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Bone metastasis in hepatocellular carcinoma: Need for reappraisal of treatment

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ABSTRACT

Bone is an uncommon site of metastasis in patients with hepatocellular carcinoma (HCC), and often overlooked. We report two cases that had isolated bone metastasis; one of them had prolonged disease-free survival. The present series, along with the literature review, reinforces the idea that HCC should be considered in the differential diagnoses in patients presenting with metastases in bone. The presence of isolated bone metastases need not necessarily indicate poor prognosis, and all such patients need to be offered chemotherapy and at least one of the bone-directed therapies (either local radiation in cases of localized disease or bisphosphonates in the presence of extensive disease) as they may have a better outcome with therapy.

KEY WORDS: Bone metastasis, hepatocellular carcinoma

Bone is an uncommon site of metastasis in patients with hepatocellular carcinoma (HCC), and is a site that is often overlooked during investigation of patients. However, autopsy series have shown that it is the 3rd commonest organ to be affected, next only to the lung and adrenal gland. The incidence of bone metastasis is 3-20% and shows a definite upward trend.[1-3] There are multiple case reports in literature, where bone metastasis has been the presenting symptom in patients with HCC. It is unique among the hematogenous metastases of HCC in that it occurs before the other clinical manifestations of HCC become apparent, with the majority of the patients with bone metastases being symptomatic.[2] The prognosis is usually good and presence of isolated bone metastasis does not necessarily confer a poor prognosis.[4] We present two patients of HCC in whom bone metastasis was incidentally detected and was found to be the only site of metastasis.

CASE REPORTS

Case 1

A 56-year-old female presented with symptoms of pain abdomen; the initial evaluation done at the primary care center showed multiple hypoechoic lesions in the liver. The evaluation at our center showed that patient had Child-Pugh 'A' disease The histology of the lesion was suggestive of HCC. She was hepatitis-B positive; serology for HCV was negative. X-ray chest revealed lytic lesions in the ribs as well as the clavicles. A Tc^{99}-labeled bone scan showed that the patient had metastasis (increased uptake of the isotope) in the humerus, right femur, and left tibia. X-ray of the lesions confirmed the presence of lytic lesions involving the same regions. Metastatic workup was otherwise within normal limits. In view of the advanced (stage IV) disease and the inoperability of the primary lesion (because of involvement of the inferior vena cava and the presence of multiple lesions involving both lobes), the patient was treated with combination chemotherapy with adriamycin 60 mg/m^2 and cisplatin 75 mg/m^2 given every 3 weeks, along with zoledronic acid for the bone metastasis. After six courses, the primary lesion regressed by 90% and the bone lesions showed decreased activity on Tc^{99} scan (indicating healing); the patient also reported improvement in symptoms. She remained asymptomatic for the next 2 years. Later, she had seizures and was diagnosed as having brain metastasis. She died of progressive disease.

Case 2

A 64-year-old male presented with pain abdomen, progressively deepening jaundice, anorexia, and a weight loss of 12 kg over the last 6 months. He was a known alcoholic who had been diagnosed as having cirrhosis and advised conservative management. The primary care physician referred him to us when the patient developed features consistent with HCC. The evaluation at our center showed that the patient had Child-Pugh 'C' disease. Histology of the liver mass was suggestive of HCC. CT scan of the abdomen showed multiple

hypodense lesions involving both lobes of the liver and lytic lesions in the lumbar as well as lower thoracic vertebra. A Tc^{99}-labeled bone scan showed that the patient had metastasis (increased uptake of the isotope) in the right iliac bone, and T_{10}-L_2 vertebrae. The rest of the metastatic workup, including CT thorax, was within normal limits. In view of the stage IV disease and the inoperability of the primary lesion, the patient was offered symptomatic care or combination chemotherapy as options; he opted for the former. He died of progressive disease the following month.

DISCUSSION

Bone involvement in patients with HCC is on the rise and one of the main reasons for this is the better survival of HCC patients due to recent progresses made in both the diagnosis and treatment of the disease.[1] Some authors support the view that metastasis to the bones occurs via portal vein-vertebral vein plexuses (owing to either portal thrombus and/or portal hypertension which allows bypass through plexus), thus explaining the more frequent craniospinal and pelvic bone metastases. However case reports of upper and lower limb involvement[1] argue against the same and in the present series too, the first patient had long bone involvement. The diagnosis is usually made by Tc^{99}-labeled scan, as is done in bone metastases in other malignancies.[5]

There is enough literature to suggest that HCC should always be considered in the differential diagnoses in patients presenting with bone metastasis, with a few reports suggesting that this could be the first manifestation of HCC.[1-8] The importance of the recognition of this entity is enhanced by some reports that patients with HCC and bone metastases do well and show long-term survival after hepatectomy and radiotherapy to the bone metastases.[4] However the use of bisphosphonates in this condition is not widely studied. In our first case, the patient was given chemotherapy along with zoledronic acid, as the patient had extensive bone disease. In accordance with the literature, the patient had a considerably long progression-free survival with the treatment. However, in the second patient, the outcome was poor as he did not receive any therapy and also because the residual hepatic function (Child-Pugh score C) was poor. Therefore, while treating patients of HCC with bone metastasis, other prognostic factors also should be kept in mind, and all patients with bone metastasis should preferably be given the option of treatment as the prognosis is better than with metastasis at other sites.

CONCLUSION

One of our cases had long bone involvement, which is unusual. The present series and the review of literature reinforces the view that HCC should be considered in the differential diagnoses in patients presenting with bone metastasis. The presence of 'bone-only' metastasis confers a better prognosis, and all such patients need to be offered chemotherapy and at least one of the bone-directed therapies - either local radiation in cases of localized disease or bisphosphonates in the presence of extensive disease.

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