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HEPATOCELLULAR CARCINOMA IN A NON-CIRROTIC PATIENT WITH CHRONIC HEPATITIS B VIRUS INFECTION: CASE REPORT

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Abstract: Hepatocellular carcinoma (HCC) is a primary cancer that affects the liver and usually arises in the context of liver cirrhosis, but in 20% of cases it develops in a non-cirrhotic liver. It may be associated with several causes, including chronic infection by the hepatitis B virus (HBV). HCC is an aggressive disease and its diagnosis is usually made in advanced stages, as it is a silent morbidity in its early stages. In this study, we report the case of a non-cirrhotic patient diagnosed with advanced HCC secondary to chronic HBV infection. The description of this case aims to alert about the risk of HCC emergence in non-cirrhotic patients, with chronic HBV infection, showing the importance of surveillance in this group of patients, thus enabling early diagnosis and adequate treatment of the aforementioned tumor.
Keywords: Hepatocellular carcinoma; Hepatitis B; Hepatical cirrhosis.

INTRODUCTION

Hepatocellular carcinoma (HCC) is characterized as a primary cancer that affects the liver and is the most frequent primary liver tumor. It usually arises in a context of liver cirrhosis, however, in about 20% of cases, it develops in a non-cirrhotic liver (DESAI et al., 2019).

The incidence of this pathology gradually increases with advancing age, reaching a peak around the 7th decade of life and is found at a frequency about three times higher in men than in women (HEMMING et al., 2016).

Liver cirrhosis is the greatest individual risk factor for HCC development and all its etiological forms can be complicated by the formation of said tumor, however, the risk is high in patients with chronic viral hepatitis (IOANNOU et al., 2017).

Worldwide, about 50% of all cases of HCC, among cirrhotic and non-cirrhotic patients, are caused by chronic HBV infection, and among these, at least 30% develop HCC even in the absence of HBV. cirrhosis (BEASLEY, 1988).

The present work describes the case of a previously healthy patient, hospitalized for investigation of abdominal pain and weight loss, where he was diagnosed with advanced stage HCC, in the absence of liver cirrhosis and in the context of chronic infection. by HBV. In order to carry out this case report, clinical data from the patient's history and complementary exams, recorded in the medical records during hospital stay, were used. The description of this case is justified to warn about the risk of developing HCC in patients with chronic HBV infection, even in the absence of liver cirrhosis, thus showing the importance of carrying out surveillance in this group of patients to ensure early diagnosis. and allowing adequate treatment of said tumor.

CASE REPORT

A 50-year-old male patient, active alcoholic and without known comorbidities. He was admitted to the emergency room due to a 3-month evolution of moderate intensity abdominal pain in the epigastric region and right hypochondrium, associated with hyporexia and weight loss of about 10 kg. It did not identify factors that improved or worsened the referred pain. He denied increased abdominal volume, nausea or vomiting, choluria, fecal acholia, change in bowel habits, fever or any other symptoms. Laboratory workup was performed with evidence of increased transaminases and canalicular enzymes. 108 Oxalacetic glutamic transaminase (reference value (RV) < 35); Pyruvic glutamic transaminase (TGP) of 128 (VR < 45); 359 gamma glutamyltransferase (RV < 60); Alkaline phosphatase of 218 (RV < 100). Ultrasonography (USG) of the upper abdomen was also performed, which showed increased liver volume, associated with

irregular contours, heterogeneous texture, associated with several nodular formations of 1.4x1.4cm, 1.9x1.8cm and 5.4x5.7cm, with the diagnostic impression of chronic liver disease associated with nodules to be clarified. Due to the lack of medical resources and the need to establish the diagnosis of the referred case, the patient was referred to a referral hospital, for a propaedeutic extension and elucidation of the case. He was admitted in good general condition, with performance status 0, without stigmata of chronic liver disease, the only alteration on physical examination being moderate abdominal pain on deep palpation in the right hypochondrium. On admission, a contrast-enhanced computed tomography (CT) scan of the abdomen and laboratory tests were performed.

Abdominal CT showed an enlarged liver at the expense of the right lobe, lobulated contours and heterogeneous parenchyma at the expense of multiple hypodense lesions of varying sizes and varying kinetics of post-contrast enhancement, some hypervascular, some low uptake, others without enhancement in between. of contrast and all of them with imprecise limits due to the great confluence between them, the largest being partially individualized in segment VIII, measuring 6.4x6.1cm. At the conclusion, a marked hepatomegaly was described at the expense of diffuse involvement of the parenchyma by expansive lesions, with a secondary neoplastic appearance.

The diagnostic hypothesis of hepatic neoplasm of secondary origin was raised, and upper digestive endoscopy and colonoscopy were performed to search for the primary site, which came without alterations.

A complete laboratory review was also performed, with viral serology and alpha-fetoprotein (AFP). The results of such exams showed maintenance of the elevation of transaminases and canalicular enzymes. And they also showed chronic infection by HBV, through hepatitis B surface antigen (HBsAg) reagent, antibodies against HBsAg (Anti-HBs) non-reactive, total antibodies against hepatitis B antigen c (Anti-HBc total) reagente, IgM antibodies against Hepatitis B C antigen (Anti-HBc IgM) non-reactive, Hepatitis B antigen E (HBeAg) non-reactive, antibodies against HBeAg (Anti-Hbe) reagent and viral load (HBV-DNA) of 680,000 IU/ml (RV not detectable); In addition, an AFP of 80,000 (VR < 8) was visualized. Once the diagnosis of chronic hepatitis B was made, it was decided to start treatment with entecavir.

After an examination showing a significant increase in AFP, in addition to the diagnosis of chronic hepatitis B, the diagnostic hypothesis of HCC secondary to chronic HBV infection in a non-cirrhotic patient was raised, despite inconclusive imaging tests. Thus, it was decided to perform a liver biopsy, which in its results suggested the possibility of well-differentiated HCC, but could not rule out the possibility of other hepatocellular lesions.

In this context, the material from the liver biopsy was sent for immunohistochemistry, which showed foci of atypical hepatocytic proliferation, revealing expression for hepatocyte-1 and glypican-3; The set of these findings favors the diagnosis of hepatocarcinoma.

DISCUSSION

The development of HCC in a context of chronic HBV infection is associated with risk factors such as elevated and persistently elevated viral load, HBeAg positivity, HBsAg levels >1000 IU/mL in patients with chronic inactive HBV, genotype C HBV infection, male gender, advanced age, viral coinfection with HCV, hepatitis D or HIV, chronically elevated levels of TGP, family history of HCC, chronic perinatally transmitted infection, and alcohol abuse (BEASLEY, 1988).

HBV is a DNA virus that is capable of integrating into the host genome, inducing both genomic instability and mutagenesis of several cancer-related genes. This integration into the human genome may explain the incidence of HCC in the non-cirrhotic patient (HEMMING et al., 2016), supporting the idea that HBV plays a direct role in liver transformation, triggering common and etiology-specific oncogenic pathways, in addition to stimulating the host immune response and leading to chronic liver necroinflammation (LEVERO; ZUC-MAN-ROSSI, 2016).

It is described that some of the protective factors for HCC are the prevention of chronic HBV infection through vaccination, which is recommended by the World Health Organization for all newborns and adults in high-risk groups, and treating such an infection with antivirals.

Hepatocarcinoma in non-cirrhotic patients is generally silent in its early stages due to a greater hepatic reserve in this population. Generally, at the time of diagnosis, they are already in advanced stages and this is mainly due to the aggressive nature of the tumor. The most common initial symptom is mild to moderate abdominal pain. Symptoms such as abdominal distension, weight loss, hyporexia, malaise, fatigue, diarrhea, jaundice and fever of undetermined origin may also be present (DESAI et al., 2019). The most common sites of extrahaptic metastases are pulmonary, intra-abdominal, bone, and adrenal gland lymph nodes.

Most patients with chronic HBV infection are at high risk of developing HCC and therefore, when they are considered high or medium risk patients, they must be subjected to strict surveillance, which aims to obtain a reduction in mortality related to the disease. disease, which is achieved through an early diagnosis. Such patients who are considered to be at high and medium risk of developing HCC include those with active hepatitis, a family history of HCC, Africans and African-Americans, Asian men over 40 years of age, and Asian women over 50 years of age (KANWAL; SINGAL, 2019).

Screening for HCC must be performed every 6 months and abdominal US is the modality of choice, due to its low cost and lack of risk exposure to the patient (HEMMING et al., 2016). And during such screening, if lesions ≥1cm are visualized, propaedeutic extension with more sensitive and specific imaging exams is recommended for better evaluation of the lesion and diagnosis of the condition (MARRERO, J. A. et al., 2018).

The diagnosis of HCC can usually be made with imaging tests alone, with contrast-enhanced CT of the abdomen or magnetic resonance imaging (MRI) of the abdomen being the choice. The radiological appearance of HCC seen in such exams is arterial hyperenhancement and "washout" of the contrast medium in the portal or late phases.

The liver lesions seen in such exams are classified according to their characteristics, and thus the probability of being a HCC can be estimated. This classification was proposed by the American College of Radiology and is known as Liver Imaging Reporting and Data System (LI-RADS) and has a high specificity for the diagnosis of HCC. The LI-RADS System assigns imaging findings to 1 to 5 categories, with LI-RADS 1 being a definitely benign image and LI-RADS 5 being definitely a HCC (HEMMING et al., 2016).

Histological diagnosis by liver biopsy may be necessary only if imaging studies are inconclusive for the diagnosis of HCC.

AFP is the most used tumor marker to aid in the diagnosis of HCC and despite its low sensitivity, it can be useful for diagnosis when applied in conjunction with other tests (HEIMBACH, J. et al., 2017).

When establishing the diagnosis of HCC, tumor staging must be performed and although there is no universally adopted staging system, currently, American and European guidelines recommend the use of BCLC for staging, prognosis prediction and treatment. This classification divides patients with HCC into 5 stages (0 very early, A early, B intermediate, C advanced and D terminal) according to the size and number of nodules, vascular invasion, performance status and liver function. At all stages, except BCLC-D, the proposed treatments offer increased survival (HEIMBACH, J. et al., 2017).

In cases of patients with chronic hepatitis B, in which treatment is indicated, antiviral therapy must be instituted, with a view to persistent suppression of HBV replication (BEASLEY, 1988).

Treatments for HCC can be divided into surgical, locoregional and systemic. Surgical resection is the treatment of choice for resectable HCC that occurs in the absence of cirrhosis and must be performed in patients with a single nodule, confined to the liver, with no invasion of the hepatic vasculature and no portal hypertension. For patients who are not candidates for surgical resection, therapeutic options include liver transplantation, locoregional therapies, and systemic therapy. Patients eligible for liver transplantation must meet the Milan criteria, with the presence of a single liver nodule ≤5 cm or up to three lesions < 3 cm and absence of vascular invasion and metastases.

The locoregional therapies include ablative techniques or chemoembolization.

For patients ineligible for surgical or locoregional treatment, due to evidence of multiple bilobar nodules, vascular invasion and/or extrahepatic metastasis, systemic therapy is an option if performance status and underlying liver function are adequate. Sorafenib, which inhibits tumor cell proliferation and tumor angiogenesis, is the first-line systemic therapy of choice. In the case of patients with very advanced disease and no treatment indication, it is recommended that they have only the best supportive care (HEIMBACH, J. et al., 2017).

CONCLUSION

HCC is a cancer that is usually silent in its early stages, and because it is considered an aggressive tumor, the median survival after diagnosis is usually approximately 6 to 20 months.

The development of this tumor is the result of the interaction of multiple factors such as genetic predisposition, exposure to environmental factors and/or chronic viral infection.

HCC can develop even in the absence of liver cirrhosis and one of the most relevant risk factors for such development is chronic HBV infection. As patients chronically infected with HBV have a high risk of developing HCC, when indicated, they must be submitted to a rigorous surveillance, with the objective of obtaining an early diagnosis of the referred tumor.

The diagnosis of HCC is made through imaging tests such as CT of the abdomen with contrast or MRI of the abdomen. And in case of diagnostic doubt, a liver biopsy is performed. The choice of treatment for this tumor can be complex, and in each case it is individualized based on many factors such as size and number of nodules, vascular invasion, extrahepatic metastases, performance status and adjacent liver function.

Although vaccination programs against hepatitis B have already been instituted and treatment for this virus is available, there are still millions of people worldwide who are chronically infected with HVB, thus remaining at risk of developing HCC.

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