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Case Report

Sofosbuvir and daclatasvir combination therapy for current hepatitis C virus genotype 4 achieves SVR: a case report of HCV genotype 4 from the Amazon

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Abstract

Hepatitis C is a worldwide endemic disease. However, hepatitis C virus genotype 4 (HCV GT-4) has rarely been reported in Brazil. HCV GT-4 demonstrates high sustained virological response (SVR). Here, we report the case of a 62-year-old HCV GT-4 positive woman complaining of a headache, nausea, and arthralgia. The patient was treated according to the protocol for genotype 4 (12 weeks administration of 400mg sofosbuvir and 60mg daclatasvir daily) and achieved SVR. Although this is not an Amazonas autochthonous case, the presence of genotype 4 is rarely reported in the region.

Keywords: Hepatitis C. Genotype 4. Sustained viral response.

INTRODUCTION

According to the World Health Organization (WHO), hepatitis C virus (HCV) affects millions of people worldwide; it is estimated that approximately 71 million people are chronically infected with HCV, causing a serious global public health problem[1].

There are seven HCV genotypes including 67 subtypes, which are geographically distributed throughout the world[2]. In Brazil, the genotype distribution pattern consists of genotype 1, followed by genotypes 3, 2, 4, and 5[3-4].

The treatment recommended by the Brazilian Ministry of Health for chronic HCV infection involves oral combinations of direct-acting antivirals (DAAs); sofosbuvir in association with simeprevir or daclatasvir. These drug combinations are well tolerated and have been reported to increase sustained virological response (SVR) rates to approximately 90%[5-7].

CASE REPORT

A 62-year-old woman was admitted to the *Fundação de Medicina Tropical Doutor Heitor Vieira Dourado* (FMT-HVD) in November 2015. Upon admission, the patient complained of a headache, nausea, and an extrahepatic manifestation of neurological motor impairment. The patient had received blood transfusion eight years prior in Alenquer, during an upper digestive endoscopy procedure. Follow-up tests prior to treatment are detailed in **Table 1**. The patient was treated according to the protocol for genotype 4 (12 weeks administration of 400mg sofosbuvir and 60mg daclatasvir daily); SVR was achieved and hepatic markers values returned to normal six months after the end of treatment (**Table 1**).

DISCUSSION

Hepatitis C virus genotype 4 (HCV GT-4) represents approximately 1518 million cases of the total global HCV infections. It is prevalent in lower income countries in Northern and Equatorial Africa, the Middle East, and Caribbean and Indian regions[8,9].

The frequency of the geographical distribution of the genotypes in the Amazon region is similar to the pattern in Brazil and other world regions; a higher prevalence of genotypes 1 (64.9%) and 3 (30.2%) and a lower prevalence of genotypes 2 (4.6%), 4 (0.2%), and 5 (0.1%)[3]. However, genotype 4 is rarely reported in the State of Amazonas[10].

The current global distribution of HCV genotypes has undoubtedly been influenced by historical events and modified by contemporary human migration trends. Although genotype 1 has been established as the most prevalent genotype worldwide, including in the Amazon region, we must be aware of the introduction of other genotypes into the region.

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TABLE 1: Patient laboratory test results.

Laboratory tests	Admission	Post-treatment*	Reference values
Hemoglobin	12.9g/dL	13.73g/dL	12g/dL–18g/dL
Hematocrit	39.8%	41.1%	37%–52%
Platelets	196,000/mm^3	239,000/mm^3	130,000/mm^3–400,000/mm^3
Leukocytes	6,190/mm^3	6,340/mm^3	5.2/mm^3–12.4/mm^3
Albumin	5.1g/dL	5.0g/dL	3.5–5.0g/dL
INR	1.13	1.12	1.0
TGO/AST	81IU/L	20IU/L	2IU/L–38IU/L
TGP/ALT	116IU/L	20IU/L	2IU/L–44IU/L
HCV-RNA	541,978 (Log= 5.73)	Undetectable	12IU/mL (Log=1.08) – 100$_x$10^6 IU/mL (Log=8)
FIB-4**	2.38	1.20	FIB 4 > 3.25 (≥ F2)
Child pugh score	A5	A5	A-C

INR: international normalized ratio; **TGO/AST:** transaminase glutamic-oxalacetic/aspartate aminotransferase; **TGP/ALT:** transaminase glutamic-pyruvic/alanine aminotransferase; **HCV-RNA:** hepatitis C virus- ribonucleic acid; **IU/mL:** international units/milliliter; **FIB-4:** index for liver fibrosis; **APRI:** AST-to-platelet ratio index; **METAVIR:** score that quantify the degree of inflammation and fibrosis using the results of a liver biopsy. *Post -Treatment tests were performed six months after the end of treatment. **The treatment is indicated for HCV mono infected patients with APRI > 1.5 or FIB-4 > 3.25, characterizing METAVIR ≥F2. HCV.

In this case, the patient is a native of Tracuateua, a small City in Pará, in the Amazon region; however, she lives in Alenquer, another city in Pará closer to Manaus. Thus, this is not an autochthonous case as the patient temporarily moved to Manaus for HCV treatment. Migratory flow may contribute to the dissemination of genotype 4 originating from other states in the region into Amazonas via virus carriers prior to SVR.

The origin of the region of Tracuateua is linked to the construction of the Belém-Bragança railroad (completed in 1908), during which many African descent, Portuguese, and Spanish immigrants began to colonize the vicinity. Although this migratory phenomenon is not recent, it has been increasing; thus, new and unusual genotypes may be more prevalent than thought[11].

Because of the low prevalence of HCV GT-4 in Brazil, this genotype has not been studied extensively in prospective trials evaluating treatment outcomes. The lack of genotype 4 in our samples indicates that it is absent or rarely present in our population. Because many people in Bahia are of African descent and Brazil is a country with continental proportions, it is possible that uncommon Brazilian HCV strains in other regions of Brazil may be the result of multiple introductions of genotype 4[12].

Therefore, we believe that HCV patient numbers are inexact in some municipalities of the state of Amazonas, a poor region of the country affected by this endemic disease, where the only public access to advanced technology for diagnosis and treatment is at the FMT-HVD and Araújo Lima Ambulatory, the Federal University of Amazonas. In addition, the natural history of hepatitis C and the limited education of the population in some of these municipalities hinder patient notification and treatment.

This case report may contribute to demonstrate that there is HCV GT-4 in the North of Brazil and these individuals carrying this genotype have developed response to the DAAs.

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Conflict of interest

The authors declare that there is no conflict of of interest.

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