

Multiple skeletal metastases as unusual manifestations of hepatocellular carcinoma in a noncirrhotic liver

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ABSTRACT

Hepatocellular carcinoma is the most frequent primary malignant tumor of the liver. Bony metastases of hepatocellular carcinoma are usually rare, in which most common sites involved are vertebra and pelvis. Still rarer are metastases to the chest wall and skull. We report a case of a 45-year old man with unusual metastases of hepatocellular carcinoma to skull, sternum and ribs. These combinations of metastases have rarely been reported in literature.

Keywords: Sternal metastases; skull metastasis; osteolytic lesions; aflatoxin B; cirrhosis.

Hepatocellular carcinoma (HCC) is the most frequent primary malignant tumor of the liver.¹ It is usually seen in the sixth and seventh decades of life in the western world, whereas in Asia and Africa, it usually occurs in the fourth decade of life.² It is found more commonly in the males.² A definite association between HCC and cirrhosis has been found, with chronic hepatitis B viral infection being described as the most common cause.³⁻⁵ It has been found to metastasize commonly to the lungs, regional lymph nodes, kidneys, bones and adrenals.⁴⁻⁹ Multiple bony metastases to the skull and the chest wall have rarely been reported before. This report presents a middle aged male with unusual metastasis of HCC which manifested initially as multiple swellings on the mid sternum and anterolateral aspect of the chest wall and the skull.

CASE REPORT

A 45 year old male presented to our hospital with complaints of swelling in the central and right anterolateral region of the chest and the right side of the skull, loss of weight, loss of appetite and general weakness of 3 months duration. There was no history of pain over the swellings, jaundice, fever, night sweats. He was nonalcoholic. His physical examination revealed a 3 × 2 cm fixed hard swelling in the right side of the skull and two hard swellings of varying sizes at the mid sternum and right anterolateral region of the chest. There was no pallor, icterus or ascites. On abdominal examination, he had mild nontender hepatomegaly. He was anemic with hemoglobin of 8.5 mg/dL. Total and direct bilirubin and liver enzymes were within normal limits. Viral marker profile was not reactive for both HBsAg and HCV. Other causes of liver disease were eliminated by assessment of antinuclear, anti-

mitochondrial, anti-smooth-muscle and anti-microsomal antibodies. Iron metabolism study was also normal.

The radiograph of the skull demonstrated an osteolytic lesion involving the right frontal bone. Computerized tomography (CT) of the skull revealed a destructive lesion with erosion of the right frontal bone (Fig. 1). CT scan of the thorax revealed soft tissue lesions on the central and right anterolateral aspect of the chest with erosion of the sternum and right 5th and 6th ribs respectively (Fig. 2). Abdominal CT scan detected a 4.6cm x 4.1cm well circumscribed heterogenous lesion in the right lobe of the liver (Fig. 3). The rest of the liver parenchyma was normal. There was no lymphadenopathy on thoracic, abdominal or pelvic scan. Microscopic examination of the biopsy specimen from the skull and chest wall lesions revealed pleomorphic tumor cells with eosinophilic cytoplasm, prominent nucleoli and mitosis arranged in trabecular and solid



Fig.1. Axial CT scan of the skull (bone window) showing a lytic lesion in the right frontal bone.

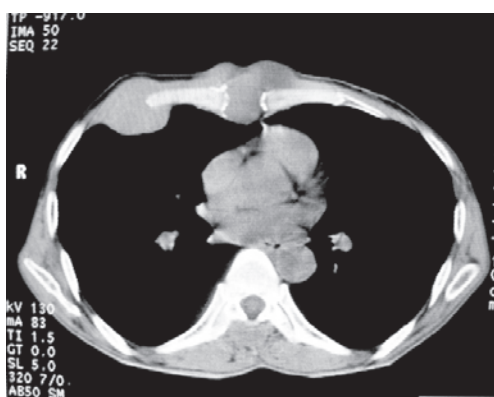


Fig.2. CT scan of the thorax showing lytic lesions involving the sternum and right 5th rib adjacent to the costochondral junction with soft tissue extension.

pattern, suggestive of metastatic hepatocellular carcinoma (Fig. 4). Cytological examination of a fine needle aspirate taken from the lesion in the liver was consistent with the diagnosis of hepatocellular carcinoma (Fig. 5). The serum alpha-feto protein (AFP) level of the patient was elevated (33,566 ng/mL; normal 0-13.6 ng/ml). The patient was discharged on palliative treatment. After 2 months of diagnosis and 5 months of appearance of the symptoms, he is still continuing with follow-up. No other swellings have appeared, he has weight loss and increase in size of the described swellings.

DISCUSSION

Bony metastases from HCC are now being reported more commonly than ever before. They are seen in 3.0-10.0% of HCC patients.¹⁰⁻¹⁵ The bones most commonly involved are the vertebra, pelvis, ribs and skull.¹⁶ Isolated metastases to the ribs, sternum and the skull have been reported.¹⁷⁻²⁴ Multiple metastases to the chest wall and the skull in the same patient have rarely been reported in the literature.

The bony lesion due to metastatic HCC in this case was osteolytic and discrete. However, multiple osteolytic

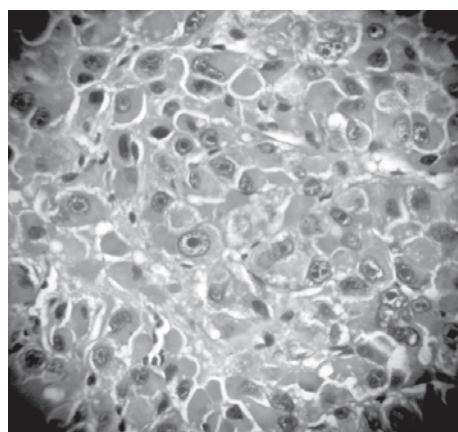


Fig.4. Photomicrograph of the biopsy taken from the chest wall and skull lesions shows malignant hepatocytes, consistent with metastatic hepatocellular carcinoma. (X 400 Haematoxylin and Eosin stain)

lesions simulating multiple myeloma can be due to metastatic HCC.²⁵

The etiology of HCC is still unknown in this patient. There were no clinical or laboratory parameters or radiological features of chronic liver disease. HCC has been found usually to develop on a background of cirrhosis (cirrhomimetic) but can also originate in normal or nincirrhotic hepatic parenchyma (non-cirrhomimetic).²⁶ In fact, in South African black population, 37.0% of primary HCC occurs in patients without cirrhosis.²⁶ One cause that can be attributed is aflatoxin B produced by aspergillus species which grows as a contaminant in stored cereals and grains in a hot humid climate. A close correlation between the degree of fungal contamination and frequency of HCC has been reported in tropical areas like sub-Saharan Africa and South East Asia, though the frequency is less well established in our part of the world, due to lack of studies.^{27,28} We believe such a relation might exist in our patient. Studies using histochemical detection of aflatoxin B in patients with HCC will be needed further to establish the causative role in our region also.

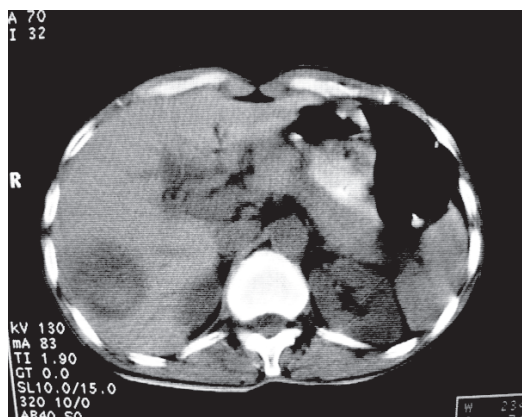


Fig. 3. CT scan of the abdomen showing a well defined heterogeneous mass lesion in the right lobe of the liver.

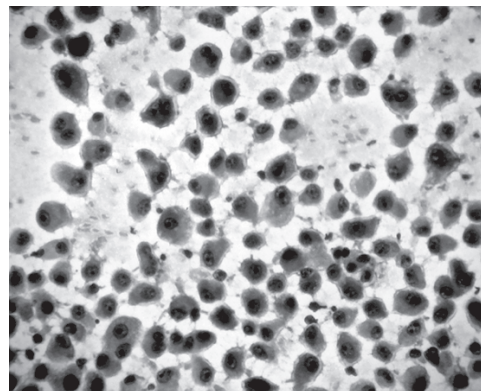


Fig.5. Cytological examination from the lesion in the liver shows malignant hepatocytes, suggestive of hepatocellular carcinoma (X 400 Papanicolaou stain)

Metastatic HCC without an unknown primary is a definite subset that poses a great challenge in the diagnosis.^{17,18,24} The cause has been postulated to be ectopic liver carcinogenesis and hepatoid adenocarcinoma found to occur in the stomach, ovary, uterus, renal pelvis, bladder, pancreas and lungs.^{24,29-31} In our case, there was little difficulty in the detection of the primary which was confirmed by the fine needle aspiration cytology.

We conclude hereby that metastasis of HCC should be included in the differential diagnosis of bony swellings even in the absence of chronic liver disease.

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