Case Report

Spontaneous Cure of Acute Hepatitis C

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ABSTRACT: The statistics proved that approximately 25% of the patients with acute HCV present with jaundice, and only 10-20% develop gastrointestinal symptoms. We present the case of a 58 year-old woman, with prior antecedents of arterial hypertension and diabetes mellitus since 25 years old, hypercholesterolemia and hypertriglyceridemia, psoriasis, epilepsy and depressive syndrome. She clinically presents asthenia, anorexia, itching, jaundice and choluria. The objective examination showed an orientated patient, without flapping, hemorrhagic dyscrasia or signs of chronic hepatic disease, with icteric mucosa and skin, abdominal pain, with hepatomegaly and splenomegaly. The laboratory tests have been compatible with acute hepatitis with colestatic pattern: AST/ALT 969/798 UI/ml, FA 796 UI/ml, GGT 2476 UI/ml, BT/BD 7.39/6.10, INR 0.9. The abdominal echography showed: hepatomegaly, regular borders, hepatic steatosis, splenomegaly without ascitic fluid. The viral serological tests revealed protection for hepatitis A (IgM neg/IgG pos), negative for HVB infection (AgHBs neg, anti-HBc neg), negative for HVE and other viruses (CMV Herpes virus, Epstein Barr, HIV), positive antibodies for HCV and positive RNA VHC (164200 UI/ml), HCV genotype 3a, IL-28B CT, negative autoimmunity. The previous HCV tests were negative, sustaining the recent infection. We assumed an acute hepatitis C. The patient was symptomatically treated with hydroxyzine for the skin itch, with vitamin K for INR correction and she was closely monitored. She had good clinical and laboratorial evolution and she was discharged after one week, maintaining hepatology consultation. She spontaneously cleared HCV infection after 3 months, maintaining negative RNA VHC 6 months after infection. The patient has cured the HCV infection with no need for antiviral treatment.

KEYWORDS*: acute hepatitis C, spontaneous clearance, polymorphisms, laboratory tests*

Introduction

The diagnosis of acute hepatitis C virus (HCV) infection is infrequently made, primarily because more than 70% of patients do not have symptoms associated with the acute infection. Overall, approximately 25% of all patients with acute HCV present jaundice, and 10 to 20% develop gastrointestinal symptoms (nausea, vomiting, or abdominal pain) [1].

Spontaneous resolution of the HCV typically occurs within 1 year after infection. The factors associated with greater probability of spontaneous viral clearance in acute hepatitis C (AHC) are the presence of jaundice at the time of initial infection [2, 3], more rapid decline in viral load during the first 4 to 8 weeks after infection [3, 4] and the CC polymorphism on the IL28B gene.

The diagnosis is made on laboratory studies that show positive HCV RNA levels, an elevated ALT level, and a positive HCV antibody test. It is important to evaluate recent risk factors for infection and have normal analytical studies and negative HCV antibodies prior the event.

The treatment options are a regime of peg-interferon (Peg-INF) during 24 weeks of therapy that seems to be sufficient to provide excellent response rates for patients with acute hepatitis C infection. There are many individuals who clear HCV infection spontaneously in the first three months (2), so it is better to wait a period before expose the patients to unnecessary medications and side effects. Several studies have employed a strategy of delaying therapy for 8 to 12 weeks after the disease onset and impressive SVR rates were preserved [5].

Clinical Case

We present the case of a 58 years old woman, with prior antecedents of arterial hypertension and diabetes mellitus since 25 years old, hypercholesterolemia ad hypertriglyceridemia, psoriazis, epilepsy, depressive syndrome. She refers with asthenia, anorexia, skin itch and icteric mucosa with one month evolution. She also refers with choluria and acholia fecal with weight loss, about 5 kg in the last period. She denies fever, night chills and vomits. The habitual medication is: Depakine, Efexor, Bromalex, Atorvastatina, Fenofibrat, Betaserc, Alprazolam, Co-diovan, Metformina, Paracetamol in SOS. She doesn't refer introduction of other new medication. She admits having a new partner, with chronic HCV that she had shared recently the same depilatory device.

At the objective examination at hospital admission the patient is orientated, without flapping, hemorrhagic dyscrasia or signs of

chronic hepatic disease. She presents icteric skin and mucosa, abdominal pain, with hepatomegaly and splenomegaly at abdominal examination. Analytically at entry she reveals an acute hepatitis with colestatic pattern:

AST/ALT 969/798 UI/ml, FA 796 UI/ml, GGT 2476 UI/ml, BT/BD 7.39/6.10, and INR 0.9. The patient is admitted in the Clinic of Gastroenterology-Hepatology with the diagnosis of acute hepatitis of unknown etiology. The abdominal echography shows hepatomegaly, normal regular borders, with hepatic steatosis and splenomegaly, without ascitic fluid. Viral serological tests are performed during the admission, that reveal protection for hepatitis A (IgM neg/IgG pos), negative for HVB infection (AgHBs neg, AcHBc neg), negative for HVE, negative for other viral infections (CMV Herpes virus, Epstein Barr, HIV) with positive antibodies for HCV and positive RNA VHC (164200 UI/ml).The patient has HCV genotype 3a and IL 28B rs12979860 CT. She has negative autoimmunity (ANA, AMA, anti-dsDNA, anti-LKM). The patient had anterior laboratorial exams that showed negative HCV infection, which sustain the hypothesis that she has recently been infected. We assume that is an acute hepatitis C. She receives symptomatically treatment with hydroxyzine for skin itch, vitamin K for INR correction and is closely monitored during internment. She has a good clinical and laboratory evolution and she is discharged from hospital after one week, maintaining hepatology consultation. She spontaneously clears HCV infection after 3 months, maintaining negative RNA VHC 6 months after the infection (Table 1). The patient has cured the HCV infection with no need for antiviral treatment.

Table. 1. Evolution of laboratory parameters

Date	16/7/2014	30/7/2014	31/07/2014	1/8/2014	4/8/2014	6/08/2014	11/08/2014	15/10/2014	15/01/2015
AST	798	589	490	383	91	91	59	23	21
ALT	969	622	535	483	154	154	81	34	40
GGT	2476	1937	1657	1553	1376	1376	780	150	
FA	796	829	720	712	574				
INR	0.9	2.43	1.85	0.9	0.8				
BT/BD	7.39/6.10	14.9/ 2.3	11.78/ 9.8	14.9	6.1	4.48	2.85	0.26	
LDH	629	535	514	386	277				
RNA VHC	164200 UI/ml							undetected	undetected

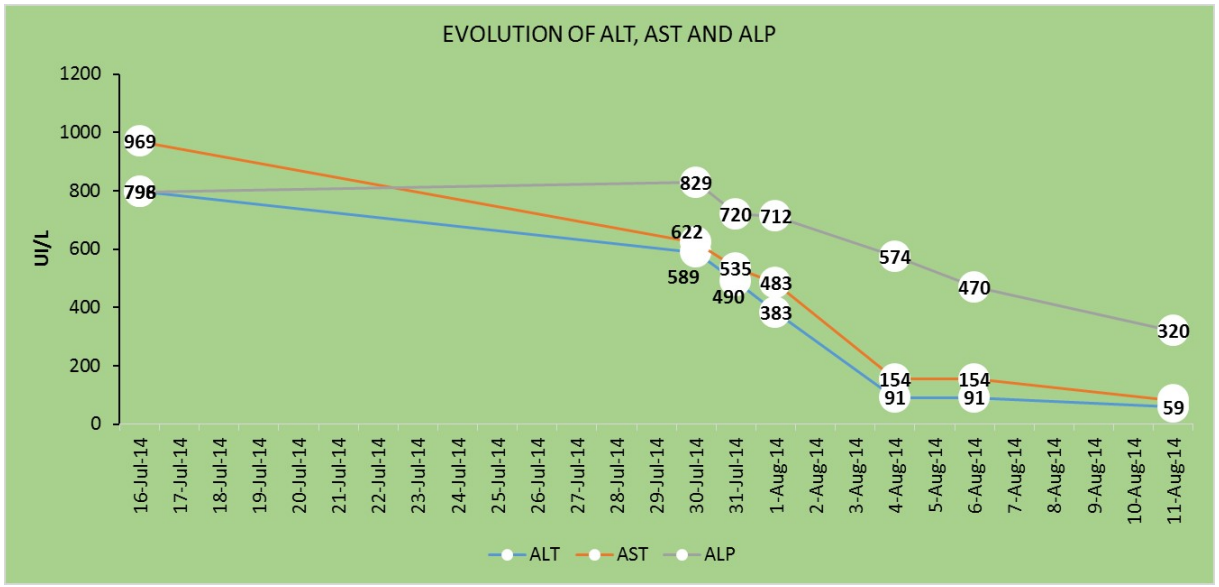

Fig.1.Evolution of ALT, AST and ALP

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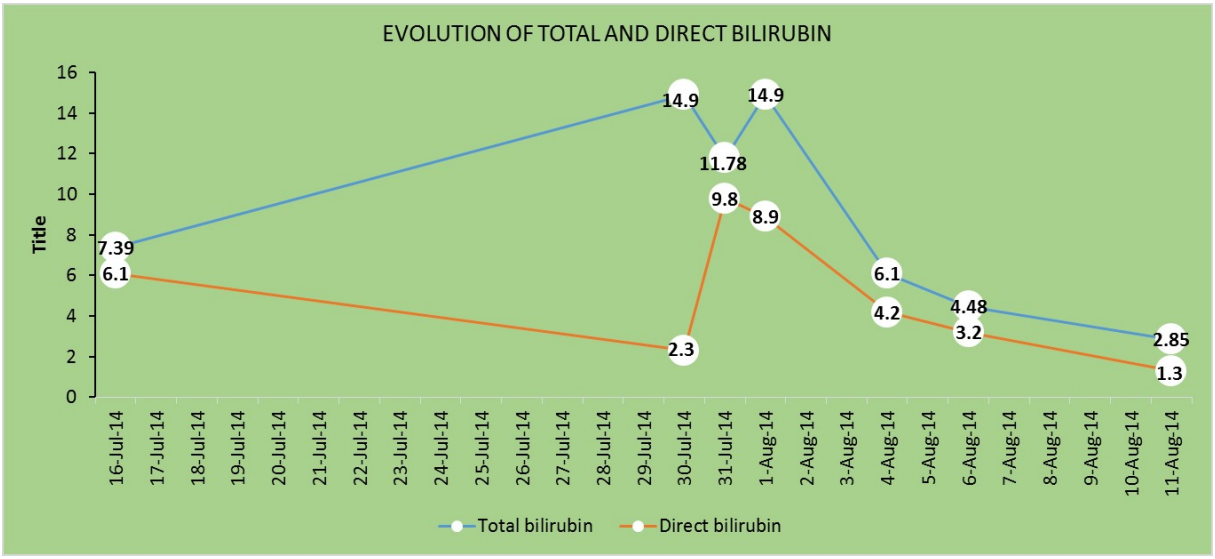

Fig.2. Evolution of total and direct bilirubin

Discussion

Hepatitis C infection has a chronic evolution in most of the cases even there is a 20% chance to eliminate the virus. The patients with an acute phase that present clinical symptomatology seem to have higher rate of spontaneous cure [6]. Optimal timing and management are still discussed but it seems that a "wait and see" period of 8-12 weeks is accepted. Genotypes 2 and 3 seem to have a better outcome; the presented patient had genotype 3 a [7]. A six month treatment with Peg INF, one injection weekly, showed a good efficacy with a 95% SVR. The efficiency of a 24 weeks treatment with Peg-Inf alpha-2b is demonstrated in a study that enrolled 28 patients with acute HCV. The timing of waiting 12 weeks from onset revealed that 11 (39%) patients had a spontaneous clearance with normal ALT and undetectable HCV RNA. Seventeen patients still viremic after this period were considered to have evolution to chronic hepatitis so a treatment regime with PEG-IFN alpha-2b at 1.5 mcg/kg once weekly for 6 months was applied. After therapy discontinuation, none of the patients had evidence of a virological relapse and ALT levels normalized [8]. Additional Ribavirin shows no differences [9]. One meta-analysis that collected data from 12 studies sustains that a daily induction treatment with Interferon improves sustained virological response [10]. In a study that includes 40 subjects, two lots of patients are compared, one treated with Peg INF-alpha alone and the other one with Peg INF and ribavirin. They show no significant difference between the two groups (85% in first group vs. 80% in the second one). They explain the importance of Peg INF-alpha therapy in acute hepatitis through its early efficient stimulation of multispecific HCV-specific CD4 (+) T helper 1 responses [11].

Various studies tried to optimize the treatment and find some predictive factors that influence the spontaneous clearance and the SVR. There is one study made on a cohort of 178 Italian patients with AHC, from different institutions. The patients were treated with either Peg-INF alone or in combination with ribavirin. They chose to investigate the frequency of IL28B rs12979860 SNP and HLA class II alleles. IL28B CC was associated with favorable outcome. The role of HLA alleles as an additional genetic predictor factor showed frequency of DRB1*1101, DRB1*1104 and DQB1*0301. Other factors that were considerate important were age of infection, sex and clinical symptomatology (presence of jaundice). In conclusion DQB1*0301 and viral clearance was modulated by the age at infection. IL28B CC seemed to be a good predictive factor, but jaundice played an additional role only in IL28B non-CC patients [12]. Our patient had IL28B rs12979860 CT genotype and presented clinical symptomatology with icteric coloration of the skin and mucosa. We could consider that this was a favorable predictive factor for spontaneous clearance.

A diagnostic score for predicting the spontaneous resolution of HCV was elaborated in a study made on 168 Caucasian subjects. The aim of the study was to differentiate the subjects that have a high probability to cure spontaneous from those who tend to evaluate to chronicity. They tested blood samples from acute HCV

patients and made genetic determination of IL28B rs12979860 (CC/CT/TT), serum IP-10 levels (with a cut-off <546.0 pg/ml), total bilirubin (peak bilirubin >6 mg/dl), initial HCV RNA as well as at 4 weeks after infection. The score cut-offs for variables also included age at infection (before 35 or after 35 years old) and the presence of HCV-specific CD4 (+) Th1 cells at first presentation. The Score was based on points and the most simple was composed of three variables: IL28B rs12979860 genotype, serum bilirubin at presentation and age at infection. If the patient had a score more than 3 points then the chance of spontaneous cure was higher (6). Appling this predictive Score to our clinical case we could affirm that she had 2 points as she was a young female (<35 years), presented analytically total bilirubin more than 6 mg/dl (7.39 mg/dl) but had IL28B rs12979860 genotype CT. The RNA VHC was negative at 3 months so the choice of waiting for the outcome of the disease was probably the best option.

Conclusion

In the end we could affirm that in the clinical practice it is important to identify an acute HCV, observe and wait before deciding to apply the treatment. Using a mix of predictive factors, as a favorable score, could be one of the options, as well as the strategy "wait and see". We should avoid a useless and harmful treatment of the patients with a self-limiting acute hepatitis C. It is better to differentiate patients with high probability of spontaneous clearance from those who could benefit from an early antiviral therapy.

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