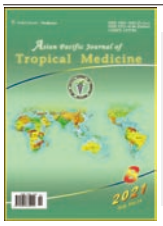

Case Report

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Pediatric perspectives on treating uncommon genotypes of hepatitis C in the United States

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ABSTRACT

Rationale: Hepatitis C in the pediatric population is a large health burden globally. With its diverse genotypes as well as genotypic subtypes, there is a discrepancy in the genotypes used in research compared to their prevalence. HCV genotype 6 which is endemic to South China and Southeast Asia comprises approximately one-third of all HCV infections worldwide, but make up a minority of cases studied in HCV research.

Patient concerns: We report a case of HCV-6 seen in an 11-year-old Burmese immigrant to the U.S. and describe the new direct acting antiviral treatment guidelines for pediatrics with HCV genotype 6.

Interventions: The patient completed a 12-week course of ledipasvir/sofosbuvir (90 mg/400 mg), per FDA weight-based recommendations for treatment-naive HCV genotypes 4-6, without any complications.

Outcomes: The patient was treated successfully with an undetectable HCV viral load one month after treatment completion.

Lessons: HCV-6, although previously uncommon in the U.S., is becoming more prevalent. Updated guidelines include the use of direct acting antivirals, which have been proven effective for HCV-6. Lessons on barriers to care in the immigrant population as well as the value of HCV genotyping are also discussed.

KEYWORDS: Hepatitis C; Genotype 6; Pediatrics; Direct acting antivirals; Immigrant health; Refugee health

1. Introduction

There are 3.5-5 million cases of chronic hepatitis C infection (CHC) in children worldwide[1,2], with a large financial burden given need for screening, monitoring, and treatment for a 10-year study duration. Until 2017, the standard of care for patients under 18 with CHC was pegylated interferon with ribavirin, which requires 48 weeks of therapy with adverse effects such as flu-like symptoms, cytopenias, and autoimmunity. HCV treatment has changed drastically over the last decade with the Food and Drug Administration's (FDA) approval of direct acting antivirals (DAAs) in 2017. DAAs have also proven to have higher sustained viral response (SVR) rates compared to traditional interferon-based treatments[3]. In particular, the DAA regimen with ledipasvir-sofosbuvir (with or without ribavarin) has shown a favorable efficacy and safety profile in patients aged 12-17 years old. Currently, treatment data is largely based on experience treating HCV genotypes 1a and 1b (which are of highest prevalence in the

Significance

HCV-6 is uncommonly seen, studied, and treated in the U.S. though it is becoming more prevalent due to immigration to this country. Most treatment experiences reported are on genotypes 1a and 1b. It is known that response to antivirals varies among different genotypes. Direct acting antivirals (DAAs) are a more recent therapy recommended for HCV, including HCV-6. This study serves to emphasize the efficacy of DAAs in treating HCV-6, which is underrepresented in the literature, especially in the pediatric population. This study also emphasizes other barriers to care for these patients given their immigrant status.

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U.S.). However, with the rise in immigration to the U.S., other HCV genotypes like genotype 6, which is endemic to South China and Southeast Asia[4], have been discovered. With consent, we present a case of HCV genotype 6 in a Burmese immigrant and review current guidelines for HCV management from a pediatric perspective.

2. Case report

An 11-year-old Burmese immigrant male with sensorineural hearing loss and developmental delay presented with a history of failure to thrive (FTT) and a maternal history of CHC. He was born in Myanmar and lived in Thai refugee camps with his family before moving to the U.S. at age 11. Added to his FTT work-up was HCV antibody which was positive, likely *via* perinatal transmission. He had not received any blood products since birth. There is a maternal history of end stage liver disease due to suspected CHC and was awaiting liver transplant. His physical examination revealed a notable body mass index of 13.3 kg/m^2 (0.16th percentile for age), though there was no evidence of jaundice or hepatosplenomegaly. He presented for follow-up after discharge from the outside hospital, with improved FTT growth parameters. His initial hepatic function panel was normal [ALT: 21 U/L (normal range: 0-37 U/L); AST: 18 U/L (normal range: 0-40 U/L); alkaline phosphatase: 61 U/L (normal range: 100-320 U/L); total bilirubin: 0.2 mg/dL (normal range: 0-1.2 mg/dL); total protein: 5.9 g/dL (normal range: 6.0-8.2 g/dL); albumin: 3.0 g/dL (normal range: 3.5-5.3 g/dL); PT: 9.8 s (normal range: 9.4-11.6 s); APTT: 21.9 s (normal range: 2.9-30.6 s)]. His hepatitis B and HIV screen were negative. His alphafetoprotein tumor marker was 2.0 ng/mL (normal range: 0-10 ng/mL). His initial HCV viral load was 3 252 785 IU/mL (normal range: <5 IU/mL) and was noted to be genotype 6a. Because of his likely prolonged HCV infection and therefore risks for liver cirrhosis/cancer, an abdominal ultrasound was performed, which showed a liver normal in size and echogenicity without a mass. His liver fibrosis score was 0.23. Fibrosis stage was F0-F1.

We followed him annually with labs until he became eligible for ledipasvir/sofosbuvir treatment at age 12, per 2017 FDA requirements. Due to his FTT, he did not initially meet weight requirements (>35 kg) for the medication. In between his yearly visits, his social situation changed and he was taken into foster care for unclear reasons. Eventually, he completed a 12-week course of ledipasvir/sofosbuvir (90 mg/400 mg), per FDA weight-based recommendations for treatment-naive HCV genotypes 4-6, without any complications. His HCV RNA was undetectable one month after treatment completion. He also had a SVR 12 weeks later.

3. Discussion

Numerous challenges exist in immigrant healthcare. Immigrants in the U.S. may be characterized by socioeconomic characteristics which disadvantage them in terms of accessing healthcare. Additionally, though guidelines recommend testing for anti-HCV antibodies at 18 months of age in children born with maternal hepatitis C[5], HCV is not on the list of communicable diseases tested during U.S. immigration/refugee screening[6]. With this, hepatitis C may continue to be an under-detected and under-diagnosed entity. Public health policies regarding new immigrants may also impede access to healthcare[7]. Fortunately, because DAAs have become FDA-approved and recommended for treatment in children, out-of-pocket cost and prior authorization processes, which may require additional labs or diagnostic testing depending on insurance type, are no longer major barriers. Of note, patients who are immigrants, compounded by being taken into foster care as seen with this patient, may be at risk for even poorer health outcomes, and thus should be followed closely.

HCV genotype 6 comprises approximately one-third of all HCV infections worldwide[8], yet composes a minority of cases in clinical trials. It is prevalent in Northern Myanmar, with subtypes 6f, 6n, and 6m predominating. HCV-6, particularly subtype 6a, is the most common genotype among ⅣDU drug users[5]. Furthermore, response to antivirals varies between different genotypes. As such, not only does genotyping provide valuable information in determining the most effective treatment course, it also yields actionable insight on infection source, both on an individual as well as public health level. DAAs show higher SVR rates for HCV genotype 6 than interferon therapies with similar efficacy to genotype 1 and 3 treatment[9]. High success rates in adults with DAAs have been replicated in children, though not specifically for genotype 6. DAA-based therapies are shorter in duration and avoid toxicities associated with interferon and ribavirin including temporary growth impairment, which is particularly undesired in the pediatric population. DAAs are currently recommended for HCV patients 3 years and above irrespective of disease severity. Prompt antiviral therapy is indicated in the presence of extrahepatic manifestations and advanced fibrosis[5]. Previously uncommon genotypes like HCV-6 are becoming more prevalent in the U.S. Fortunately, DAA treatment has proven to be effective for HCV genotype 6. Thus, an understanding of the updated recommendations is essential.

Conflicts of interest statement

The authors declare that there is no conflict of interest.

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Authors' contributions

V.S. and W.K. contributed to data acquisition and manuscript preparation. V.S., M.K.A., and W.K. contributed to edition and revision of the manuscript. W.K. was responsible for conception and supervision of the research project and manuscript.

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