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Clinical Characteristics and Prognostic Factors of Hepatocellular Carcinoma in HIV-Infected Patients

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Abstract

From 1998 to 2012, we looked at 53 HIV-positive individuals with Hepatocellular Carcinoma (HCC) who were diagnosed at our facility. All of the patients had hepatitis virus infection (77% HCV, 12% HBV, and 11% HCV+HBV), and 95% had cirrhosis of the liver. In 41% of individuals, HCC was discovered while they were being monitored. Patients were offered potentially curative therapy in 32% of cases and palliative care in 30% of cases. Median survival was 2 months in those diagnosed from 1998 to 2005, and 11 months in those diagnosed from 2006 to 2012, P=0.16. HCC stage, alpha-fetoprotein serum levels, MELD score, and any treatment were all independently linked to survival.

Keywords: Hepatocellular carcinoma; Human immunodeficiency virus; Hepatitis C virus; Chronic hepatitis C; Liver cirrhosis

Introduction

From 1998 to 2012, we looked at 53 Human Immunodeficiency Virus (HIV)-positive individuals with Hepatocellular Carcinoma (HCC) who were diagnosed at our facility. All of the patients had hepatitis virus infection (77% HCV, 12% HBV, and 11% HCV+HBV), and 95% had cirrhosis of the liver. In 41% of individuals, HCC was discovered while they were being monitored. Patients were offered potentially curative therapy in 32% of cases and palliative care in 30% of cases. Median survival was 2 months in those diagnosed from 1998 to 2005, and 11 months in those diagnosed from 2006 to 2012, P=0.16. HCC stage, alpha-fetoprotein serum levels, MELD score, and any treatment were all independently linked to survival. According to several findings, patients with HIV infection are younger and more frequently symptomatic with advanced tumors at the time of diagnosis of HCC than non-HIV-infected patients [1]. However, little is known regarding HCC surveillance procedures in at-risk HIV-infected individuals, as well as HCC prognostic variables in this group. Our purpose was to analyses clinical features, therapy, and survival in HIV-infected individuals with a particular emphasis on discovery of predictive markers.

Methods of Clinical and Administrative Data

We reviewed the Minimum Basic Data Set (MBDS) of our institution to identify all HIV-infected patients diagnosed with HCC at our institution from 1998 to 2012. The MBDS is a computerized database of clinical and administrative data generated from the medical records of discharged patients that is used in hospital management processes and clinical and epidemiological research. Patient medical records were reviewed, and data were extracted according to a protocol and recorded in a working database.

Diagnosis of HCC was based on noninvasive imaging tests or pathology findings according to well-defined criteria [2]. HCC was staged following the Barcelona Clinic Liver Cancer (BCLC) classification [3]. We compared patients with HCC diagnosed before and after 2005, when the new HCC guidelines of the American association for the study of liver diseases were published [4]. For the purposes of the study, we considered that the diagnosis of HCC was made during surveillance when ultrasonography of the liver (with no evidence of HCC) was performed within the 12 months before the diagnosis of HCC. During the study period, a multidisciplinary liver cancer committee met regularly to review cases, outline treatment plans, and follow outcomes of patients with liver cancer. This committee comprises hematologists, interventional radiologists, and transplant surgeons with expertise in the diagnosis, treatment, and management of liver tumors. Diagnosis of HCC was based on noninvasive imaging tests or pathology findings according to well-defined criteria [2]. HCC was staged following the Barcelona Clinic Liver Cancer (BCLC) classification [3]. We compared patients with HCC diagnosed before and after 2005, when the new HCC guidelines of the American association for the study of liver diseases were published [4].

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We analyzed the characteristics, treatment, and outcome of 53 HIV-infected patients with HCC attended in our institution over a 14-year period (1998 to 2012). HCV-related cirrhosis waste most frequent underlying disease, although in a large number of patients, profound immunosuppression and alcohol consumption well known enhancers of fibrosis progression in HI/HCV-co infected individuals were associated with advanced liver disease.

Of note, only 40% of tumors were detected in surveillance programs, irrespective of the period analyzed, this differs little from data reported elsewhere. It must be remembered that ours is a referral center for liver-transplantation and that a substantial proportion of patients were already diagnosed with [6] HCC when first seen by us. We found that HCC was more frequently diagnosed using noninvasive imaging tests after 2005, thus reflecting current recommendations. At diagnosis, HCC was frequently advanced, and half of the patients had decompensated liver disease, these findings are concordant with those of other studies in this field.

A significantly higher proportion of patients received treatment for HCC after 2005. The explanation for this finding is multifactorial: In recent years, a more generalized approach to managing malignant diseases in HIV infected patients has been applied following the appropriate-for-stage recommendations [7] used in the general population, in addition, new treatments for HCC, such as sorafenib, have become available.

An on significant trend towards increased survival was observed after 2005. However, given that the statistical power of the comparisons of mortality between the 2 periods ranged from 20% for 3-year survival and 40% for 1-year survival, a type II error could not be excluded. We found that survival was independently associated with tumor burden (BCLC stage and serum alpha-fetoprotein concentration), liver function (MELD score), and treatment of HCC. Detectable HIV-RNA was associated with an increased hazard of mortality by uni variate analysis but not by multivariate analysis.

Transient Elastography

Our study is limited by its retrospective design, and by the small number of patients included. In addition, although the AASLD screening guidelines were enforced in our institution after their publication in 2005; we have no data about how diligently they were followed by clinicians. We recognize that the definition of diagnosis of HCC during surveillance used in this study (ultrasonography within the 12 months before the diagnosis of HCC) doesn't match with current recommendations that surveillance be undertaken at 6 monthly intervals. However, it must be taken into consideration that the ideal surveillance interval is not known; and that a surveillance interval of 6 months-12 months has been proposed based on tumor doubling times [8]. Moreover, a retrospective study has reported that survival is no different in patients screened at 6 monthly or 12 monthly intervals. Nevertheless, our results reflect the experience of a single institution in which a multidisciplinary team reviewed HCC cases and outlined treatment plans. Our findings allow us to draw some conclusions that we believe are relevant for clinical practice. First, HCV-related cirrhosis was by far the most frequent underlying disease in patients with HCC, many of whom had a history of severe immunosuppression and/or alcohol consumption. Consequently, key preventive measures for HCC among HIV/HCV-co infected individuals should include interventions that modify the natural history of HCV infection, such as antiviral therapy for HCV and HIV and avoidance of alcohol and injection drugs. Second, most cases of HCC were detected outside surveillance programs. Third, at the time of diagnosis, half of the patients already had decompensated liver disease and the tumor was frequently advanced [9]. These findings highlight the need to prioritize identification of patients at risk of HCC, particularly those with liver cirrhosis. Patients can be identified accurately using noninvasive methods such as transient elastography and serum tests. Following current guidelines, patients at risk should be screened for HCC with 6-monthly liver ultrasound with or without serum alpha-fetoprotein testing, a procedure that is associated with significant improvements in early tumor detection, administration of curative therapy, and overall survival in patients with cirrhosis.

Shortening the interval for HCC screening has been proposed for HIV-infected patients with liver cirrhosis, since development of HCC could be more rapid in this group than in cirrhotic patients without HIV-infection. This approach warrants further analysis in prospective studies, particularly in patients at high risk of developing liver-related events such as those with liver-stiffness values >40.

A no significant trend towards tumors with better prognostic characteristics was found in the second period in comparison with the first period. A solitary lesion was found in 38% of patients, and lesions greater than 5 cm in diameter were found in 52% of patients. Portal vein invasion was detected in 36% of patients, and metastases in 15%. The tumor was advanced (BCLC stage C or D) in 55% of patients, and alpha-fetoprotein serum levels were above 200 mg per ml in 38% of patients [10]. 60% of patients received treatment for HCC. Of note, patients in the second period received treatment for HCC more frequently than patients in the first period. Potentially curative therapy was given to 32%of patients and no curative therapy to 30% of patients.

The median (IQR) duration of follow-up was 10 months. The median (IQR) survival was 2 months in the first period and 11 months in the second period, P=0.16. A no significant trend towards improved survival during the first 3 years after diagnosis of HCC was observed in the second period (1-year survival, 62%; 2-year survival, 37%; and 3-year survival, 28%) in comparison with the first period (1-year survival, 37%; 2-year survival, 26%; and 3-year survival, 14%). Variables associated with survival by univariate and multivariate cox regression analysis. Survival was independently associated with tumor-related factors (such as BCLC stage), serum alpha-fetoprotein levels, liver-related factors (such as MELD score), and any treatment.

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