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Original article

Strong correlation by ultrasonography of hepatomegaly and the presence of co-infection in HIV/HCV cirrhotic patients

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ABSTRACT

Objectives: Progression of hepatic fibrosis is accelerated in patients co-infected with human immunodeficiency virus and hepatitis C virus compared to hepatitis C virus mono-infected patients. This study aimed to compare ultrasound features and selected clinical and biochemical variables between patients with human immunodeficiency virus/hepatitis C virus co-infection ($n = 16$) versus hepatitis C virus mono-infection ($n = 16$).

Methods: Each patient underwent abdominal ultrasound, and a specific evaluation was performed in order to detect findings consistent with chronic liver disease. Characterization of spleen size, liver structural pattern, diameter of the portal, spleen, and mesenteric veins was based on classical ultrasound parameters. Propensity score was used for control of selection bias and performed using binary logistic regression to generate a score for each patient. The Fisher and Mann–Whitney tests were used to evaluate categorical variables and continuous variables, respectively.

Results: On univariate analysis right hepatic lobe size was larger in human immunodeficiency virus/hepatitis C virus patients (157.06 ± 17.56 mm) compared to hepatitis C virus mono-infected patients (134.94 ± 16.95 mm) ($p = 0.0011$). The left hepatic lobe was also significantly larger in human immunodeficiency virus/hepatitis C virus patients (115.88 ± 22.69 mm) versus hepatitis C virus mono-infected patients (95.06 ± 24.18 mm) ($p = 0.0177$). Also, there was a strong correlation between hepatomegaly and co-infection ($p = 0.005$).

Conclusion: Human immunodeficiency virus infection was the primary variable influencing liver enlargement in this population. Hepatomegaly on ultrasound was more common among cirrhotic human immunodeficiency virus/hepatitis C virus co-infected patients than among cirrhotic hepatitis C virus mono-infected patients. This aspect is very important in the management of human immunodeficiency virus/hepatitis C virus co-infected patients, because screening for hepatocellular carcinoma is necessary in this population.

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Introduction

Chronic hepatitis is one of the most relevant co-morbidities of patients co-infected with human immunodeficiency virus (HIV) and hepatitis C virus (HCV).[1] HIV-infected patients are at increased risk for HCV infection, with an estimated HCV prevalence of 30–35% in this population.[1] Among HIV-positive drug users, the reported prevalence of HCV is up to 80%.[2,3] Patients co-infected with HIV and HCV develop liver disease more rapidly, and earlier progression to liver cirrhosis has been described in this population.[4–7]

Liver cirrhosis is usually suspected on the basis of abnormalities in standard liver function, biochemical (blood) tests, non-invasive methods of evaluating fibrosis, and ultrasound (US) examination. The role of radiology in the evaluation of liver cirrhosis is primarily to characterize the morphologic manifestations of the disease, evaluate hepatic and extrahepatic vasculature, assess the effects of portal hypertension, and detect liver tumors.

There are scarce data in the literature regarding US studies in HIV/HCV co-infected patients, particularly those with liver cirrhosis. US findings could influence the management of these patients in terms of identifying indications for liver biopsy, treatment, and surveillance for hepatocellular carcinoma.

The aim of this case–control study was to compare US features and selected clinical and biochemical variables among HIV/HCV co-infected versus HCV mono-infected patients with hepatic cirrhosis matched for age, gender, and body mass index (BMI). We aimed to answer two questions: (1) Is there any difference in liver size between co-infected and mono-infected cirrhotic patients? (2) Are there demographic and clinical variables related to liver size?

Methods

Study population

The initial study population was 45 patients, including 28 HIV/HCV co-infected and 17 HCV mono-infected patients. We applied a propensity score using three demographic characteristics (age, gender, and BMI) and identified 16 patients with HIV/HCV co-infection (study group) and 16 patients with HCV mono-infection (control group). The co-infected patients were selected among patients seeking regular care at the AIDS Outpatient Clinic of the Hospital das Clínicas, Medical School, Universidade de São Paulo. HCV mono-infected patients were selected from those registered at the Department of Gastroenterology, Universidade de São Paulo School of Medicine. Patients were selected from January 2006 to January 2007.

All patients had a diagnosis of HCV infection (seropositive for HCV-RNA) and a histopathological diagnosis of liver cirrhosis. Each patient underwent abdominal US, and a specific evaluation was performed in order to detect findings consistent with chronic liver disease (liver and spleen size, liver texture, diameter of the portal, splenic, and superior mesenteric veins). We analyzed the following additional variables: history of high ethanol consumption (daily intake of more than 60 g for females or more than 80 g for males for more than 10 years), HCV genotype, US parameters, and the presence of steatosis on liver biopsy.

Patients were excluded if they had a history of chronic liver disease from other etiology (including hepatitis B virus co-infection), opportunistic infections, or other serious medical conditions.

Liver biopsy

Liver biopsy was indicated in all subjects to evaluate the severity of hepatic disease. The decision to proceed with a liver biopsy was made during routine work-up for chronic hepatitis C, and was in accordance with accepted clinical practice by physicians staffing the Department of Gastroenterology and Infectious Diseases at the University of São Paulo School of Medicine. Steatosis on liver biopsies was graded according to the following categories: 0 (minimal, <5%), 1 (mild, 5–33%), 2 (moderate, 34–66%), or 3 (severe, >66%). Biopsy was performed at a mean of 12 (standard deviation [SD] 3.6) months after US examination.

Ultrasound examination

All patients underwent US of the abdomen. The operator was an experienced US examiner and was blinded to other patient variables. Patients were in the supine position for all examinations. For better access to the liver, patients were instructed to raise their hands behind the head, thus increasing the intercostal spaces and the distance from the lower costal margin to the iliac crest. US examination was performed during deep inspiration and with a relaxed abdominal wall. In each case, the liver was examined and visualized in three planes: longitudinal, cross-sectional, and diagonal. Patients fasted for an average of 6 h prior to US.

A specific protocol was performed to evaluate the characteristics consistent with chronic liver disease (liver and spleen size, liver texture, diameter of the portal, splenic, and mesenteric veins). The right hepatic lobe size was measured in accordance to prior research: the cranio-caudal diameter was determined in the conventional section in the mid-clavicular line, by measuring from the hepatic dome to the inferior hepatic tip.[8–10] The left hepatic lobe was measured at the median line of the abdomen, parallel to the aorta.

Normal liver size was defined as follows: in men with BMI between 22 and 26 kg/m^2 and women with BMI between 22 and 25 kg/m^2, normal liver size was 13.5 ± 1.7 cm; in men with BMI > 26 kg/m^2 and women with BMI > 25 kg/m^2, normal liver size was 14.5 ± 1.7 cm.[10] Characterization of other features (spleen size, liver structural pattern, diameter of the portal, spleen, and mesenteric veins) was based on classical US parameters.[11]

Portal hypertension was defined by the following criteria: (1) portal vein diameter larger than 12 mm; (2) mesenteric and splenic veins larger than 9 mm; (3) the presence of collateral routes; and (4) spleen index larger than 20 cm^2 [9]. Liver steatosis was defined on US by the observation of a bright liver echo pattern or by the loss of portal venous walls.[12]