Clinical Case

Bone Metastases as the Main Clinical Manifestation of Hepatocellular Carcinoma: A Report of Two Cases

Métabases osseuses comme principale manifestation d'un carcinome hépatocellulaire: à propos de deux cas

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ABSTRACT

Hepatocellular carcinoma accounts for more than 85% of primary liver cancers. Recently, progresses in diagnostic modalities and therapeutic procedures have prolonged the survival in patients with HCC. Bone involvement is reported as uncommon in HCC. Axial skeleton is the most frequent localization of bone metastases. Few reports have appeared in the literature concerning patients who presented with skeletal metastases as the clinical manifestation of HCC. We describe our experience with two patients with skeletal metastases as the dominant clinical manifestation of hepatocellular carcinoma.

RÉSUMÉ

Le carcinome hépatocellulaire (CHC) représente plus de 85% des cancers primitifs du foie. Récemment, les progrès réalisés sur les plans diagnostique et thérapeutique ont permis de prolonger la survie des patients atteints de CHC. L’atteinte osseuse est signalée comme peu fréquente dans le CHC. Le squelette axial est la localisation la plus fréquente des métastases osseuses. Peu d’études dans la littérature concernent les patients qui présentent des métastases squelettiques comme une manifestation clinique du CHC. Nous rapportons notre expérience avec deux patients présentant des métastases squelettiques comme manifestation clinique dominante du CHC.

INTRODUCTION

Hepatocellular carcinoma accounts for more than 85% of primary liver cancers (1). Globally it represents the sixth cancer and the fourth cause of death from cancer in the world (2). Recently, progresses in diagnostic modalities and therapeutic procedures have prolonged the survival in patients with HCC. However, in some patients, this led to a concurrent worsening of the tumor progression beyond the liver and the development of bone metastases (3). Although bone involvement is reported as uncommon in HCC, its incidence has significantly increased in the last decade due to the improvement of overall survival of these patients (4,5). Axial skeleton is the most frequent localization of bone metastases with a prognostic correlation of the time between the primary HCC occurrence and bone metastases detection (6). Few reports have appeared in the literature concerning patients who presented with skeletal metastases as the clinical manifestation of HCC (7-10). We describe our experience with two patients with skeletal metastases as the dominant clinical manifestation of hepatocellular carcinoma.

CASE REPORTS

Case report 1

A 69 years old nonalcoholic Togolese woman, with no known defects, admitted to the gastroenterology department of the Campus teaching hospital of Lome in March 2019 for early post-meal prandial vomiting occurring 48 hours before hospitalization, with no other associated signs. In her history she reported low back pain of moderate intensity, mixed schedule, never explored, evolving for 3 months. The examination had found a general state preserved, an abdomen of normal volume, flexible, depressible and painful at the right hypochondrium, without mass, nor ascite. We notice an absence of spinal static disorder, absence of gibbosity, severe pain on palpation of the L1 vertebra. The abdominal CT Scan requested in the context of the exploration of this pain had found lytic images...
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Concerning the body of T9 (figure 1) and the spinous process of L1, associated with an enlarged liver, with irregular contours, of structure modified by a voluminous formation weakly enhanced after injection of contrast product, developed at the expense of segments II, III, IV and VIII, hypodense (figures 1 et 2). The alphafetoprotein was 1314 IU/ml; Liver enzymes were disturbed with a cholestatic pattern predominance: AST 145 IU/L (<34 IU/L), ALT 300 IU/L (<49 IU/L), GGT 258 IU/L (<38 IU/L), alkaline phosphatase (AP) 322 IU/L (<104 IU/L), total bilirubin 3.7 mg/dl (<1.0 mg/dl) and direct bilirubin 3.3 mg/dl (<0.2 mg/dl), as well as prolonged INR: 1.33. The HCV antibody was positive.

The diagnosis of hepatocellular carcinoma complicated by spinal metastasis was made, and the patient started on analgesic treatment, which made it possible to obtain a partial regression of the pain. The patient was released on symptomatic treatment before being readmitted one month later and died of hepatic encephalopathy.

![Figure 1: destructive spinal lytic lesion (red arrow)](image1)

**Case report 2**

A 39 years old patient, with no known chronic pathologies, seen in a general consultation for inflammatory pain and relative functional impotence of the left pelvic limb, which occurred suddenly without any notion of trauma two months before admission. An X-ray of the pelvis was requested, finding an osteolysis of the left iliopubic branch for which the patient was put on analgesic. Before the progressive installation of diffuse abdominal pain two weeks later, the patient consults in the gastroenterology department of the Campus teaching hospital of Lome. The examination found a deterioration of the general state, an absolute functional impotence of the left pelvic member, a bulky hepatomegaly tumor with free ascites of average quantity.

The abdominal CT Scan requested showed significant lysis of the left iliopubic branch, associated with an enlarged liver, with irregular contours, of structure altered by a mass of heterogeneous enhancement after injection of contrast product developed at the expense of the right liver (figure 2). The alpha-fetoprotein was 422 IU/ml, Liver enzymes were disturbed: AST 223 IU/L (<34 IU/L), ALT 265 IU/L (<49 IU/L), GGT 158 IU/L (<38 IU/L), alkaline phosphatase (AP) 262 IU/L (<104 IU/L), total bilirubin 2.7 mg/dl (<1.0 mg/dl) and direct bilirubin 1.3 mg/dl (<0.2 mg/dl), as well as prolonged INR: 1.31; The HBs antigen was positive.

The diagnosis of hepatocellular carcinoma complicated by pelvic metastases was made, and the patient put on morphine therapy in front of the persistence of pain with the usual analgesics. On the 8th day of hospitalization, the patient had discharged.

**DISCUSSION**

Hepatocellular carcinoma is an aggressive and rapidly lethal disease (11, 12). This clinical course can be explained by some of its anatomopathologic characteristics. Diffuse multinodular or solitary tumors grow rapidly and ultimately replace the normal liver parenchyma (13, 12). Portal and hepatic vein invasion by tumor is a common manifestation (13, 14). This explains the high frequency of distant metastases at the time of diagnosis (11). HCC tends to metastasize late in its course, with most patients dying of liver failure due to tumour replacement without clinically significant extra hepatic metastasis. However, in autopsy series, extra hepatic metastasis are found in over half the cases (15). Among these metastasis, bone metastases from HCC are infrequent, with a reported incidence ranging from 3 to 20% (16). The discovery of a bone metastasis during the evolution of HCC is a recognized incident and which has become more and more frequent given the improvement in the survival time of affected patients due to major advances in early detection, diagnosis and treatment of hepatocellular carcinoma. But the fact that these bone metastases reveal HCC is exceptional, reported in 7% of cases. These bony localizations are the spine, the ribs, the pelvis, the skull and more rarely the sternum (17). In our study, we noted spinal and pelvic localizations of HCC. To our knowledge this is the first time that cases of metastatic bone disease in patients with HCC have been reported to Togo. In the two cases that we report, patients presented bone metastasis at the time of initial HCC diagnosis, whereas others in literature (9,10,18) developed bone metastasis during disease progression. Axial skeleton is the most frequent localization of bone metastases with a prognostic correlation of the time.
between the primary HCC occurrence and bone metastases detection (6) as in the first reported case. They are mainly osteolytic, resulting in significant morbidity and reduced quality of life for patients due to associated events related to the skeleton (defined as a pathological fracture, spinal cord compression and pain) (19). Our patients had a moderate to severe child score. Among all the clinical and pathological parameters predicting the appearance of metastasis, only the Child Score resulted independently correlated early bone progression. This is the first report that indicates the Child Score not only as a predictor of overall survival, but also of a greater tendency to bone metastatization and biological osteotropism of HCC (8). In the two cases reported, they were large liver tumors. Indeed hepatocellular carcinoma is an aggressive and rapidly fatal disease (11, 12). This clinical evolution can be explained by some of its anatomopathological characteristics. Multinodular or solitary diffuse tumors grow rapidly and eventually replace the normal hepatic parenchyma (12, 13). In both cases we did not find any invasion of the portal vein. Portal and hepatic venous invasion by tumor is a common manifestation (13, 14). This explains the high frequency of distant metastases at the time of diagnosis (11). The AFP rate was very high in our two cases. Among patients with HCC and extra hepatic disease who have had bone metastases as the site of extrahepatic disease, elevated AFP levels have been shown to predict a poor prognosis (10). The etiology of HCC in our reported cases as in the literature (10,20) was viral hepatitis B and C, which could be explained by the high prevalence of these viruses in our country.

CONCLUSION

Hepatocellular carcinoma is the most common primary tumor of the liver, most commonly occurring on cirrhosis. Bone metastasis are rare in the evolution of hepatocellular carcinoma, however vertebral locations are the most common in these cases.

Conflict of interest: none declared

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