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Case Report

Multifocal Hepatocellular Carcinoma or Liver Metastases?

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Abstract

Metastases are the most common malignant liver lesions and are about 18-40 times more common that primary liver tumors.

On the other hand, hepatocellular carcinoma (HCC) is the fifth most common cancer in men, accounting for more than 500,000 deaths per year worldwide.

We present the case of a 64-year-old male, chronic ethanol consumer, which declared having chronic hepatitis HBV, who performed an abdominal computed tomography which revealed enlarged liver with multiple nodular lesions, and a macronodular lesion which occupied almost entirely the caudal lobe. The CT features have allowed differentiation between multifocal hepatocellular carcinoma and liver metastases as well as the starting point of neoplasia.

Keywords: *CT; liver metastases; multifocal hepatocellular carcinoma*

Abbreviations

CT: Computed Tomography; HCC: Hepatocellular Carcinoma; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; ESR: Erythrocyte Sedimentation Rate; CRP: C - Reactive Protein; CEA: Carcinoembryonic Antigen; HBsAg: Surface Antigen of The Hepatitis B Virus

Introduction

Metastases are the most common malignant liver lesions and are about 18-40 times more common that primary liver tumors [1,2,3].

The most common sites of primary malignancy that metastasize to the liver are gastrointestinal tract (via portal circulation), breast cancer, and lung cancer [3].

The accurate detection and characterization of metastatic disease at the time of diagnosis or during the course of treatment remains crucial to patient management [2,3]. Early identification provides the opportunity for resection, which has been shown to prolong survival [4].

On the other hand, hepatocellular carcinoma (HCC) is the fifth most common cancer in men, accounting for more than 500,000 deaths per year worldwide [5].

It is the most common primary liver cancer with nearly three quarters of cases in the world occurring in Asia secondary to the high prevalence of chronic viral hepatitis [6].

HCC incidence varies with age, sex, and geographic region, the major number of cases coming from Asia, followed by Europe, Africa, North America, Latin America and Caribbean [7].

The distribution of HCC cases among different populations reflects the differences in the exposition to different etiological factors [8].

HCC is associated with chronic liver disease and cirrhosis regardless of the etiology. Only about 10% of HCCs develop in non-cirrhotic livers [9].

A major risk factor is chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) [10]. Approximately 70% to 90% of all cases of HCC occur in cirrhosis due to chronic infection by hepatitis B virus (HBV) and hepatitis C virus (HCV), toxic injury from excessive alcohol consumption, or metabolic liver disease primarily associated with obesity and diabetes [11].

Chronic HBV infection is a leading cause of HCC in most Asian and African countries and HCV predominates in some southern European countries [6]. Coinfection with HBV and HCV may have a synergistic effect on HCC development [10].

Long-term prognosis of HCC remains dire with 5-year survival rates hovering around 12% for all stages combined, although treatment interventions applied at early stages of HCC provide dramatically better results and justify regular surveillance and aggressive therapy [12].

Case report

We present the case of a 64-year-old male, chronic smoker and chronic ethanol consumer, which declared having chronic hepatitis HBV (uninvestigated for 20 years), with duodenal ulcer operated in 1986 complicated with postoperative eventration (operated in 1990), with type 2 diabetes (diagnosed in 1998), insulin dependent for the last 10 years, with multiple micro and macrovascular complications, hypertensive, is present to the hospital for palpitations with rapid and irregular rhythm and pain in the upper abdominal area, for several months, almost permanent, sometimes accompanied by heartburn.

It should be noted that was presented to the emergency room a month earlier, where was detected atrial fibrillation with rapid ventricular response, but at that time he refused admission and not expected test results, returning the next day for them, being a non-compliant patient.

At current admission, the physical examination detected an overweight patient, with average overall status, median line postoperative edematous erythematous scar, with increased local temperature, important varices in the lower limbs, palmar erythema, abdominal angiomas, lack of hairiness at the lower leg, abdominal excess fat represented at the abdominal level, discrete leg and abdominal wall edema, normal blood pressure and normal pulse, liver with the lower edge at about 4 cm under the right rib cage, palpable spleen with inferior margin at approximately 5 cm under the left rib cage, painless to palpation.

Blood tests had detected mild hyperchromic macrocytic anemia, mild thrombocytopenia, neutrophilia, and an inflammatory syndrome (ESR-49mm/l/h, and CRP 7,6mg/dl), increased glycosylated hemoglobin, increased CEA tumor marker, hypoalbuminemia, with hepatic cholestasis, and HBsAg and anti-HCV negative results.

Diagnostics after physical examination and blood tests were permanent atrial fibrillation, hepatic cirrhosis of toxic etiology, insulin-requiring diabetes with micro- and macrovascular complications.

Given that the patient claims to have lost approximately 17 kg in the last month, without selective loss of appetite, and increased CEA marker, he was directed to the Department of Radiology and Medical Imaging for a CT examination with the suspicion of hepatocellular carcinoma due to liver cirrhosis.

The CT scan was performed native and with administration of intravenous and oral contrast medium.The abdominal CT revealed the liver with slightly elevated dimensions (19.5 cm cranio-caudal diameter) with regular contours, with inhomogeneous structure by the

presence of multiple nodular isodense lesions, with well-defined contours, homogeneous, some with moderate contrast enhancement in arterial phase, with rapid wash-out, the largest of 1.4 cm, located in segment 8 (Figure 1), and some with low contrast enhancement, the largest of 2cm in segment 4 (Figure 2). Also, it was noticed a macronodular lesion of 4cm, hypodense on native scan, with low contrast enhancement, ill-defined contour, which occupied almost entirely the caudal lobe (Figure 3).

Also perihepatic fluid was identified, with maximum thickness of 2cm (Figure 2).

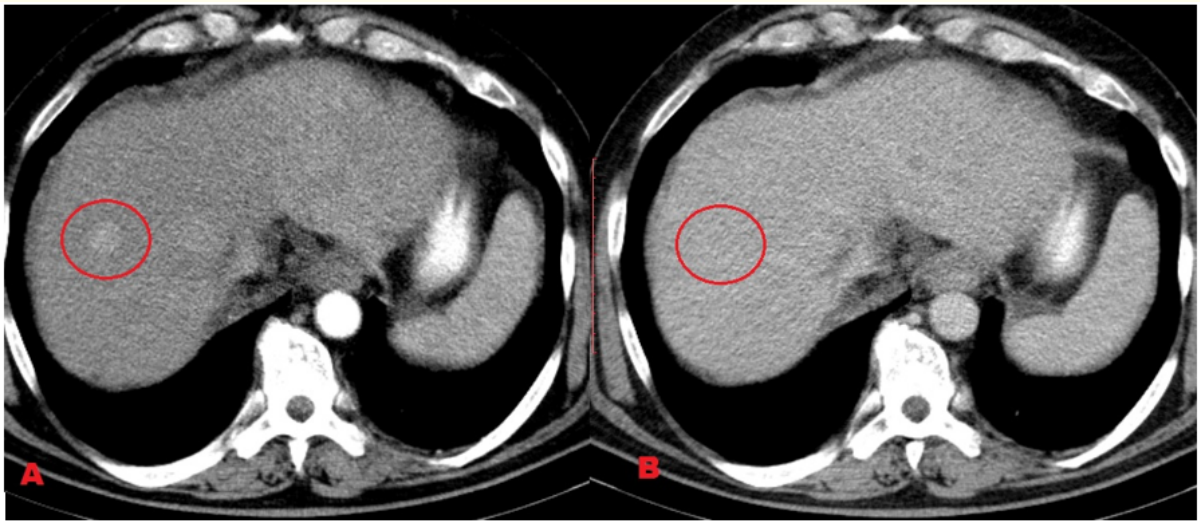

Figure 1: *abdominal CT: A – arterial phase, B – venous phase: nodular lesions with moderate contrast enhancement in arterial phase, with rapid wash-out (red circle).*

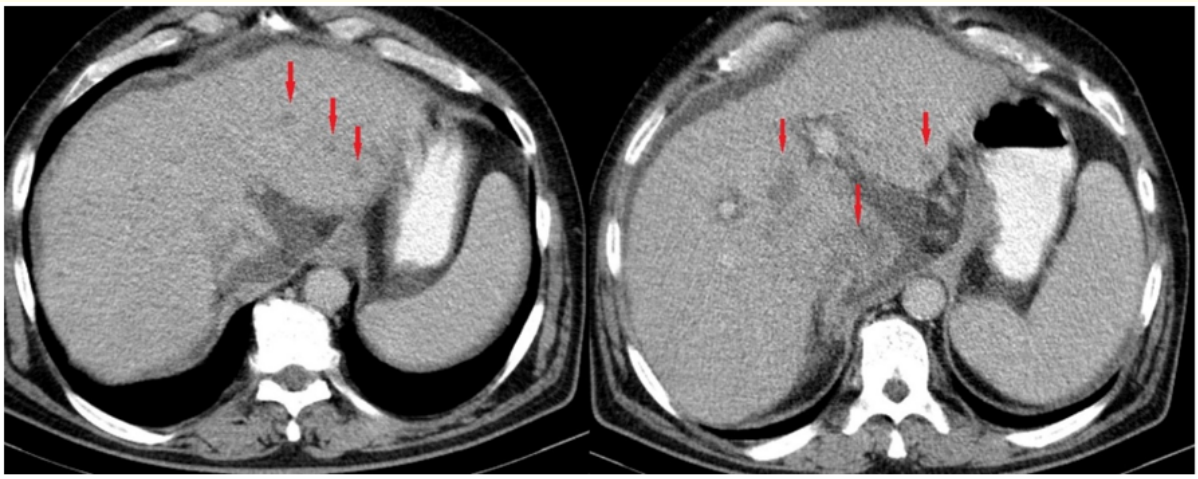

Figure 2: *abdominal CT: venous phase: nodular lesions with low contrast enhancement (red arrows).*

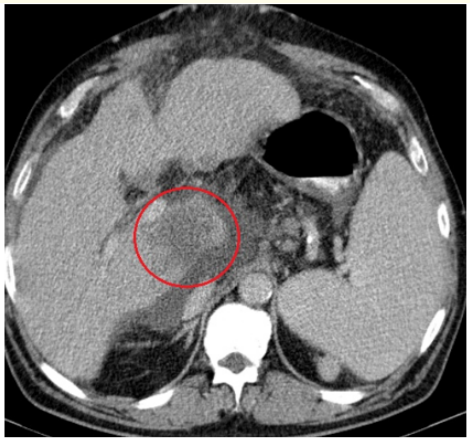

Figure 3: *abdominal CT: venous phase: nodular lesions with low contrast enhancement, and ill-defined contour, which occupies almost entirely the caudal lobe (red circle).*

The portal vein had a maximum caliber of 1.8cm, and splenic vein had a maximum caliber of 1.4cm, without signs of thrombosis.

Withal it was detected collateral pathways (peripacreatic, perisplenic, perigastric, and in the anterior abdominal wall) and spleen enlargement (21 cm cranio-caudal diameter), but with homogeneous structure, as well as a parietal defect on the median line above the navel with protrusion of large omentum and intestines, without signs of occlusion, and some renal bilateral cysts.

It has also been highlighted parietal irregular, asymmetric thickening (up to 1.7cm) of the wall of descending duodenum, with the involvement of papilla (Figure 4B), extended to the common bile duct at a length of about 2 cm (having a maximum thickness of 0.5 cm), as well as to the duodenal bulb and the posterior surface of the stomach, but without revealing tumor masses at these levels.

The choledoch had the maxim caliber of 1 cm (Figure 4A).

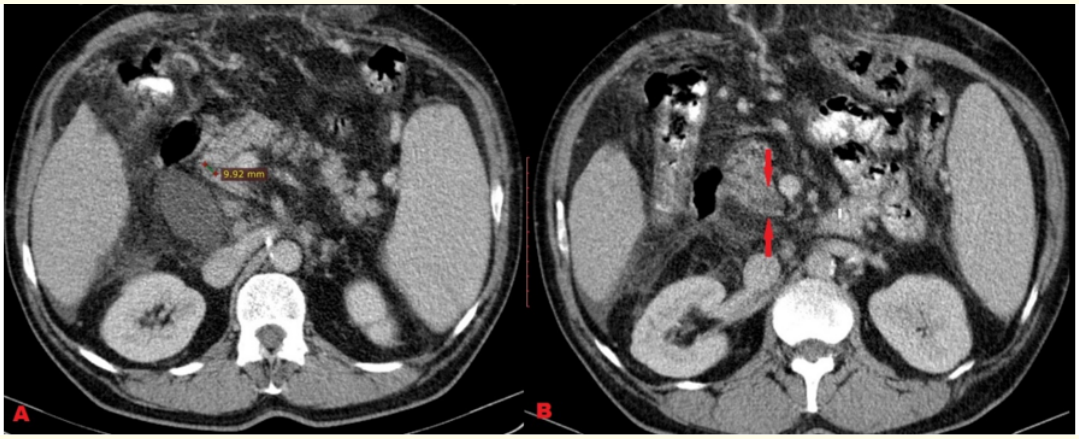

Figure 4: *abdominal CT: venous phase: parietal irregular, asymmetric thickening involving the papilla (B – red arrows) and with dilation of the choledoch with maxim caliber of 1 cm (A).*

We found also adenopathies, in celiac group up to 1.2 cm, peripancreatic groups up to 1 cm, interaorticocaval group up to 1.2 cm, and para-aortic groups up to 1.4 cm (Figure 5).

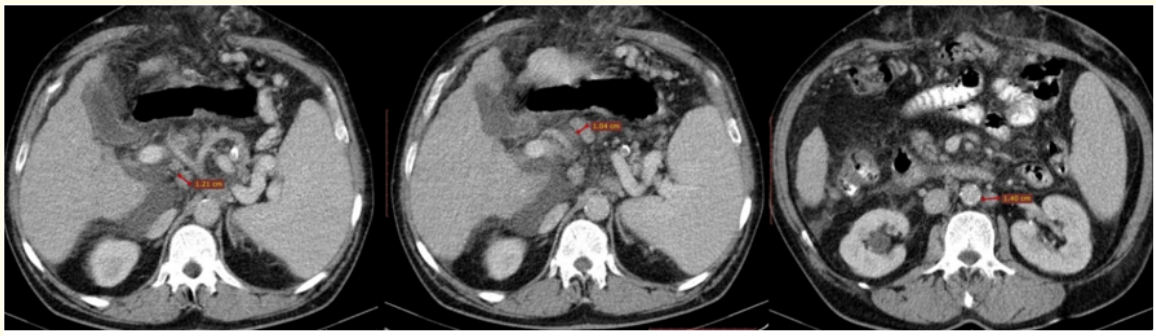

Figure 5: *abdominal CT: venous phase: abdominal adenopathies.*

The CT examination conclusion was tumoral thickening of the duodenum, with the involvement of the papilla and common bile duct, with liver metastases and adenopathies. Also, hepatosplenomegaly and portal hypertension were among conclusions.

We mention that the patient underwent upper GI endoscopy in the context of biopsy acquisition and histopathological confirmation, which revealed the diagnosis of poorly differentiated adenocarcinoma.

During hospitalization, evolution was favorable with improvement of symptomatology under treatment.

Discussion

Hepatocellular carcinoma (HCC) is a frequent and deadly human disease, with 0.25-1 million new cases per year [13], and ranks sixth in cancer incidence and third in cancer mortality worldwide [14], with growing incidence of HCC [15].

However, liver is the most common site of distant metastasis [16,17], and liver metastases are the most common indication for abdominal imaging [18].

Detection and characterization of liver lesions has been greatly improved due to advances in scanning techniques and the understanding of liver and lesion conspicuity on unenhanced and contrast-enhanced CT and magnetic resonance imaging [19].

Also, dynamic and multiphase contrast-enhanced computed tomography (CT) and magnetic resonance imaging are the standard diagnostic methods for HCC [20].

Liver metastases are usually asymptomatic and found during workup of a malignancy which has presented in other ways. Symptoms like hepatomegaly, jaundice, and ascites due to liver metastases are discovered much later and bring about worse prognoses [21].

In the study of Izzo., *et al*. [22] the histological diagnosis was HCC in 73.5% of cases, 23.8% of patients had metastases, and few (2.8%) were diagnosed with cholangiocarcinoma. Kim., *et al*. [23] found liver metastasis in 10 patients in their analysis.

Liver metastases are typically hypoattenuating on unenhanced CT [1.3]. If there is concomitant hepatic steatosis, then the lesions may be iso- or even slightly hyperattenuating [1], and central low attenuation may be the result of necrosis or cystic change [3]. Depending on lesion size, the margins tend to be irregular, but margins can be sharp and well-defined [3].

On unenhanced images, the appearance of HCC is variable and depends on the surrounding liver parenchyma and etiology of chronic liver disease [20]. Most often, HCC appear hypodense or isodense to the liver on unenhanced images but may appear hyperdense when they develop in a background of fatty liver [20]. Other typical imaging features of HCC include internal mosaic pattern, presence of fat, vascular invasion, and interval growth of 50% or more on serial images obtained less than 6 months apart [24].

Is well known that most liver metastases are hypovascular [3], and they are enhancing less than surrounding liver following contrast administration [1]. During the arterial phase they show a complete ring of enhancement [3], which during the portal venous phase of imaging, this thickened rind enhances progressively but to a lesser extent than liver [3]. Although, on portal venous phase, there may be seen a central filling in [1]. The delayed phase will show washout, being helpful in distinguishing a metastasis from a hemangioma [1].

Classic HCC shows arterial phase enhancement followed by a washout in the portal and/or delayed phase with a pseudocapsule around the nodule [20]. Portal vein tumor thrombosis (PVTT) is a well-known complication of HCC, the presence of which modifies typical imaging features [20].

In oncological pathology, duodenal neoplasm is relatively rare entity [25], and comprises <0.5% of all gastrointestinal malignancies [26]. These neoplasms are usually grouped as periampullary carcinoma because most tumors arise in the periampullary region [27].

Although they are considered to be very rare, there are studies that have shown that primary duodenal tumors are found in 15- 25 % of cases of malignant tumors of the small intestine [28].

In primary duodenal malignant tumors, the most common histopathological form is the adenocarcinoma [28]. This was also the diagnosis in the case presented by us.

Because the incidence of duodenal cancer is low, most studies have been performed retrospectively with relatively few patients and a longer period of inclusion than other periampullary malignancies [23]. Therefore, several points such as the extent of surgery including the extent of lymph node dissection and prognostic pathological factors are still controversial [29,30].

The 5-year survival rate of duodenal cancer is reported to be less than 30% [31,32]. On the other hand, it is reported that resection improves 5-year survival [33]. Several clinicopathological factors have been reported to affect survival for primary duodenal adenocarcinoma [16,27,29,30].

Duodenal adenocarcinoma is usually diagnosed late, because symptoms are nonspecific and resemble those of duodenal ulcer [34,35]. The surgical procedure for duodenal adenocarcinoma varies and usually depends on the location of the tumor. Segmental resection of the duodenum or pancreaticoduodenectomy is performed most commonly [23]. In our case, the diagnosis assumed as a result of the CT examination was possible due to manifestations caused by liver metastases, but which raised the initial suspicion of HCC.

Conclusions

It is well known that HCC occurs most frequently as a result of cirrhosis of the liver. Diagnosis can be determined by radio-imaging examinations, along with laboratory tests, patient symptomatology, and clinical examinations.

The CT examination with intravenous contrast media is the most reliable imaging method for diagnosing liver lesions, along with MRI.

The CT scanning protocol for identifying and diagnosing liver lesions should include a native phase and arterial, venous and parenchymal phases, as well as the late phase that is essential in the differential diagnosis of benign and malignant lesions. These postcontrast phases must be performed as standard, because the lesion characteristics on CT images can help differentiate HCC from other liver lesions that can mimic HCC. The appearance of these different pathologies must be known, especially when differentiating between multifocal HCC and liver metastases of different etiologies, as the therapy used differs.

Conflict of Interest

There is no conflict of interest.

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