Hepatocellular carcinoma with hepatic and pulmonary metastasis, inferior vena cava and left pulmonary artery thrombosis in a patient with asymptomatic hepatitis C. Case report

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Abstract
During the virus C infection the presence of cirrhosis is the major risk factor for the development of hepatocellular carcinoma. In the absence of cirrhosis the estimated prevalence hepatocellular carcinoma ranged from 6.7% to 50.1%. We present the case of a 64 year-old-man admitted to the hospital with 3-days history of nespecific symptomatology. Screening abdominal ultrasound showed an enlarged liver with 4 parenchimatous nodules in the right lobe and malignant thrombosis of the inferior vena cava. Chest CT revealed multiple metastasis in both lungs and left pulmonary arterial thrombosis. The patient died 5 weeks later. The particularity of the case is the presence of the end-stage hepatocellular carcinoma in a patient with asymptomatic C virus infection.

Keywords: hepatocellular carcinoma, hepatitis C, abdominal ultrasound

Introduction
Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related deaths worldwide [1]. Chronic hepatitis B virus (HVB) and hepatitis C virus infection (HCV) are the most important causes of hepatocellular carcinoma (HCC). The presence of cirrhosis is a major risk factor for the development of HCC. However, HCC can occur in the absence of cirrhosis, suggesting that both HBV and HCV may be directly involved in hepatocarcinogenesis [2]. Various HCV proteins, including the core, envelope and non-structural proteins, have been shown to have oncogenic properties [2]. The estimated prevalence of noncirrhotic hepatocellular carcinoma ranged from 6.7% to 50.1% [3]. The pooled prevalence estimated for HCV in non-cirrhotic HCC ranged from 0% and 68.4% according to the geographic location [3]. Reports from Japan had the highest estimated pooled prevalence of HCV (55.01%), followed by Italy (29.95%) [3,4]. HCV can occur in patients with HCC without cirrhosis, but the true incidence and prevalence are very difficult to ascertain [3, 5]. We report a case of a hepatocellular carcinoma with hepatic and pulmonary metastasis, inferior vena cava and left pulmonary artery thrombosis in a patient with asymptomatic hepatitis C.
Case presentation

A 64 year-old-man was admitted presenting with a 3-days history of right-sided abdominal pain, poor appetite, and low fever. There was no history of weight loss, past medical history, alcohol drink, and smoking. At physical examination, the liver was 5 cm below the lower edge of the ribs. There was no ascites, edema, hepatic failure signs or cirrhosis stigmata. The patient had diminished vesicular breath sounds over the right lung base, blood pressure 170/80 mmHg, heart rate 70/bpm, and pain at palpation of the right upper abdomen. Laboratory evaluation revealed leucocytosis (13800/mm3), neutrophilia (74.3%), high erythrocyte sedimentation rate (32 mm/h), serum aspartate aminotransferase (110 u/L), and serum alanine aminotransferase (62 u/L). The other routine blood tests were in normal range.

Screening abdominal ultrasound showed an enlarged liver with 4 hyperechoic nodules in the right lobe, with the largest up to 100 mm, heterogenous, with less defined capsule and hypervascularized (fig 1). The largest mass infiltrated the inferior vena cava with thrombosis. The others masses were between 20 and 40 mm and showed different, some of them in target (fig 2, fig 3). The spleen was slightly enlarged with an accessory spleen of 20 mm. This aspect was confirmed at abdominal CT (enlarged liver with multiple lesions, some of them with necrosis, the right lobe with an extensive heterogenous lesion, malignant thrombosis of inferior vena cava, and multiple lymph nodes between aorta and inferior vena cava, less than 10 mm) (fig 4).
Chest radiograph demonstrated multiple variable sized nodules in both lungs. Chest CT revealed multiple variable sized well-defined nodules in both lungs, between 5 and 25 mm (fig 5) and left pulmonary arterial thrombosis (fig 6). Cerebral CT was normal. The alpha-fetoprotein level was above 300 ui/ml, hepatitis C antibody were positive, and hepatitis B antibody negative. Upper and lower endoscopy were negative for collateral circulation and a primar digestive tract cancer was excluded.

Since the disease was at a very advanced stage the patient was given palliative treatment. The patient died 5 weeks later and the family refused necropsy.

Discussion

Hepatitis C virus has a major impact on public health, infects around 170 million people in the world, with an estimated global incidence of three to four million new infections per year [6]. Most patients infected with HCV are unaware of their exposure and remain asymptomatic during the initial stages of the infection. The majority of these infections will progress to chronic HCV. HVB and HCV infection can cause chronic injury to the liver, with subsequent progression to severe fibrosis and cirrhosis. The presence of cirrhosis is a major risk factor for the development of HCC. However, HCC can occur in the absence of cirrhosis.

Early diagnosis of HCC is critical for its effective treatment. The tumor frequently metastasizes via the lymphatic system, intrahepatic blood vessels or direct infiltration [7]. The lung is the most common site for extrahepatic spread and its involvement is associated with poor prognosis [8,9]. The therapeutic interventions are generally ineffective in advanced stages [10]. Imaging of the liver is a key component in detection, diagnosis, management and follow-up of patients with HCC [11].

This case report describes an unusual presentation of HCC in an asymptomatic patient with no past history of hepatitis virus infection. Although he had few symptoms at the moment of diagnosis, his tumor was already at an advanced stage, with multiple pulmonary metastases, inferior vena cava thrombosis, left pulmonary arterial thrombosis. The presence of cirrhosis is a major risk factor for the development of HCC, but our patient had no clinical sign of cirrhosis. Because the blood tests need time, it is almost a rule in the emergency room to investigate the patients by ultrasound, after the clinical exam. It is a rapid and noninvasive investigation, well accepted by the patients and very useful. In our case abdominal ultrasound was the first method used in diagnosis, before laboratory evaluation. The aspect was a multifocal HCC in the hepatic right lobe. The largest nodule, had more than 10 cm, and the smallest nodule had 2 cm. The ultrasound aspect of these tumors was heterogeneous: hyperechoic, hypoechoic, and in target. On color Doppler, the nodules had classical intratumoral flow signals, with the vessels flowing into the lesions and branching within it. The larger tumor infiltrated the inferior vena cava with metastatic thrombosis. In our case the ultrasound guided the next exams. Alpha-fetoprotein level was above 300 ui/ml, with positive hepatitis C antibody and negative hepatitis B antibody. Alpha fetoprotein is considered to be the serum marker for HCC. The endoscopic evaluation of the digestive tract, abdominal, thoracic and cerebral CT were negative for other primary tumors. The patient presented to the hospital with advanced disease,
and the prognosis in this situation was very poor and the treatment was only palliative.

In conclusion HCC can arise in livers chronically infected with hepatitis C, but without cirrhosis. Most patients infected with hepatic C virus are unaware of their exposure and remain asymptomatic until an advanced stage. Hepatitis C virus infection might evolve into chronic disease, cirrhosis, and/or HCC, depending on the host immune response. Ultrasonography is the technique of choice for screening focal hepatic lesions, targeted at the population at risk.

References