
CASE REPORT

Bone Metastasis as the First Presentation of Hepatocellular Carcinoma

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ABSTRACT

This report is of a patient with multifocal bilobar hepatocellular carcinoma who presented with bone pain related to bone metastasis. Radiograph of the pelvis showed an expansile osteolytic bone lesion in the right superior pubic ramus. Review of the literature showed that the radiographic appearance was typical of bone metastasis from hepatocellular carcinoma, as well as renal cell carcinoma and thyroid carcinoma. This entity is not usually included in the differential diagnosis of expansile lytic bone lesion, possibly due to the rarity of hepatocellular carcinoma in western countries. If a patient presents with an expansile osteolytic bone lesion, bone metastasis from hepatocellular carcinoma should be considered in addition to renal cell carcinoma and thyroid carcinoma, especially in areas such as Hong Kong where the incidence of hepatocellular carcinoma is high.

Key Words: Carcinoma, hepatocellular; Neoplasm metastasis; Radiography

中文摘要

骨轉移作為原發性肝癌首發表徵個案報道

梁錦榮、梁禮賢、施雅倫、鄭志成、陳鉅發

這份病例報告是關於一個肝臟兩葉有多處原發性肝癌的病人以骨痛骨轉移作為首發表徵的描述。骨盆X光片顯示右側恥骨上支有膨脹溶骨性病變。經翻查文獻，發現該X光片的外觀是典型的原發性肝癌、腎細胞癌或甲狀腺癌的骨轉移。可能是由於原發性肝癌在西方國家比較罕見，原發性肝癌骨轉移通常不包括在鑑別診斷膨脹性溶骨性病變之內。如果在原發性肝癌發病率很高的地方，例如在香港，遇到一例膨脹溶骨性病變的病人，除了要考慮腎細胞癌和甲狀腺癌的骨轉移之外，還要考慮原發性肝癌的骨轉移。

INTRODUCTION

Hepatocellular carcinoma (HCC) is commonly seen in Hong Kong due to the high local prevalence of chronic hepatitis B infection. It is well known that HCC usually presents with local symptoms such as right upper

quadrant pain and systemic symptoms of malaise and weight loss.¹ Bone metastasis as the initial presentation of HCC is rare. This report is of a patient who presented with bone metastasis without local or systemic symptoms related to HCC.

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CASE REPORT

A 61-year-old man presented to the Pamela Youde Nethersole Eastern Hospital, Hong Kong, in September 2008 with left hip pain for 1 week. He had no recent history of injury. The patient did not have systemic symptoms such as malaise, weight loss, or fever. Physical examination showed local tenderness over the left iliac crest. Clinical examination of abdominal, respiratory, cardiovascular, and neurological systems was unremarkable. Blood tests showed mildly elevated alkaline phosphatase of 142 U/L (reference range, 50–120 U/L) and alanine aminotransferase of 53 U/L (upper limit of normal, 41 U/L). The serum bilirubin level was normal, as was haemoglobin level, platelet count, and coagulation profile.

Radiograph of the pelvis showed an expansile osteolytic bone lesion in the right superior pubic ramus (Figure 1). In view of the radiographic appearance of the right superior pubic ramus lesion, investigations for a provisional diagnosis of bone metastasis were performed. Technetium-99m methylene diphosphonate whole-body bone scintigraphy showed an increase in tracer activity over the left iliac crest and the right superior pubic ramus on blood-flow, blood-pool, and delayed images. Tests for the tumour markers carcinoembryonic



Figure 1. Magnified view of the pelvis radiograph showing an expansile osteolytic bone lesion in the right superior pubic ramus.

antigen and prostate-specific antigen were negative, but serum α -foetoprotein was 3477.8 $\mu\text{g/L}$ (reference range, $<10 \mu\text{g/L}$) and hepatitis B surface antigen was positive. Computed tomography (CT)-guided biopsy of the right pubic bone lesion (Figure 2) was done for histological examination. The biopsy cores comprised tumour tissue

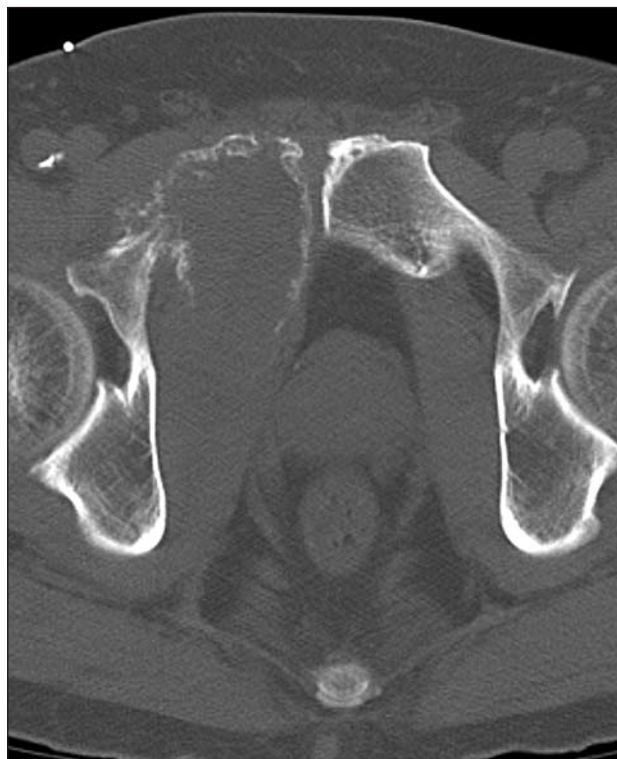


Figure 2. Computed tomography image showing the expansile osteolytic bone lesion in the right superior pubic ramus.

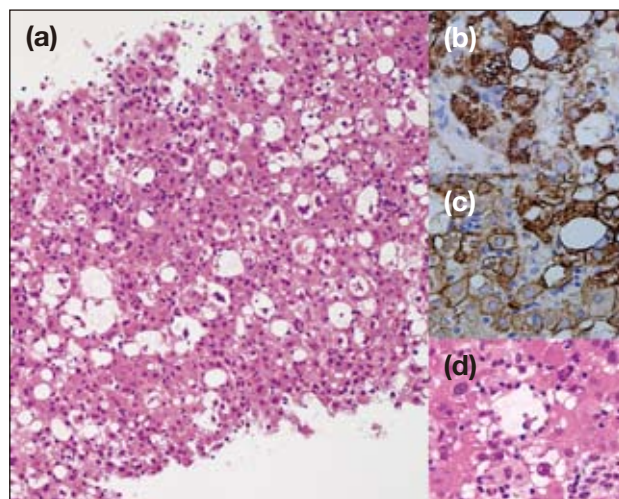


Figure 3. Immunohistochemical staining of metastatic hepatocellular carcinoma showing (a) neoplastic cells arranged in broad trabeculae (haematoxylin and eosin stain; original magnification, $\times 100$); (b) cytoplasmic granular staining for hepatocyte paraffin 1; (c) membranous staining for low molecular weight cytokeratin CK8/18; and (d) a few tumour giant cells under high magnification (original magnification, $\times 200$).

with morphology consistent with that of a metastatic hepatocellular carcinoma (Figure 3). The neoplastic cells were moderately pleomorphic with pale to eosinophilic granular cytoplasm arranged in broad trabeculae and sheets. Occasional giant tumour cells were present. The neoplastic cells expressed low molecular weight cytokeratin (CK8/18) and showed typical cytoplasmic granular staining for hepatocyte marker (hepatocyte paraffin 1) on immunochemical staining.

F-18 fluorodeoxyglucose positron-emission tomography CT (^{18}F FDG PET-CT) fusion study was performed to check for suspected primary liver cancer and exclude other metastases. ^{18}F FDG PET-CT showed multiple hypermetabolic lesions involving both lobes of the liver, in addition to the bone lesions over the left iliac crest and right superior

pubic ramus (Figure 4). Complimentary ^{11}C -acetate (^{11}C -ACT) PET-CT showed multifocal ^{11}C -ACT uptake over both lobes of the liver, which supported the diagnosis of multifocal HCC. The bone lesions in the left iliac crest and right superior pubic ramus were also ^{11}C -ACT avid consistent with bone metastases from HCC.

Palliative radiotherapy to the left iliac and right pubic bone metastases was given. The patient refused systemic chemotherapy or targeted therapy after the completion of palliative radiotherapy.

DISCUSSION

HCC is the most common primary malignant tumour of the liver. This tumour accounted for 1745 new cases and 1462 cancer deaths in 2006.² In Hong Kong, HCC

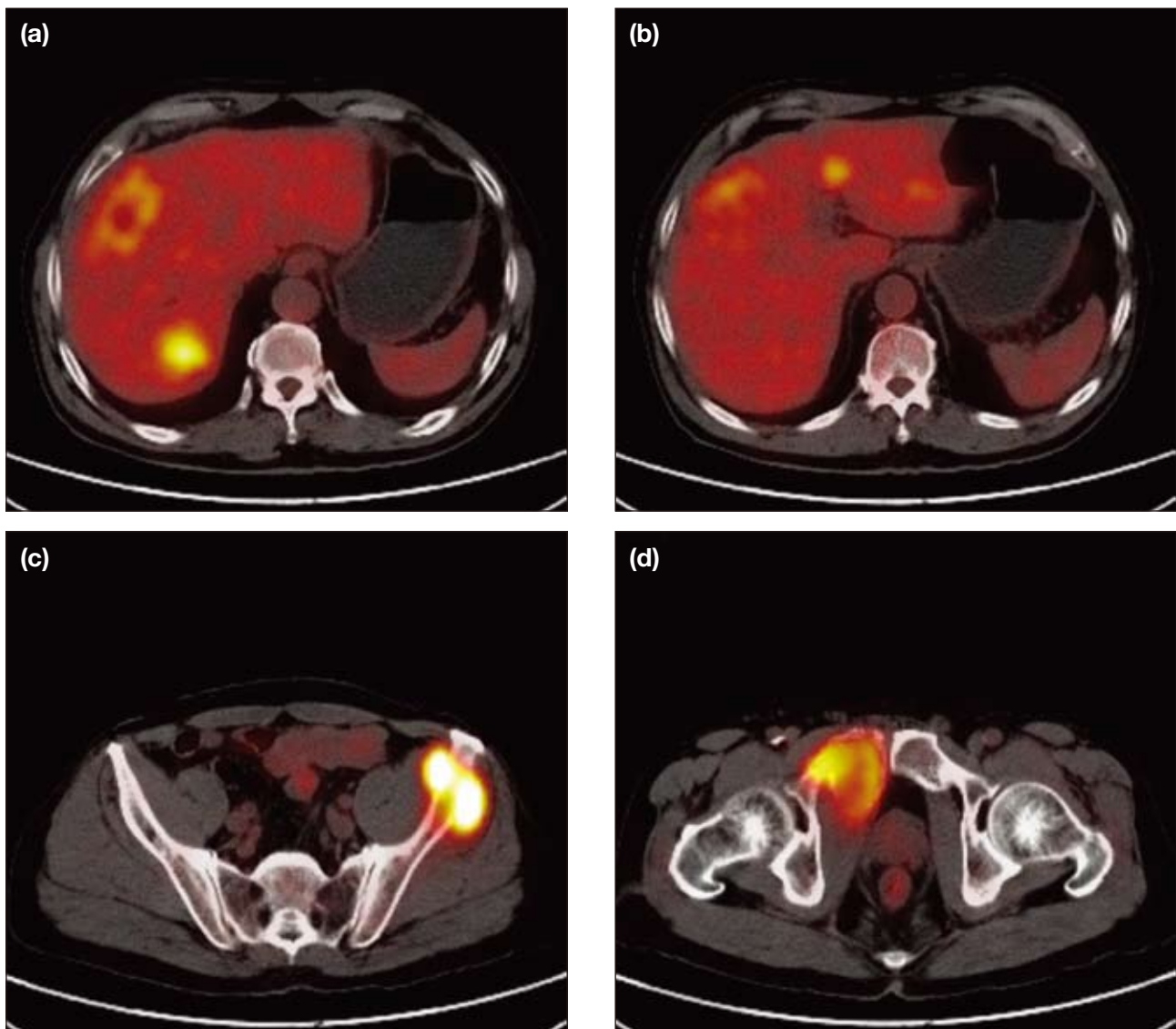


Figure 4. F-18 fluorodeoxyglucose positron-emission tomography computed tomography images showing multiple hypermetabolic lesions involving (a and b) both lobes of the liver; (c) the left iliac crest; and (d) the right superior pubic ramus.

ranks third and eighth for cancer incidence and second and fourth for cancer mortality for men and women, respectively.²

Extrahepatic metastases of HCC have been reported to occur in 13.5% to 36.7% of patients in large-scale studies.³⁻⁸ The most frequent metastatic site is the lung (53.8% to 54.7%) followed by the lymph nodes (33.8% to 52.7%) and bone (5.8% to 38.5%). The commonest site of bone metastasis is the spine, followed by the ribs, pelvis, and femur.⁵⁻⁷ Although bone metastasis is common in HCC, bone metastasis as the first presentation is rare. Kuhlman et al⁶ and Liaw et al³ have reported incidences of 3.3% (10/300) and 5.1% (20/395), respectively. The series by Okazaki et al shows a higher incidence of 6.9% (6/87), which may be related to the small sample size, and only autopsy patients were included in the study.⁵

All bone metastases from HCC are osteolytic in nature.^{3,5,6,8} Bone metastases from HCC tend to be expansile and lytic in appearance on plain radiograph and CT.^{3,6,9} Dual-tracer PET-CT using ¹¹C-ACT and ¹⁸F-FDG as radioisotope tracers is an advanced imaging modality for evaluating and staging HCC. The pattern of tracer uptake correlates with the degree of tumour cellular differentiation. Well-differentiated HCC preferentially accumulates ¹¹C-ACT, whereas poorly differentiated tumours tend to be ¹⁸F-FDG avid.¹⁰ A hypervascular mass corresponding with the osteolytic lesion may be demonstrated at angiography.^{3,9} Caution should be taken when taking a biopsy from these bony lesions as significant haemorrhage related to the hypervascularity has been reported.^{6,9,11}

In radiology textbooks written by western authors, the most common differential diagnoses of expansile osteolytic bone metastasis are renal cell carcinoma and thyroid carcinoma. HCC bone metastasis is seldom included in the list of differential diagnoses.^{12,13} Nevertheless, this entity ranked eighth in the differential diagnosis of osteolytic metastasis with features of expansile lytic appearance in Reeder and Felson's *Gamuts in Radiology*,¹⁴ which is a comprehensive textbook of radiological differential diagnosis. Although the radiographic features

of HCC bone metastases have been well documented in various studies,^{3,6,9} they are not well recognised among radiologists, probably due to the rarity of this condition in western countries.

In conclusion, HCC presenting as bone metastasis is uncommon. However, if a patient presents with an expansile osteolytic bone lesion, bone metastasis from HCC should be considered in addition to renal cell carcinoma and thyroid carcinoma, especially in areas with a population in which the incidence of HCC is high, such as Hong Kong.

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