Radiology Case Reports 19 (2024) 6440–6444

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Appendicular skeleton multiple bone metastasis as first manifestation of hepatocellular carcinoma ☆

*Kongni Fokou Gervais Camille, MD**, *Orfanos Xenia Alexandra, MD*

CHU Brugmann, Brussels, Belgium

ARTICLE INFO

Article history:
Received 17 August 2024
Revised 2 September 2024
Accepted 3 September 2024

Keywords:
Hepatocellular carcinoma
Bony metastasis
Appendicular skeleton
X-ray

ABSTRACT

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. It is the fourth leading cause of cancer related deaths in the world. Major risk factors for HCC occurrence are Alcoholic liver disease, viral hepatitis B and C, and nonalcoholic fatty liver disease. In westerns countries, patients with such risk factors are followed up regularly, to avoid late detection and complications of HCC. Bony metastasis of HCC are a usually considered a late presentation in the course of HCC disease, and are associated with poor prognosis. They occur most frequently on the axial skeleton. Appendicular skeletal bony metastasis are not frequent, and it is rare to have it as first manifestation of the disease, without a known primary liver lesion. We present the case of a 55 year old male with known hepatitis B viral infection, who came consulting for elbow and thigh pain since 8 months. X-rays and subsequent computed tomography (CT) scans and positron emission tomography (PET) CT revealed multiples appendicular skeletal bony metastasis of a primary unknown liver HCC. This denotes poor follow up of this patient with risk factors of HCC. The medical team should therefore be more aggressive in their investigation methods whenever faced with skeletal unusual painful areas, in patients with high risk of HCC even if primitive liver lesion is not yet diagnosed, and not hesitate to use MRI or CT scans if X-rays are not contributory.

Introduction

Heptocellular carcinoma (HCC) is one of the leading causes of cancer related deaths in the world, according to 2020 Globocan statistics [1]. The main etiology of the disease varies across the world. Nonalcoholic fatty liver disease and alcohol related cirrhosis are leading causes in western world. Whereas chronic viral liver infections are predominant in eastern Asia and sub-saharan Africa. HCC liver lesions are asymptomatic and only frequent screening can prevent late detection with many metastatic complications. Metastatic complications of HCC occur mostly in the lung, lymph nodes and adrenal glands. Bony HCC metastasis are not frequent, and it's more rare to have them as first manifestation of an unknown primary liver disease [2]. The spinal Column remains the predominant site

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: kofogecam23@yahoo.fr (K.F. Gervais Camille).

https://doi.org/10.1016/j.radcr.2024.09.016

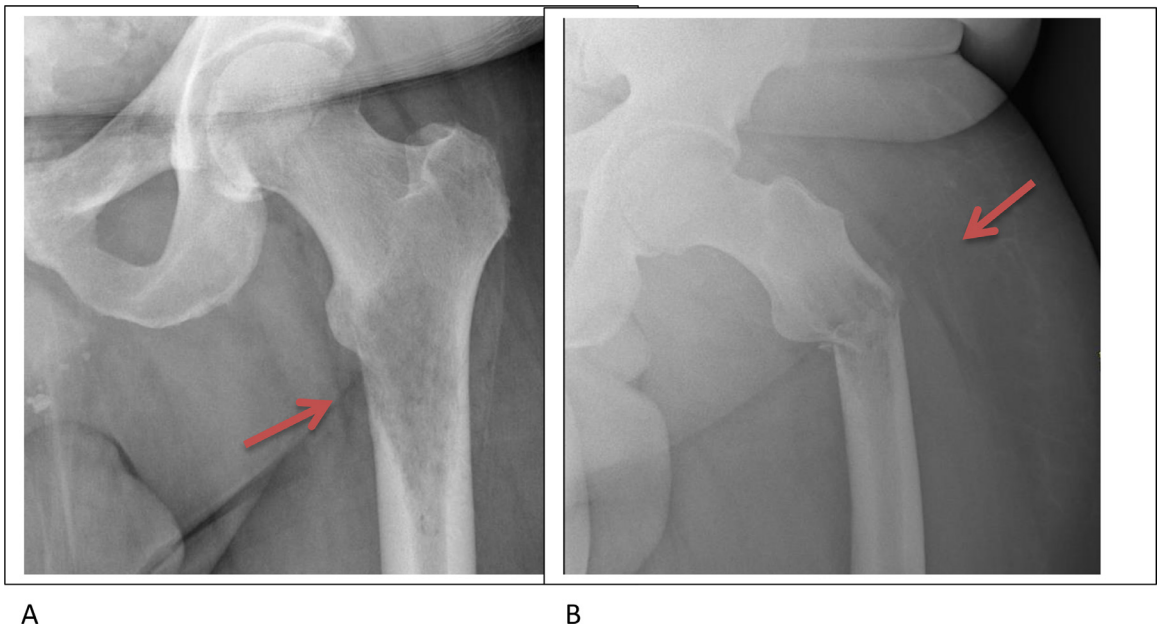

Fig. 1 – X-rays of the hip showing a lucent area around the proximal femur, with poor delineated margins, but conserved cortical bone(A) Same lesion femoral lesion few Weeks after with a pathological fracture (B).

of secondary bony lesions [3]. Bony HCC metastasis are known to be a factor of poor prognosis in the course of the disease [4]. The median survival without any intervention from the diagnosis of bony metastasis has only shifted from 3 months before the 21st century to approximately 7 months in recent studies [5]. Up to a decade ago we only had few published cases with unusual bone metastasis to distant appendicular skeleton, presenting as first manifestation of an unknown primary HCC [2,6]. We present here a case of an unusual distant multiple skeletal metastasis as first manifestation of HCC.

Case presentation

A 55 year old male, known to be living with hepatitis B infection. He was referred by the family doctor for the investigation of shoulder pain and of the left upper limb impotence. He also complained of pain in the thigh upon walking and at night. The symptoms had been present for 8 months and worsening. The patient's past medical history revealed that he was diagnosed of hepatitis B infection 3 years ago in his home country, few months before he emigrated into European Union. He was not on any long term therapy. He had consulted a family doctor few times during the year, first for abdominal discomfort, and then for muscular pain around the left shoulder and the thigh. No blood samples were required by the family physician, according to the patient. X-rays of the left shoulder and the hip were required by the physician, and they did not reveal any suspicious lesion. Six Weeks later, the patient came back to the emergency department of our hospital for exacerbation of the pains on the shoulder and the thigh. Upon arrival, X-rays of the left shoulder and the femur on frontal and lateral views were carried out. They revealed a heterogeneous lytic lesion of the scapula involving the acromio-clavicular joint (Fig. 2). On the femur they revealed a translucent lesion of the proximal third of the femur, and cortical erosion (Fig. 1A). We then continued our investigation with a thoraco-abdomino-pelvic (TAP) enhanced CT scan. CT scan confirmed the presence of an osteolytic tissue mass, at the superior margin of the left scapula and extending towards the deltoid muscle. There was a second tissue mass at the level of the anterior glenoidal surface. They were both hyper vascularized with irregular non well delineated margins. On the left femur we found an osteolytic lesion on its proximal segment with periosteal reaction and cortical erosion. There was a second lesion of the middle segment of the femur eroding the bony cortex on its lateral portion, affecting soft tissues around the bone. In the abdomen, the liver was almost completely infiltrated and replaced by an inhomogeneous mass, partially necrotic, hypervascularized in the arterial phase, with wash out on late phases (Fig. 4A,B). There was thrombosis of the portal vein, and varicose vessels at the liver hilum. Adrenals were also enlarged bilaterally, infiltrated by tissue mass. PET CT revealed that all the above listed bony lesions displayed hypermetabolic activity (Fig. 3). Biopsy of the shoulder and liver lesions confirmed the presence of hepatocellular carcinomatous tissue. During additional workup that was required before treatment, patient was ambulatory. Few days after the CT scan, the patient suffered pathological fracture of the femur (Fig. 1B). He was then hospitalized and underwent surgery of the femoral fracture. He was put on chemotherapy for both HCC and Hepatitis.

Discussion

Hepatocellular carcinoma represents more than 75% of all primary liver cancer incidence [7,8], and accounts for the fourth

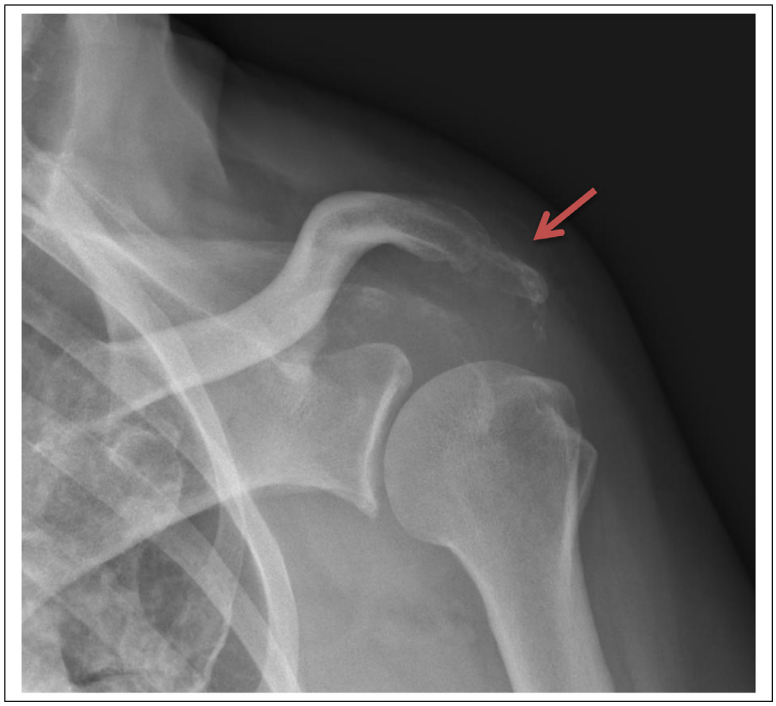

Fig. 2 – Shoulder X-ray with heterogeneous calcified soft tissue around the acromio-clavicular joint (arrow) and also clavicular and acromial luciencies.

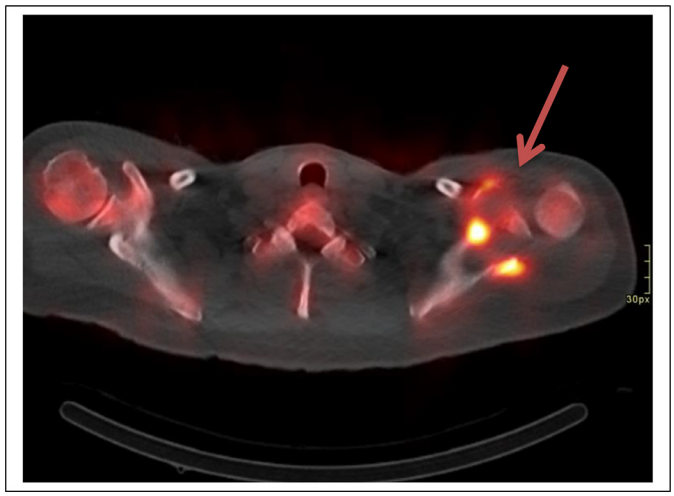

Fig. 3 – Hypermetabolic activity of the bone and soft tissue on the shoulder lesion with PET-CT.

highest number of cancer-related death in the entire world [9]. The overall survivability of patients with HCC was estimated above 2 years a decade ago [10]. Overall survivability of patients has increased due to increased performances of detection techniques such as CT/MRI, PET-CT and bone scintigraphy [1]. Patients with HCC who develop bone metastasis have a poor prognosis, and median survival time of only 4-10 months [11]. Patients with bone metastasis tend to have multiple metastatic spread elsewhere as well [2]. Unlike in developing countries, early detection of HCC is more likely in western countries, due to frequent screening of patients with risk factors [12,13]. Distant appendicular skeletal metastasis as first revelation of HCC in westerns world may be attributed to inadequate follow-up of patients with risk factors. As confirmed by literature data, notably those of Bukhari et al., our patient had other secondary lesions in addition to those on the skeleton. The patient also suffered pathological bone fractures that could maybe have been prevented if they had been detected earlier. This brings upfront the usefulness of imaging techniques in accurate and early diagnosis of HCC com-

Fig. 4 – infiltrative hypodense liver mass occupying the 7th end 8th segments of the liver, and displaying a characteristic hyper enhancement on arterial phase (A) with wash out on portal acquisition (B).

plications. Imaging techniques used to detect bone metastasis have different levels of sensitivity and specificity. MRI and 18 F-fluorodeoxyglucose (18 FDG) Positron Emission Tomography have highest sensitivity for the detection of bone metastasis [4]. X-ray has low sensitivity and will only detect lesions at a late phase with massive bone destruction, due to the soft tissue composition of HCC metastasis in bone. But X-ray is still used in primary investigation of bone pain and search of fractures, especially on the appendicular skeleton. Distant secondary lesions on the appendicular skeleton from HCC are rare as primary manifestation of HCC [14]. Exhibiting more than 1 appendicular skeletal lesion as first presentation of HCC is rarer. These patients will present symptoms such as pain and limb impotence, that are not specific. Due to its low sensitivity, X-ray mays not reveal lesions early enough as in our case. Perhaps patients with high risk factors of HCC in whom skeletal symptoms are present and X-rays noncontributory, should benefit from more sensitive imaging modalities. In our case the patient was diagnosed late, with large lesions and suffered pathological fractures before treatment could be carried out.

Conclusion

Bony metastasis can be one the complications of HCC, but it is not considered a frequent finding to have it without a known primary liver tumor. Our patient's case highlights the hypothesis of secondary bony lesions in patients with high risk factors of HCC who present with atypical skeletal pain. As X-ray has low sensitivity for detection of these lesions in their early phase, the medical team should perhaps be more aggressive in the investigations even when common radiographs are not contributory.

Patient consent

We declare having obtained a signed informed consent from the patient for the use of his personal data for scientific purposes. The data are to be used anonymously without any disclosure of patient's identity.

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