

# SOLITARY BONE METASTASIS WITH PATHOLOGICAL FRACTURE: A RARE ATYPICAL INITIAL PRESENTATION OF HCC

Vineeta Ojha,<sup>1</sup> Partha Samui,<sup>1</sup> Debashis Dakshit,<sup>1</sup> Soumik Das<sup>2</sup>

<sup>1</sup> Department of Radiodiagnosis, Medical College Kolkata, India.

<sup>2</sup> Department of Neuro Radiology, NIMHANS, Bangalore, India.

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## ABSTRACT

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver which metastasizes by hematogenous and lymphatic routes commonly to the lungs, & regional lymph nodes, soft tissues, brain, adrenal and rarely to the bones. In particular, symptomatic bone metastasis as a primary presentation in HCC is extremely rare. In this extremely rare case, the patient had no known liver disease, but presented with swelling and inability to lift his left arm. Core biopsy from left humerus was compatible with metastasis from adenocarcinoma in left humerus. Further investigations led to a diagnosis of hepatocellular carcinoma with solitary bone metastasis. It should be noted that while evaluating a patient who has bone metastasis with unknown primary, metastasis from HCC should be put into consideration as a rare possibility.

## Introduction

Hepatocellular carcinoma is the most common primary malignancy of the liver. The usual clinical features consist of right upper quadrant pain or tenderness, and less often, jaundice, fever and haemorrhage. High grade fever and leukocytosis described in poorly differentiated HCC may mimic the clinical picture of liver abscess. Haemorrhagic ascites with malignant cells is found in about half the patients. Rarely, systemic endocrine manifestations such as hypercalcemia due to paraneoplastic syndrome are observed. Extrahepatic spread occurs via hepatic or portal veins to different sites like lungs, brain, adrenals, by lymphatic route to regional lymph nodes and rarely to the bones.

## Case Report

A 50 year old male patient presented with swelling and inability to lift his left arm for 2 months (Fig. 1). There was no history of fever, jaundice, or blood



**Figure 1:** Clinical image showing pathological fracture of left arm with arm sling.

**Correspondence :** Dr. Vineeta Ojha  
Department of Radiodiagnosis,  
Medical College, Kolkata,  
India.  
Email: vineetao17@gmail.com

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transfusion. The patient was admitted in department of orthopedics and was referred to our department for X-ray of left arm which showed an expansile osteolytic lesion with cortical destruction in the proximal shaft of left humerus with pathological fracture and overlying soft tissue swelling, radiological features suggestive of a neoplastic lesion (Fig. 2).



**Figure 2:** X-ray of left arm AP view showing an expansile osteolytic lesion in the proximal shaft of left humerus with pathological fracture and overlying soft tissue swelling.

Hematological and biochemical examinations revealed elevated levels of SGOT, SGPT, and alkaline phosphatase. Ultrasonography of abdomen and contrast enhanced CT of chest and abdomen was done for primary site workup and for searching other secondaries.

Ultrasonography of abdomen revealed a fairly large heterogeneously hypoechoic hypervascular lesion in Segment 6 and 7 of right lobe of liver. Rest of the liver parenchyma appeared normal. Contrast enhanced CT scan of abdomen and thorax (Fig. 3) was done in our department and the following findings were noted:

i. A large heterogeneously enhancing hypodense lesion in right lobe of liver without any significant change in background liver architecture.

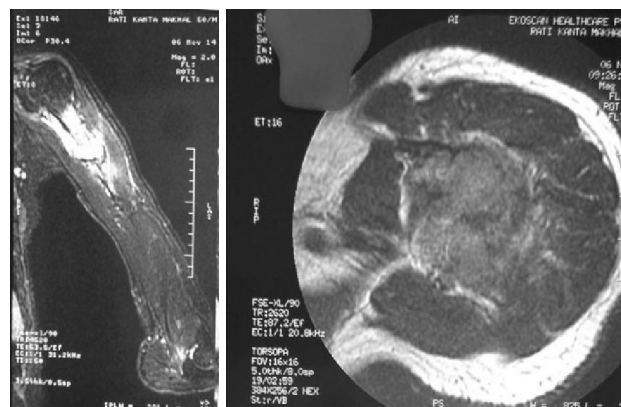


**Figure 3:** Contrast enhanced CT scan of whole abdomen showed a large heterogeneously enhancing hypodense lesion in right lobe of liver, and a large hypodense lesion in proximal left humeral shaft with breach of overlying cortex

ii. A large lytic lesion in proximal left humeral shaft with pathological fracture and adjacent large soft tissue mass.

No obvious lung metastasis or abdominal lymphadenopathy was detected.

MR images of left arm revealed pathological fracture of proximal shaft of left humerus with heterogeneous signal changes. Para-cortical involvement was seen with edema in proximal and distal segment. Marked soft tissue swelling and signal changes noted in adjoining areas (Fig. 4)



**Figure 4:** MR images of left arm showing pathological fracture of proximal shaft of left humerus with heterogeneous signal changes with edema and marked signal changes in the adjacent soft tissues

Among the tumour markers, serum carcinoembryonic antigen, serum CA 19.9, & serum -HCG levels were within the normal range, but serum alpha fetoprotein level was mildly elevated (20.8 ng/ml). Bence Jones protein was absent in urine.

Initially, there was a dilemma about the primary site-whether bone lesion or the hepatic lesion as the patient presented with pathological fracture of humerus

and he had no symptoms of hepatic disease, To add to the dilemma, the serum alpha fetoprotein level was not markedly raised as is expected of hepato-cellular carcinoma.

Subsequently, we did CT guided core biopsy from the hepatic and left humeral lesion in single sitting in an attempt to find out the primary site. Core biopsy from left humerus showed fibrocollagenous tissue, trabeculae of bone and malignant cells, findings consistent with a non specific neoplastic lesion, most likely a metastatic disease. Core biopsy from the liver lesion was done and histopathological diagnosis was hepatocellular carcinoma. Meanwhile, bone scan was done and it revealed no other abnormal uptake except for solitary humeral lesion.

The features were compatible with hepatocellular carcinoma with solitary bony metastasis in left humerus and that was our final diagnosis. Fixation of the pathological fracture in the left humerus and palliative treatment with sorafenib and bisphosphonates was done as management strategy in this case according to BCLC guidelines.

## Discussion

Hepatocellular carcinoma is the most common primary malignancy of the liver in adults. It is the third most common carcinoma and constitutes 11.3% of all tumors. It accounts for 22.6% of all cancer related deaths. Overall survival rates are 11.8% in men and 13.3% in women. The causes of hepatocellular carcinoma are- cirrhosis, alcohol abuse, autoimmune diseases of the liver, hepatitis B or C virus infection.<sup>1</sup> Hepatic cancer may remain undetected initially because it often occurs in patients with underlying cirrhosis.<sup>2</sup> The usual clinical features consist of hepatomegaly with palpable mass in the liver, right upper quadrant pain or tenderness, and less often, jaundice, fever and haemorrhage from oesophageal varices. Laboratory findings yield nonspecific results like anaemia, markedly elevated serum alkaline phosphatase as found in cirrhosis, and high serum alpha-fetoprotein (AFP).<sup>3</sup>

The HCC can have both intrahepatic and extrahepatic spread which faithfully reproduces the structure of the primary tumour. Intrahepatic spread occurs by haematogenous route and forms multiple metastases

in the liver. Extrahepatic spread occurs via hepatic or portal veins to different sites, mainly to the lungs, adrenal, brain, soft tissues and by lymphatic route to regional lymph nodes. Review of literature reveals bone metastasis as an uncommon occurrence as far as hepatocellular carcinoma is concerned.<sup>4</sup>

In this extremely rare case, the patient had no known liver disease and the only clinical presentation was swelling and inability to lift his left arm for 2 months. Metastatic symptoms are common in diagnosed HCC patients, but presentation of unknown HCC with metastatic symptoms has been described only rarely in literature. And that too, in a patient without any background chronic liver disease, such a presentation i.e with a solitary bone lesion is extremely uncommon.<sup>5</sup> Another striking aspect is that in patients with diagnosed HCC, most common site for bone metastasis is spine (LS>D>C) followed by pelvis and ribs. Solitary metastasis in an extremity is extremely uncommon even in known HCC patients.<sup>6,7</sup>

Management of HCC is based on the BCLC staging system for hepatocellular carcinoma. Early stage HCC patients (< 3 nodules, < 3 cm) are considered for curative treatments like resection, RF ablation, and transplantation. Intermediate stage patients (multinodular, < 3 cm) are managed with chemoembolization whereas in advanced stage (Portal vein invasion, metastasis, nodal spread) management is done by sorafenib. Finally, end stage patients receive palliative care only.<sup>8,9</sup> The usual outcome in treated HCC is poor, because only 10–20% of hepatocellular carcinomas can be removed completely using surgery. The median survival is 7 months.<sup>10,11</sup> The prognosis for metastatic or unresectable hepatocellular carcinoma has recently improved due to the approval of sorafenib for advanced hepatocellular carcinoma. It inhibits VEGF, thereby reduces progression of HCC. Sorafenib also helps in pain management in case of bone metastases, whereas bisphosphonates increase the bone strength in affected areas. Overall, these therapies along with radiotherapy, help in palliative care in bone metastases. Amputation is not fruitful in cases of advanced HCC and further deteriorates quality of life of the patient. Our patient was managed with sorafenib and bisphosphonates.

## Conclusion

Considering the exceptional increase in incidence of HCC in this era, it is indispensable to keep in mind its various atypical presentations including a solitary bone metastasis, especially when survival rate is as low as <1 year in untreated HCC. It may also be concluded that if a patient has expansile osteolytic bone lesion proven to be bone metastasis on HPE, then metastasis from HCC should be included in the differential diagnosis as a remote possibility while workup to search for primary. In such cases, sorafenib plays a unique role in pain palliation without deteriorating quality of life of such patients.

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