

Bone Metastases Indicative of Post Viral Hepatitis C Hepatocarcinoma: About Two Observations

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How to cite this paper: Houzou, P., Oniankitan, S., Bouglouga, O., N'Timon, B., Mba, E.D., Koffi-Tessio, V.E., Kakpovi, K., Tagbor, K.C., Fianyo, E., Atake, A.-E., Oniankitan, O. and Mijiyawa, M. (2021) Bone Metastases Indicative of Post Viral Hepatitis C Hepatocarcinoma: About Two Observations. *Open Journal of Rheumatology and Autoimmune Diseases*, 11, 144-151.

<https://doi.org/10.4236/ojra.2021.114015>

Received: July 25, 2021

Accepted: September 14, 2021

Published: September 17, 2021

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Abstract

Background: Hepatocarcinoma is the most common primary malignant tumor of the liver with rare bone metastases, electively residing in the vertebrae, ribs and sternum. They remain exceptionally revealing. **Cases reports:** We report two cases of bone metastases indicative of hepatocellular carcinoma in patients with viral hepatitis C. Through these two observations, we describe the various clinical, paraclinical and therapeutic aspects of this condition whose prognosis is poor. **Conclusion:** Although unusual, osteolytic bone metastases may be indicative of hepatocellular carcinoma, the diagnosis must be made in the event of any tumor bone involvement in a patient with chronic liver disease, particularly viral.

Keywords

Bone Metastasis, Hepatocarcinoma, Viral Hepatitis, Togo

1. Introduction

Hepatocellular carcinoma (HCC) or hepatocarcinoma is the most common type of primary liver cancer that accounts for around 90% of all cases and is the fourth leading cause of cancer death worldwide [1] [2]. Although, its geographical distribution is heterogeneous with the highest incidence in sub-Saharan Africa and Eastern Asia where infection of endemic hepatitis B virus (HBV) is the ma-

major cause around 70%, while in Europe and North America countries, hepatitis C virus (HCV) infection ranges from 50% - 70% and excessive alcohol consumption contributes for around 20% of all cases [1] [3]. The most frequent secondary locations of HCC are the lung, lymph nodes and kidneys [4]. However, an increase of bone metastases (BM) has been noted in recent decades, probably related to the lengthening of life expectancy following diagnostic and therapeutic advances in patients with HCC [5] [6]. These BMs are rarely revealing and are often located in the vertebrae, ribs and sternum [7]. We report two cases of HCC revealed by bone metastases with vertebral locations and an exceptional scapulo-humeral location in Togolese (West African) patients with viral hepatitis C.

2. Cases Reports

Observation 1: Mr. M.B., 69 years old, chronic ethyl, was known to be carrying viral hepatitis C diagnosed 5 months ago and not followed up consulting for mechanical low back pain developing for 9 months which became inflammatory and debilitating 3 weeks before admission. There was abdominal pain that appeared during hospitalization, with no other associated signs. The clinical examination found an altered general condition, lumbar spinal syndrome without neurological deficit. There was also pain on palpation of the ribs and painful swelling of the stump of the right shoulder. Examination of the abdomen revealed hepatomegaly at 14 cm arrow, hard with a sharp edge, without associated signs of hepatocellular insufficiency. The examination of the other devices was normal. X-rays of the lumbar spine and right shoulder revealed lytic images of the right transverse vertebral process of the first lumbar vertebra, the upper end of the right humerus and the right scapula (**Figure 1**). An abdominopelvic tomodensitometry (CT) performed noted a normal size liver with regular contours, seat of two nodules taking the contrast (**Figure 2**). Biology noted a biological inflammatory syndrome with a sedimentation rate of 50 mm, pancytopenia (hemoglobin level at 9.8 g/dL; white blood cells at 2300/mm³ and platelets at 98,000/mm³), cytotoxicity (elevated AST at 158 IU/L and ALT high at 96 IU/L) and hepatic cholestasis (γ -GT at 172, normal alkaline phosphatase at 212 IU/L). Serum protein electrophoresis noted hypoalbuminemia and polyclonal hypergammaglobulinemia. Prostate-specific antigen levels were normal at 2 ng/mL, and alphafoetoprotein (AFP) levels were elevated at 4000 IU/L. The diagnosis of HCC in post viral C cirrhosis with bone metastasis was very probable given the history of viral hepatitis C and the clinical, radiographic and CT scan of the liver and laboratory features. A bone and liver biopsy puncture with pathological examination could not be performed due to insufficient technical facilities. The presumptive diagnosis thus retained was HCC in viral C cirrhosis revealed by bone metastases. Due to the advanced stage of neoplastic disease; the therapeutic attitude was symptomatic treatment with analgesics (tramadol, morphine sulfate and prednisone), three infusions of zoledronic acid and vitamin C and E therapy. He got also a plastered corset for one month. The patient died five months after the diagnosis.



Figure 1. X-ray image of osteolysis of the scapula and humeral head (red arrow).



Figure 2. Ct axial section of the abdomen passing through the liver, with injection of the contrast medium, showing two hepatic masses of the right lobe (red arrows) partly necrotic, with enhancement of the tissue part in arterial time.

Observation 2: Mr. T.A., 65 years old with known hypertension of irregular follow-up, was admitted for an exacerbated right lumbaradiculalgia of mechanical schedule two weeks before his admission. The clinical examination found a deterioration of the general condition, a lumbar spinal syndrome and a radicular syndrome without sensory-motor deficit. Examination of the abdomen revealed tender hepatomegaly within 15 cm of hepatic arrow with blunt inferior border, without clinical sign of portal hypertension. The remainder of the physical examination was normal. A lumbar scanner objectified the presence of lysis of the vertebral body of the fourth lumbar vertebra in favor of a bone tumor (**Figure 3**). On the abdominal CT, it was noted a multinodular faith taking the contrast and of which the largest measured 75 mm × 81 mm and dilation of the portal trunk. Laboratory work-up showed a biological inflammatory syndrome with



Figure 3. CT appearance of L4 lysis (red arrow).

hypochromic microcytic anemia at 10.1 g/dL and a sedimentation rate of 100 mm, and polyclonal-looking hypergammaglobulinemia with beta-gamma block by electrophoresis of serum proteins. There was also cytolysis (AST elevated to 162 IU/L and ALT elevated to 85 IU/L) and hepatic cholestasis (γ -GT elevated 464 IU/L, alkaline phosphatases elevated to 645 IU/L, total bilirubins at 12.79 IU/L and direct at 6.10 IU/L). The anti-HCV antibodies were positive, and the alphafoetoprotein level was greater than 40,000 IU/L. The diagnosis retained being HCC on liver of cirrhosis post hepatitis C with revealing bone metastasis. But bone and liver biopsy puncture with pathological examination was not performed due to insufficient technical facilities. Treatment was mainly symptomatic with analgesics (tramadol and morphine sulfate), vitamin C and E therapy and two infusions of zoledronic acid. Two months after this diagnosis, the patient died.

3. Discussion

HCC is the most common primary malignant tumor of the liver and the fifth most common cancer in the world [5]. It is a major cause of death in sub-Saharan Africa and South-East Asia where it is the most frequent visceral cancer [8]. HCC develops in 90% of cases in cirrhosis which is a true precancerous condition, more rarely in chronic liver disease, exceptionally in a healthy liver. The main risk factors for cirrhosis or chronic liver disease are viral B and C infections and excessive alcohol consumption. The chronic hepatitis caused by infection with virus C from our two patients has been recognized as an important factor in the genesis of HCC [9]. Indeed, the oncogenic role of chronic infection with viral hepatitis B and C occurs by a direct or indirect mechanism [10]. Viral

hepatitis infection is associated with cellular inflammation, oxidative stress, and DNA damage, which may lead to subsequent hepatic injuries such as chronic hepatitis, fibrosis, cirrhosis, and finally HCC. In Egypt, the country most affected by viral hepatitis C in the world, 36.2% of patients had bone metastases which revealed HCC in subjects carrying this infection [11]. Men were the most affected as the case of our patients, however, the ribs and mandible were the most affected bones in this Egyptian study. BMs in HCC are also frequently located in the spine with a risk of spinal cord compression [12] [13]. In our patients, BM was located not only in the spine, but also in the humerus and scapula, which are exceptional locations. In a multicenter study, 77.8% developed bone metastasis after HCC diagnosis while 22.2% showed bone metastasis at the time of HCC diagnosis; 64.9% had multiple bone metastases and the remaining 35.1% showed single lesion [14]. BM revealed the HCC in our patients, and the bone lesions were osteolytic as described in the literature [11] [15] [16] [17], even osteoblastic lesions can be found in few patients [14]. Due to insufficient technical platform, bone and liver biopsy could not be performed. However, the deterioration in general condition, the lumpy appearance of the liver, and the very high rate of AFP noted in our patients were strongly suggestive of HCC. Indeed, studies have found a strong correlation between elevation of AFP and the onset of metastatic HCC [18] [19]. Indeed, AFP promoted HCC cell invasion and metastasis via up-regulating expression of metastasis-related proteins [19]. However, its prognostic role in survival remains mixed [14] [19] [20] [21]. Even patients with bone metastasis had a better prognosis than patients with lung metastasis [22], the occurrence of BM during HCC has a poor prognosis with a statistical link in spinal location [14]. Our two patients had spinal injuries, and died 5 and 2 months after diagnosis, respectively. The mean survival time during BM in HCC varied between 6 and 7 months in Korea and Italy [14] [20] [21]. This duration appears to be shorter in our country where the symptomatic management of BM, in addition to orthopedic means and analgesics, combines zoledronic acid as indicated in the literature [14] [23]. There was no radiotherapy center in Togo when our patients were admitted. However, therapeutic advances in HCC with the use of anti-monoclonal antibodies appear to improve the survival of this condition [24]. These molecules are almost inaccessible to our patients because of their very high cost.

4. Conclusion

Although unusual, osteolytic bone metastases may be indicative of HCC. The diagnosis must be made in the event of any tumor-like bone involvement in a patient with chronic viral liver disease, which prevention requires increased sensitization and vaccinations.

Ethics Approval and Consent to Participate

This study was approved by the “Comité de Bioéthique pour la Recherche en

Santé (CBRS)” (Bioethics Committee for Health Research) from the Togo Ministry of Health, Ref N0: 0101/2016/MS/CAB/DGS/DPLET/CBRS). All patients and relatives of patients had received information on the purpose and procedures of this study and provided written and informed consent. The study has been carried out in accordance with relevant guidelines and regulations.

Conflicts of Interest

The authors declared no potential conflicts of interest with the research, authorship, and/or publication of this article.

Authors Contributions

PH was responsible for the study design, undertook the field study, performed data collection, analysis and interpretation, and wrote the manuscript.

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