Eliminação Tardia de Hepatite C Crónica: A Propósito de um Caso Clínico

Late Clearance of Chronic Hepatitis C: A Rare Case Report

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Resumo:

A infeção pelo vírus da hepatite C (HCV) é uma das principais causas de doença hepática crónica em todo o mundo. As consequências da infeção a longo prazo são altamente variáveis, desde alterações hepáticas ligeiras até fibrose e cirrose, com possível progressão para carcinoma hepatocelular. A eliminação espontânea do HCV é definida como persistência carga viral indetetável de forma sustentada e acontece em 20%-25% dos infetados, geralmente nos primeiros 6 a 12 meses pós infeção.

Os autores apresentam um caso de uma doente internada numa enfermaria de medicina interna com uma provável infeção crónica por HCV, não previamente conhecida e sem contexto epidemiológico, a condicionar doença hepática com cirrose, que desenvolveu um processo de eliminação espontânea no contexto de infeção vírica aguda.

Palavras-chave: Anticorpos Neutralizantes; Hepatite C Crónica; Hepatite C.

Abstract:

Hepatitis C virus (HCV) infection is one of the leading causes of chronic liver disease worldwide. The long-term impact of HCV infection is highly variable, from minimal changes to extensive fibrosis and cirrhosis, with or without progression to hepatocellular carcinoma. Spontaneous viral clearance of HCV, defined by sustained undetectable serum viral load concentrations, occurs in about 20%-25% of those infected, usually within the first 6 to 12 months after primary infection. We present the case of a patient admitted to an internal medicine ward with a likely chronic HCV infection, without epidemiological context, but with established liver disease and cirrhosis, who developed a process of spontaneous elimination, due to acute Epstein Barr virus infection.

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https://doi.org/10.24950/rspmi.1087

Keywords: *Antibodies, Neutralizing; Hepatitis C; Hepatitis C, Chronic.*

Introduction

Hepatitis C virus (HCV) is responsible for both acute and chronic hepatitis. Acute infection is often asymptomatic, and around 20%-25% of the cases result in spontaneous eradication.[1] The remaining 75%-80% progress to chronic hepatitis within 6 months after exposure.[2] Chronic hepatitis C usually has a slow course but, in some cases, can lead to cirrhosis and hepatocellular carcinoma.

Clearance of chronic HCV infection without treatment is rare, as the virus has already escaped the host's immunity for a long time. A large Scottish trial estimated an incidence rate of 0.19 – 0.36 per 100-person-year follow-up.[2]

Host, viral and cellular factors associated with certain events seem to enhance the host's immune response leading to spontaneous clearance of the virus.[1-4] These include polymorphisms in the interleukin-28 (*IL28B*) gene, superinfection with other hepatotropic viruses (hepatitis A, B, D, cytomegalovirus), HIV coinfection treated with antiretrovirals and immunosuppressive therapy withdrawal.[4-6]

Case Report

We report the case of an 85-year-old woman, admitted to an Internal Medicine ward due to acute hepatitis of unknown cause.

She had a past medical history of type 2 diabetes with peripheral neuropathy, essential hypertension, and a recent hospital admission (three months earlier) due to thoracic trauma after a car crash. She was chronically medicated with bisoprolol, sitagliptin, metformin, gabapentin, and lisinopril/hydrochlorothiazide. Since the car accident, she was also medicated with tramadol/paracetamol and metamizole magnesium that she took for four days. She denied taking any other drugs; herbal tea ingestion; present or past illicit drug use; alcohol abuse (estimated consumption of 20 g of ethanol per week), and history of blood transfusions or tattoos. The patient was a widow for more than ten years and did not have any alleged sexual partners since then. She lived in the city with no pets or regular contact with other animals.

The patient presented with asthenia, anorexia, nausea, and jaundice for ten days. She also reported significant weight loss (10 kg in 6 months) and dark brown urine, she denied any other gastrointestinal symptoms like emesis, abdominal pain, or changes in her bowel habits. The physical exam revealed isolated mucocutaneous jaundice. Lab tests showed mild anemia (hemoglobin 11.1 g/dL), elevated total bilirubin (16.53 mg/dL, 67% direct), prolonged prothrombin time (18.1s, international normalized ratio 1.57), elevated aminotransferases (aspartate aminotransferase (AST) 1354 U/L, alanine aminotransferase (ALT) 1147 U/L), γ-glutamyl transferase (1100 U/L) and alkaline phosphatase 242 U/L; low albumin (2.97 g/dL). The serologic study revealed a positive HCV antibody with a high viral load (28100000 UI/mL; 7.45 log), afterward classified as genotype 1a.

Superinfection with hepatitis A, B, or cytomegalovirus was excluded, as were other infections such as HIV and lung or urinary tract infections. However, additional studies revealed an acute Epstein-Barr virus (EBV) infection, with positive IgM and IgG VCA (viral capsid antigens) antibodies and positive viral load (1147 UI/mL).

The autoimmune disease screening was positive for antinuclear antibodies (ANA) (titers 1:160), being negative for anti-smooth muscle antibody, anti-dsDNA antibody, anti-mitochondrial antibody, anti-liver/kidney microsome type 1, anti-liver cytosol antibody, anti-gp210, and anti-gp100 antibody and anti-soluble liver antigen/liver-pancreas antibody.

A body computed tomography (CT) scan described a dysmorphic liver with a slightly heterogeneous structure, suggesting chronic liver disease and a slightly distended gallbladder with non-thickened walls and no signs of biliary stones; and confirmed patency of portal and hepatic veins.

Chronic hepatitis C with acute EBV infection was presumed. Support therapy was given (IV fluids) and the patient's clinical status improved, as well as the levels of bilirubin and aminotransferase (bilirubin 7.16 mg/dL, 68% direct; AST 129 U/L; ALT 181 U/L).

In this setting, the patient was discharged 14 days after admission. She was reassessed one month later, in the hepatology outpatient clinic. At that point, she had normal AST and ALT levels, slightly elevated bilirubin (2.33 mg/dL), and an undetectable HCV viral load.

She maintained outpatient follow-up with persistent undetectable viral load for 12 weeks after hospital discharge, normal liver enzymes and function, but a liver elastography (Fibroscan) compatible with cirrhosis (34kPa), class A in Child-Pugh classification. Nonetheless, she remained asymptomatic since hospital discharge with no signs of hepatic decompensation.

Discussion

When this patient was admitted, all the main etiologies of acute hepatitis were considered: toxin or drug exposure was ruled-out as the patient denied any change in medication or any new herbal or dietary supplements intake, as well as heavy alcohol consumption. Abdominal ultrasound excluded biliary diseases, focal lesions, hepatic infiltrative diseases, and vascular thrombosis.

The positive serologic results for HCV with positive viral load confirmed the diagnosis. The timing of infection was unknown as the patient did not present risk factors for acute hepatitis C. We presumed a chronic, undiagnosed, hepatitis C with probable sexual transmission many years before. Supporting this hypothesis were the radiologic findings of chronic liver disease. Despite having other features that could contribute to liver damage, like obesity and type 2 diabetes, she had a normal lipid panel and controlled diabetes (HbA1c 7.5%), which ruled out fatty liver disease.

CHC has an indolent course and is often asymptomatic, with normal serum aminotransferase values. This course is sometimes complicated by the existence of a hepatic flare, in which there is an increase in necroinflammatory activity and liver fibrosis, with elevated serum liver enzymes.[3] Viral superinfection, hepatotoxic drugs, or alcohol intake may be responsible for these flares.[3,7] In this case, we considered the EBV infection the cause of it. However, we were not expecting the spontaneous clearance of HCV.

The natural history of HCV infection has not been entirely clarified because of the lack of prospective studies. Our understanding of the natural history of hepatitis C is primarily based on retrospective studies. Spontaneous clearance seems to occur in 20%-25% of individuals after acute infection, most frequently within the first 6 months, although late clearance (chronic hepatitis) can also occur, less frequently.[2] Although the mechanism through which spontaneous HCV clearance occur remains uncertain, it can be achieved by the host's immunologic arsenal alone.

According to retrospective studies, factors such as younger age at infection, female sex, race other than African American, genotype 1 infection, certain host genetic polymorphisms (*IL28B* gene), and a symptomatic acute HCV infection, seem to be associated with spontaneous clearance of HCV. On the other hand, indicators of chronicity include no reduction in CV levels of > 1 log10 IU/mL at 4 weeks or detectable viral RNA after 12 weeks from initial presentation.[2]

Most reports describe spontaneous clearance preceded by events that change host immunity, like withdrawal of immunosuppressive therapy, antiretroviral treatment, liver transplant, alcoholic hepatitis, or superinfection with a hepatotropic virus.[8-10]

In this case, we assume the acute EBV infection had a vital role, starting a vigorous immune response that caused the elimination of HCV. Despite many reports describing spontaneous clearance after viral coinfections, we did not find another one reporting a close relationship between an Epstein-Barr infection and HCV clearance.

As the patient had spontaneously cleared the infection, she is no longer a candidate for antiviral treatment; however regular follow-up must be maintained to prevent liver cirrhosis complications. ■

Declaração de Contribuição

LCN, ARM – Redação do artigo e pesquisa bibliográfica.
MM, RC – Pesquisa bibliográfica
LA, LM – Revisão do artigo
Todos os autores aprovaram a versão final a ser submetida.

Contributorship Statement

LCN, ARM – Writing of the article and bibliographical research.
MM, RC – Bibliographic research
LA, LM – Article Review
All authors approved the final draft

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Consentimento: Consentimento do doente para publicação obtido.
Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of interest: The authors have no conflicts of interest to declare.
Financing Support: This work has not received any contribution, grant or scholarship.
Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.
Patient Consent: Consent for publication was obtained.
Provenance and Peer Review: Not commissioned; externally peer reviewed.

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Recebido / Received: 2022/11/14
Aceite / Accepted: 2023/02/28
Publicado / Published: 2023/06/30

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