REPORTE DE CASO

Successful management of hepatitis B and C coinfection: a case report

Manejo exitoso de un caso de coinfección por hepatitis B y C: reporte de caso

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ABSTRACT
We report the case of a patient with chronic hepatitis B and C managed with direct-acting antivirals in an outpatient setting. Chronic hepatitis B was first treated with entecavir before initiating treatment for chronic hepatitis C. The patient achieved viral suppression for hepatitis B and sustained virological response for hepatitis C. As direct-acting antivirals become more available, healthcare practitioners should be familiar with managing patients with chronic coinfection.
Keywords: *Hepatitis B; Hepatitis C; Coinfection; Antiviral agents (source: MeSH NLM).*

RESUMEN
Reportamos el caso de un paciente con infección crónica por hepatitis B y C, tratado con antivirales de acción directa de manera ambulatoria. Primero se trató la infección crónica por hepatitis B con entecavir, antes de iniciar el tratamiento para la infección crónica por hepatitis C. Se logró la supresión viral de hepatitis B, y la respuesta virológica sostenida para hepatitis C. A medida que aumenta el acceso a los antivirales de acción directa, el personal de salud debe estar familiarizado con el manejo de pacientes con coinfección crónica.
Palabras clave: *Hepatitis B; Hepatitis C; Coinfección; Antivirales (fuente: DeCS Bireme).*

INTRODUCTION

Chronic hepatitis B and C coinfection can represent a challenge in management for healthcare practitioners, particularly when it is necessary to maintain awareness of diagnostic possibilities in patients with abnormal liver function tests and no visible signs of chronic liver disease. With the advent of direct-acting antivirals and their widespread adoption, it is expected that more physicians and other healthcare personnel, including in primary care settings, will encounter and treat patients with chronic hepatitis coinfection [(1)]. We report a case of a patient with asymptomatic chronic hepatitis B and C coinfection, successfully managed with current treatment options.

CASE REPORT

A 51-year-old patient presented to the clinic with abnormal liver chemistries. Posterior investigation revealed chronic hepatitis B and C infection. The patient was asymptomatic at the time of diagnosis. History is negative for unprotected sexual intercourse, blood transfusions, and IV drug use. The physical exam was unremarkable and particularly negative for jaundice, hepatomegaly, and chronic liver disease stigmata. Of note, there was a tattoo on the left hemithorax. BMI was normal, and there was no family history of liver disease or viral hepatitis.

Diagnostic tests were performed in July 2022 and afterward. The laboratory results and their changes over time, before and after treatment, can be found in Table 1. Of note, the hepatitis C virus had a genotype 1a. In December 2022, before treatment, transient elastography was 6.2 kPa. In January 2024, after

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treatment for both chronic HBV and HCV, a Fibroscan result was 5.6 kPa.

Based on laboratory tests and elastography, a diagnosis of chronic hepatitis B and chronic hepatitis C without cirrhosis was established. Entecavir 0.5 mg daily was initiated in December 2022 after confirming HBV suppression in July 2023 (HBV DNA: undetectable). Treatment for chronic HCV infection was initiated with sofosbuvir 400 mg-velpatasvir 100 mg 1 tablet daily for 12 weeks, which the patient completed.

The patient responded favorably to the entecavir treatment, achieving suppression of HBV viral replication, and also achieved sustained viral suppression of HCV after treatment with sofosbuvir-velpatasvir for 12 weeks. There was also a marked reduction in AFP values after treatment compared to the initial assessment (from 27.8 ng/mL to 9.2 ng/mL). The patient did not report any adverse effects.

Ethical consideration

The authors disclose using data regularly collected by the study center, guaranteeing patient confidentiality.

DISCUSSION

Hepatitis B and C coinfection is particularly concerning since it is associated with greater liver damage and faster progression to cirrhosis [2]. If a patient is a chronic carrier of either virus, superinfection may result in fulminant or subfulminant liver failure [3]. Also, there are many common risk factors for both infections [4], which may explain the varying prevalence of coinfection among some populations. A US cohort of the Veterans Affairs Clinical Registries showed that a sizable proportion of HCV-exposed patients were also exposed to HBV (34.7%), although a much smaller proportion of HCV-infected patients had coinfection with HBV (1.4%) [4]. Also, the vaccination rate for HBV in older patients tends to be lower, which may increase the risk of coinfection if a patient with chronic HCV has shared risk factors [5].

In this case, the patient's only known risk factor is exposure to needles given a tattoo. Likewise, the patient was previously asymptomatic and presented with no signs of acute or chronic liver disease, which makes it impossible to determine which infection occurred first, or whether they occurred at the same time. In some cases of coinfection, one of the viruses can become dominant [6]. If HCV was the dominant virus, HBV replication could become very low and ultimately be suppressed [6]. This has been reported as the most frequent scenario, although there are mixed reports in the literature regarding patterns of dominance and codominance, with varying patterns of activity and replication of both viruses longitudinally [6]. Likewise, HCV-related HBV suppression and latent HBV infection have become a growing concern since the advent of treatment for HCV infection, particularly direct-acting antivirals, given that HBV can reactivate after HCV cure [7]. However, this patient had a very high viral load of hepatitis B since the time of diagnosis, which suggests a state of codomination between the 2 viruses. According to US guidelines, since this patient was HBeAg (-), had a viral load of >2000 IU/mL and >2 x ULN for ALT, treatment with entecavir 0.5 mg daily was initiated [8]. In this patient, HBV DNA suppression (undetectable viral load) was achieved after 6 months of treatment.

Treatment of chronic HCV infection is recommended for almost all patients [9]. Although many regimens exist considering factors such as the presence of cirrhosis, previous treatment failure, and management of special populations, direct-acting antivirals (DAAs) are considered safe and effective in many cases, and their use is currently the standard of care in the treatment of chronic HCV infection [9]. Therefore, without cirrhosis and being treatment-naïve, this patient initiated sofosbuvir-velpatasvir for 12 weeks according to recent guidelines[9], completed with full adherence. Given the reported risk of HBV reactivation and increased viral replication with direct-acting antivirals [9], prior testing for HBV is mandatory for patients with HCV before initiating treatment [10].

In addition, liver fibrosis and the presence of portal hypertension were assessed with transient elastography. With an initial result of 6.2 kPa before treatment for either infection, compensated advanced chronic liver disease was ruled out.

Current literature recommends treatment of HBV concurrently with HCV in patients with a similar profile. However, there is also evidence to treat chronic HBV and achieve viral suppression before initiating treatment for chronic HCV [11]. In this case, suppression of HBV viral replication was achieved with entecavir before starting therapy for HCV infection, to reduce the risk of increased HBV activity during treatment with DAAs. The goal of HCV treatment with DAAs is sustained virological response, defined as HCV RNA below the limit of detection 12 weeks after finishing therapy [9], an outcome overwhelmingly correlated with sustained clearance and therefore cure of HCV infection [12]. Achieving sustained virological response also markedly decreases the risk of progression to cirrhosis, hepatocellular carcinoma development, and death [12]. In this patient, this was evidenced by absent viral replication and posterior normalization of liver function tests. Subsequent evaluation of liver fibrosis with Fibroscan 3 months after HCV eradication showed a normal value of 5.6 kPa and effectively ruled out fibrosis.

Of note, there was mild thrombocytopenia at the time of diagnosis, that normalized after treatment of HBV, and before starting DAAs. HCV infection can cause thrombocytopenia through multiple mechanisms, including immune activation against platelets, reduced synthesis of platelets, splenic sequestration, and bone marrow suppression [13]. Moreover, the degree of thrombocytopenia appears to be correlated to the degree of liver damage, since liver fibrosis may result in decreased thrombopoietin production, and portal hypertension increases splenic sequestration of platelets [13]. Platelet counts can increase

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Table 1: Laboratory results.

Date	July 2022	August 2022	December 2022	July 2023	December 2023
Treatment			Entecavir	Sofosbuvir-velpatasvir	
Laboratory tests (unit)					
ALT (U/L)	103		116	161	26
AST (U/L)	63		88	97	21
Platelet count (platelets/mm^3)	127 000		128 000	163 000	
HIV Ag/Ab	Non-reactive				
HCV RNA (IU/mL)		96 000			Non-detectable
HBsAg		Positive			
HCV Ab		Positive			
HBV DNA (IU/mL)		1 256 000	Non-detectable		
INR		1.1			
AFP (ng/mL)		27.8			
HBeAg			Negative		
Anti-HBeAg			Negative		
Quantitative HBsAg (IU/mL)			290	367	
Anti-HDAg			Negative		
Hb (g/dL)			14.4	15	
WBCs (cells/mm^3)				6800	
Albumin (g/dL)					4.2
Alkaline phosphatase (U/L)					105
Total bilirubin (mg/dL)					1
Creatinine (mg/dL)					1.18
Sodium (mEq/L)					140
Potassium (mEq/L)					4

after treatment with DAAs, even in patients with significant cirrhosis and advanced liver disease, although to a lesser degree than in patients with less advanced liver disease [14]. The increase in platelet counts after treatment reflects decreased hepatic inflammation, as evidenced by a reduction in ALT, AST, and AFP and improved hepatic synthetic function. Since scores to assess hepatic fibrosis depend directly on these values (without the AFP), treatment with DAAs usually leads to lower scores and an estimated reduction in liver fibrosis. Similarly, HCV eradication with DAAs also leads to fibrosis reversal and improved clinical outcomes (including a reduction or resolution of thrombocytopenia), although this is less predictable in advanced stages of fibrosis, which also suggests a critical point after which there is little functional improvement with sustained virological response [15,16]. In this case, the patient's platelet counts showed mild thrombocytopenia that resolved after treatment for chronic HBV with entecavir. Since platelet counts were mildly decreased, this could have been the result of HBV to some degree. Nevertheless, it is important to acknowledge chronic HCV as a cause of thrombocytopenia, even in asymptomatic patients without cirrhosis, and the effect of antiviral treatment in normalizing platelet counts.

This case highlights the importance of meticulously evaluating patients with HBV and HCV coinfection, thoroughly assessing the considerations and temporality regarding treatment initiation and evaluating viral activity and markers of liver disease during and after treatment.

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