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Case Report

Acute on Chronic Liver Failure Due to Acute Hepatitis C

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Abstract

Acute-on-chronic liver failure develops in a setting of acute decompensation of chronic liver disease, associated with organ failure and high mortality rate. Many causes have been described as the "trigger event". Viral hepatitis A, B and E is considered precipitating events and several studies have addressed this issue. Acute hepatitis C has been described as a cause of acute liver failure but no case of a worsening of a pre-existing liver disease in this setting has been reported in the literature. We present the case of a 75-year old woman who suffered cirrhosis by non-alcoholic steatohepatitis and was infected with hepatitis virus C; who developed acute-on-chronic liver failure with a fatal evolution.

INTRODUCTION

Acute-on-Chronic Liver Failure (ACLF) was first described in 2008 by consensus of the Asian Pacific Association for the Study of the Liver (APASL) [1]. It is a frequent entity defined as acute decompensation (AD) of the cirrhotic disease with ascites, hepatic encephalopathy (HE), variceal bleeding, and/or associated bacterial complications. This AD is followed by at least one organ or system failure. Overall 28-day mortality ranges around 15%. Consequently, it is not the result of the natural progression of the baseline disease but an acute deterioration of liver function in patients with cirrhosis, which is usually associated with a precipitating event and carries a high short-term mortality [2, 3]. ACLF in patients with cirrhosis and without previous history of acute decompensation who develop this syndrome is especially severe. It has been suggested to be due to a decreased tolerance to systemic inflammatory response as a consequence of the chronic inflammatory process in the disease [2].

ACLF usually occurs after a precipitating event. The most frequently described triggers are alcoholic hepatitis and bacterial infection, but other "events" may directly exaggerate liver injury such as drug-induced liver injury, superimposed viral hepatitis, portal vein thrombosis and ischemic hepatitis. Conversely, liver decompensation may be consequent upon extra-hepatic insults such as trauma or surgery [2, 3]. Interestingly, it should be noted that precipitating factors cannot be identified in 43% episodes of ACLF [1, 2].

Hepatitis A, B and E virus infection in the setting of hepatic cirrhosis has been widely reported as the trigger of ACLF [1, 2, 4-7]. In contrast, an extensive search of the literature found no reported cases of acute hepatitis C virus (HCV) infection as a trigger factor for ACLF.

We present the first case of ACLF due to acute HCV infection.

CASE REPORT

A 75-year-old female patient with a history of metabolic syndrome with diabetes mellitus 2 since 2003, treated with metformin, glipizide and insulin, arterial hypertension controlled with calcium antagonist and obesity. The patient had no macrovascular organ alteration or microvascular angiopathy.

She was referred to our service by her primary care centre in December 2006 because of increased cytolysis enzyme AST 49 U/L [0 – 32 U/L], ALT 37 U/L [10 – 31 U/L], alkaline phosphatase 142 U/L [40 - 129 U/L], GGT 245 U/L [8 - 61 U/L] and bilirubin of 1.1 mg/dl [0.1 – 1.3 mg/dl]. Ultrasound showed signs of cirrhosis (hepatomegaly, splenomegaly and nodularity) without signs of either portal hypertension or space-occupying lesions. Aetiological research showed a negative viral serology, negative antinuclear antibodies, normal ferritin metabolism and Alpha 1 antitrypsin levels. There was no history of alcohol consumption. She was diagnosed of cirrhosis due to non-alcoholic steatohepatitis with a Child-Pugh A stage (5 points). The consecutive gastroscopies performed during follow-up showed no oesophageal varices until August 2012, when small oesophageal varices were found. The patient later developed several episodes of ascites decompensation that responded to treatment with spironolactone and did not require hospital admission.

In June 2013, the patient was attended in our hospital's Outpatient Hepatology Unit for epigastric pain, pruritus and low-grade fever. Clinical exploration revealed no evidence of jaundice or fever; she was conscious and oriented without signs of encephalopathy, the abdomen was soft and depressible without clinical ascites. Diagnostic paracentesis found no ascitic fluid. The blood test performed showed cytolysis with AST 574U/L, ALT265 U/L total bilirubin 2.8 mg/dl.

Three days later, her general condition worsened with asthenia, dizziness and jaundice, without any other change in the physical examination. The blood test was repeated: AST 1040 U/L, ALT 468 U/L, total bilirubin 6,2 mg/dl and prothrombin time (PT) of 1.37 ratio (0.7- 1.2 ratio). Viral serology showed anti-VHC negative result with a RNA-VHC count of 30274782 UI/mL. anti-VHA–IgM, HBsAg, anti-VHBc-IgM, anti-CMV-IgM, anti-Herpes I/II IgM, anti-Epstein Barr IgM and HIV-1/2 were all negative. Autoimmunity test showed ANA, AML, aLKM and AMA all with tittles < 1/40.

Diagnosis of acute hepatitis C in the setting of cirrhosis secondary to NASH was established. The epidemiological risk factor considered was cohabiting with two relatives who were ex-intravenous drugs users and affected with hepatitis C virus.

During hospitalization, the patient remained haemodynamically stable with HE grade I without ascites at entry. She later developed coagulopathy with PT 1.8 ratio, increase of cytolytic activity (AST 1180 U/L, ALT 517 U/L), rise of total bilirubin to 14.8 mg/dl, as well as ascites and HE. Despite renal support with albumin solution and serum, the renal function worsened. At hospital admission creatinine was 0.7 mg/dL(0.5 – 0.9 mg/dL) progressing to 1.62 mg/dL. Hepatic insufficiency rose to a total bilirubin of 26.5 mg/dL and PT of 1.68 ratio. The MELD score reached 33. The patient suffered progressive worsening of her clinical status with persistent HE. The eleventh day of her entry, she went into coma without any response to stimulus and expired two days later.

DISCUSSION

Triggering factors of ACLF are different depending on the geographical area studied. Whereas drugs and alcoholic hepatitis predominate as precipitating factors of ACLF in the European population, reactivation of hepatitis B or superimposed viral hepatitis are more common in other geographical areas such as Asia [8].

Acute viral hepatitis is considered one of the precipitating factors of ACLF [3, 9]. In developed countries, an active vaccination with hepatitis A and B vaccine is administered to patients with cirrhosis to avoid this severe complication.

In contrast, active vaccination against hepatitis C is not available. Fortunately, the incidence of acute hepatitis C in developed countries has been decreasing in the last years. It is now about 1/100,000 per year. This low incidence is directly related to the implementation of measures to prevent transmission such as disposable sterile needles, determination of serological markers in blood donors, decrease of intravenous drug users and other measures [10, 11]. However, we have to consider that acute hepatitis C often goes unreported and under diagnosed because the majority of cases are asymptomatic (50-90%) [12]. In the developed countries, the" ACLF grade 1 is defined transmission of hepatitis C is mostly iatrogenic or related with intravenous drug injection [11]. Although acute hepatitis C is considered a precipitating factor of ACLF [1, 3, 9], no cases are described in the literature.

In our case, the source of infection could not be determined. In the previous three months, the patient was not attended in the hospital and had not undergone invasive procedures. She was cohabiting with two ex-intravenous drugs users, both affected with hepatitis C. No other reasonable source was found and it was assumed that they were the transmitters. Because of ethical reasons and in order to respect the decision of the family, phylogenetic studies were not performed on the patient or cohabiting relatives.

Fulminant hepatic failure due to acute HCV infection is very rare [13] and is more commonly related with HBV infection or reactivation [14]. Acute hepatitis C of symptomatic onset presents a higher rate of spontaneous viral clearance than the asymptomatic ones. There is scarce information about acute hepatitis C infection in the elderly. It is known that adults with acute infection older than 65 years develop cirrhosis and its complications more frequently than younger patients, particularly hepatic failure [15]. This segment of the population is generally excluded from the clinical trials for treatment options [15]. In our case, the evidence of an AD was a contraindication to antiviral treatment with interferon-based therapies. Age and previous liver cirrhosis were also contraindications for liver transplant.

Our patient presented no organ failure at the moment of hospitalization. It has been described that 10.8% of patients hospitalized for an AD of cirrhosis develop ACLF within 28 days (median 5 days) with a mortality rate of 29.6% and 51.1% at 28 and 90 days respectively [2].

Three stages of ACLF have been identified according to the onset of organ failure. ACLF grade 1 is defined by the presence of the following: single kidney failure; single failure of the liver, coagulation, circulation, or respiration with serum creatinine levels ranging from 1.5 to 1.9 mg/dL, mild-to-moderate hepatic encephalopathy, or both; single cerebral failure and serum creatinine levels ranging from 1.5 to 1.9 mg/dL. It has a prevalence of 11% in hospitalized patients with an AD and a 28-day mortality rate of 22.1%. ACLF grade 2 refers to patients who present 2 organ failures with a prevalence of 8% and a 28-day mortality rate of 32% and ACLF grade 3 defines patients who present 3 organ failures with a prevalence of 3.5% and a 28-day mortality rate of 76.7%.

In our case, the patient had ACLF grade 2 (as she presented liver and cerebral failure) with a rapid progression.

Renal dysfunction and the presence of as cites at admission are key factors in the prognosis of the patient with ACLF [2]. In this patient, the early onset of renal protection measures with albumin solution might have avoided the development of ACLF stage 3 and delayed the outcome.

To our knowledge, this is the first reported case in the literature of acute hepatitis C as the triggering factor of acute on chronic liver failure.

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