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THE DIAGNOSTIC VALUE OF ALPHA-FETOPROTEIN, ALPHA-FETOPROTEIN-L3 IN HEPATOCELLULAR CARCINOMA ASSOCIATED WITH CHRONIC VIRAL HEPATITIS

Abstract. *In the group with hepatocellular carcinoma, the level of alpha-fetoprotein was higher than in the group with cirrhosis without hepatocellular carcinoma. In addition, when comparing the level of alpha-fetoprotein in the control group, the level of alpha-fetoprotein in the group with hepatocellular carcinoma was significantly higher (p <0.001). In the group of patients with hepatocellular carcinoma, alpha-fetoprotein-L3 exceeded 15% of the main alpha-fetoprotein in 16 out of 30 patients, while in the group of patients with liver cirrhosis in the outcome of viral hepatitis without hepatocellular carcinoma and in the group of healthy volunteers; it was within the threshold value.*

Keywords: *hepatocellular carcinoma, cirrhosis, viral hepatitis B, viral hepatitis C, alpha-fetoprotein, alpha-fetoprotein-L3, screening, ELISA-enzyme-linked immunosorbent assay*

Introduction

According to GLOBOCAN for 2018, primary liver cancer ranks sixth in prevalence and fourth in cancer mortality, with approximately 841.000 new cases and 782.000 deaths annually. In the Republic of Uzbekistan, in the structure of cancer morbidity in 2018, hepatocellular carcinoma ranks seventh, with an incidence rate of

2.6 per 100 thousand population. At the same time, the share of stages 3 and 4 of hepatocellular carcinoma accounts for 63.8% of all newly diagnosed cases, while stage 1 accounts for no more than 2%. Most often, hepatocellular carcinoma develops against the background of chronic viral hepatitis B and C, which are detected in 80-90% of patients with hepatocellular carcinoma against the background of liver cirrhosis. To establish the diagnosis of primary liver cancer by practical recommendations of the World Gastroenterological Organization the following findings are sufficient: the classical picture with one from visual research methods - for example, large and / or multifocal formation in the liver, as well as an increased level alpha-fetoprotein, against the background of chronic liver disease on stages of cirrhosis.

The purpose of the study is to study the diagnostic value alpha-fetoprotein and alpha-fetoprotein-L3 as diagnostic markers of hepatocellular carcinoma associated with chronic viral hepatitis.

Material and methods

All subjects were divided into three groups. The first group included patients with a diagnosis of hepatocellular carcinoma associated with cirrhosis of the liver of viral etiology. The selection criteria for the patients were the mandatory presence of volume formation on ultrasound + computed tomography / magnetic resonance imaging with histological confirmation of the diagnosis, and markers of chronic viral hepatitis. The second group included patients with cirrhosis, viral etiology without hepatocellular carcinoma. The selection criteria for this group were the presence of viral hepatitis markers and the absence of volume formation on an ultrasound scan. The third group was composed of healthy volunteers. The study was conducted with the permission of the ethics committee of the Ministry of Health of the Republic of Uzbekistan. All subjects received written consent to take clinical material (blood) and publish the results. The diagnosis of cirrhosis was classified according to the Child-Pugh and patients with hepatocellular carcinoma on the background of cirrhosis furthermore classified according to the TNM classification used in our country. In the sera studied, we determined the level of alpha-fetoprotein and alpha-fetoprotein L3 by ELISA on a

Biotek spectrophotometer. Measurements of tumor markers were carried out in the same samples taken from patients simultaneously. To determine the level of alpha-fetoprotein, the “ALPHA-FETOPROTEIN-IFA-BEST” kit of Vector Best (Russia) was used. To determine the level of alpha-fetoprotein-L3, we used the ELISA Kit Alpha-Fetoprotein Lens Culinaris Agglutinin (a-alpha-fetoprotein-L3). The analysis was carried out according to the instructions of manufacturers.

Research results

88 people were examined. All patients were divided into three groups: a group with hepatocellular carcinoma on the background of cirrhosis due to chronic viral hepatitis, a group of patients with cirrhosis caused by chronic viral hepatitis without hepatocellular carcinoma and healthy volunteers. There were 30 patients in the group of patients with hepatocellular carcinoma associated with liver cirrhosis. The average age was 58.0 ± 5.1 years. All patients with hepatocellular carcinoma had confirmed by ultrasound and computed tomography/ magnetic resonance tomogram, as well as histologically. According to the TNM classification, there were 2 patients with stage 2 (6.6%), with stage 3 - 27 patients (90.1%), with stage 4-1 (3.3%). In the group of patients with cirrhosis, consisting of 30 people, the average age was 56.9 ± 4.95 years. In all patients, ultrasound examination did not reveal volumetric formations. In the control group, consisting of 28 healthy volunteers, the average age was 56.0 ±5.5 years old. In the group with hepatocellular carcinoma, the level of alpha-fetoprotein was within 203.9 ± 180.5 ng / ml, was higher than in the group with cirrhosis without hepatocellular carcinoma, the level of alpha-fetoprotein in which was 19.94 ± 13.4 ng / ml. Also, when comparing the level of alpha-fetoprotein in the control group, the level of which was within 2.58 ± 1.5 ng / ml, the level of alpha-fetoprotein in the group with hepatocellular carcinoma was significantly higher ($p < 0.001$). However, in 9 patients with hepatocellular carcinoma, the alpha-fetoprotein level was below 10 ng / ml. In 11 out of 30 patients with cirrhosis without hepatocellular carcinoma and in 1 healthy volunteer, the alpha-fetoprotein level was higher than 10 ng / ml, that is, above the upper limit of normal. In the group of patients with hepatocellular carcinoma alpha-

fetoprotein-L3exceeded 15% of the main alpha-fetoprotein in 16 out of 30 patients, while in the group of patients with cirrhosis in the outcome of viral hepatitis without hepatocellular carcinoma and in the group of healthy volunteers, it was within the threshold value.

Conclusions

As you know, hepatocellular carcinoma develops up to 85% of cases against the background of chronic viral hepatitis. In this regard, it becomes necessary to diagnose hepatocellular carcinoma in patients with this pathology. Ultrasound is an operator-dependent method and it is not always possible to identify and differentiate small formations on it. In this regard, tumor markers are widely used as an additional diagnostic method. In this study, we evaluated the efficacy of alpha-fetoprotein and alpha-fetoprotein-L3 in patients with hepatocellular carcinoma and compared the levels of these tumor markers in cirrhotic patients without hepatocellular carcinoma and in healthy volunteers. Currently alpha-fetoprotein is widely used in Uzbekistan as an oncological marker for hepatocellular carcinoma. However, in our study, alpha-fetoprotein was increased in patients with cirrhosis of the viral etiology without hepatocellular carcinoma, as well as in healthy volunteers. As for the alpha-fetoprotein-L3, it should be noted that its level directly depends on the alpha-fetoprotein level. Determination of levels of alpha-fetoprotein and alpha-fetoprotein-L3 in blood serum is suitable for routine diagnostics and examination of the population, since it requires a small amount of serum, is quite simple to perform and minimally invasive procedure. However, for more precise informational content, other markers more specific for hepatocellular carcinoma should be used, for example, PIVKA II.