmonary circulation or the vertebral venous plexus,<sup>[18]</sup> and the vertebrae have been reported as the most common site of bone metastasis from HCC through the vertebral vein.<sup>[19]</sup> Most of the bone lesions are osteolytic in nature, they are destructive, expansive, and often associated with large soft tissue mass.<sup>[5,16,17,20]</sup> The spinal metastasis in our patient has similar features. Since the cancellous bone is usually the first site of skeletal metastases, and the cortical bone is responsible for most of the bone density depicted on the plan-x-ray, conventional radiography and radionuclide bone scan are relatively insensitive for detecting early bone metastases from HCC,<sup>[5]</sup> as was found in the present case. Both, conventional radiography and radionuclide bone scan were falsely negative in our patient in detecting the spinal metastasis, while the CT scan was diagnostic. Indeed, CT scan and MRI scan are more sensitive than conventional radiography and radionuclide bone scan in detecting bone metastasis from HCC. These modalities, preferably MRI scan, should be performed for early detection and delineation of the extent of metastasis in order to prevent significant spinal cord compression and irreversible neurologic deficits with early intervention.<sup>[5,17]</sup>

Our patient presented with a history of upper back pain of four weeks duration, and subsequently developed significant spinal cord compression. Clinically, all

patients with vertebral metastases, had a history of back pain or neck pain as the first symptom followed by symptoms of spinal cord compression.<sup>[5,21]</sup> The prognosis of HCC in the presence of bone metastases is poor with the median survival time five months.<sup>[16,17]</sup> Our patient died three months after the diagnosis of HCC was made.

In our patient, who was a carrier of HBsAg, the HCC was accompanied with silent cirrhosis, likely due to HBV. As mentioned above, HCC is almost always associated with cirrhosis, especially due to hepatitis B and C viruses.<sup>[11,12]</sup> However, in the majority of instances, it is often asymptomatic or undiagnosed,<sup>[22]</sup> as was found in our patient. The presence of cirrhosis is associated with significantly shortened survival,<sup>[13]</sup> as happened in the present case. The HCC in our patient was well differentiated. However, in general, HCC in patients with cirrhosis tend to be less well differentiated (high grade) than those found among patients without cirrhosis, which may account in part for the poor prognosis in this group.<sup>[13]</sup>

In summary, HCC presenting as symptomatic bone metastasis is rare. However, it should be considered in the differential diagnosis of back pain in patients with underlying chronic liver disease, particularly cirrhosis, in order to prevent serious spinal cord compression with early intervention.

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