Acute Hepatitis C Virus Infection Treated with Daclatasvir/Sofosbuvir in a 9-Year-Old Boy

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Introduction

Hepatitis C is one of the most prevalent infections, which, if not treated on time, can lead to chronic infection, cirrhosis, and liver cancer. In children, acute hepatitis C virus (HCV) infection is rare, 0.05 to 0.36% in the United States; however, it may be underestimated.1 Seven different genotypes of HCV have been reported; however, in Iran, genotype I and III are the most common ones, respectively. Similarly, the usage of injections/syringes in health care facilities is one of the greatest risks of the infection in Iran.2 Some of the common comorbidities associated with HCV infection include hepatocellular carcinoma and cirrhosis.3

Treatment of acute infection is initiated by PEGylated interferon α (PEG-INFα) and ribavirin4 for 6 months; however, owing to longer duration and potential side effects, direct-acting antivirals (DAAs) are now in practice, due to shorter duration of treatment and efficacy.5 According to a recent study, use of DAA such as NS3, NS5B, and NS5A inhibitors has been recommended. These antivirals are developed in response to resistant viral strains.4 Studies have also shown that combination of PEG-INFα, DAAs, and ribavirin, is also effective for the treatment of chronic HCV infection.6

Daclatasvir (NS5A ribonucleic acid [RNA] polymerase inhibitor)/sofosbuvir (NS5B RNA polymerase inhibitor) sold under the name of Sovodak (sofosbuvir 400 mg and daclatasvir 60 mg in a tablet) is a drug used in Iran for the treatment of hepatitis C in adults.7

In this case report, we present the case of a boy with acute hepatitis C infection who was successfully treated with 400 mg sofosbuvir and 6 mg daclatasvir where complete remission was seen until 24 months of follow-up.

Case Presentation

A 9-year-old boy was reported to our center in 2015, who was presented with jaundice and elevated liver enzymes, with impalpable liver 2 cm below the edges of the ribs. His laboratory results were as follow: aspartate aminotransferase (AST): 214 U/L, alanine aminotransferase (ALT): 364 U/L, gamma-glutamyl transferase (γGT): 23 U/L, while telangiectasias and clubbing was negative. An initial ultrasound 

Keywords
► hepatitis C
► ursodeoxycholic acid
► RT-PCR
► liver enzymes

Abstract

The present study includes a case report of a 9-year-old boy who came to our center with jaundice, elevated liver enzymes, and palpable liver. He was treated with ursodeoxycholic acid, but no improvement in symptoms was seen. Reverse transcription polymerase chain reaction and liver biopsy were positive for hepatitis C virus. He was treated with daclatasvir/sofosbuvir for 3 months. Daclatasvir/sofosbuvir might be effective against the treatment of hepatitis in children, with no report of remission and minimal side effects.
showed enlargement of the liver. He had no history of any liver disease or congenital disorder. The patient was otherwise healthy.

Considering the causes of jaundice, increased liver enzymes, and liver enlargement, following laboratory results were found: anti-smooth muscle antibody, antinuclear antibody, and anti-liver kidney microsome type 1 were negative. Complete blood count: white blood cells (WBCs) = 25,500/µL (neutrophils: 42, lymphocytes: 41, monocytes: 7), hemoglobin = 12 g/dL, and platelets = 312,000/µL.

Alpha fetoprotein = 10 ng/mL, AST = 101 U/L, ALT = 42 U/L, erythrocyte sedimentation rate = 19/h, T4 = 8 mcg/dL (4.5–11.2), thyroid-stimulating hormone = 2 mIU/L, total immunoglobulin A = 82 mg/dL, anti-tissue transglutaminase = negative, α1-antitrypsin = 107 mg/dL, ceruloplasmin = 133 mg/L, and 24-hour urine copper: 40 µg/d (►Table 1).

He was treated with ursodeoxycholic acid to increase liver enzyme; however, within the period of a month, there was no improvement in the signs and symptoms, although a very slight improvement in AST. Examination of liver and lymphoblastic pathology showed an increase in the number of eosinophils. Based on the abovementioned laboratory results, the drug was discontinued, and these laboratory findings were reported:

**Table 1** A summary of the patient’s laboratory results

<table>
<thead>
<tr>
<th>Interval of tests</th>
<th>Normal range</th>
<th>Patient’s results</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the time of admission</td>
<td>Alpha fetoprotein = 10–20 ng/mL</td>
<td>AST = 214</td>
</tr>
<tr>
<td></td>
<td>AST: 10–40 U/L</td>
<td>ALT = 364</td>
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<td></td>
<td>ALT: 10–35 U/L</td>
<td>γGT = 23</td>
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<td></td>
<td>γGT: 5–24 U/L</td>
<td>WBC = 25500</td>
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<tr>
<td></td>
<td>T4 = 4.5–11.2 mcg/dL</td>
<td>(N: 42, L: 41, M: 7)</td>
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<td></td>
<td>TSH: 0.55–5.31 mIU/L</td>
<td>Hb = 12</td>
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<tr>
<td></td>
<td>IgA: 80–350 mg/dL</td>
<td>Plt = 312 × 10³</td>
</tr>
<tr>
<td></td>
<td>α1At: 100–300 mg/dL</td>
<td>Alpha fetoprotein = 10 ng/mL</td>
</tr>
<tr>
<td></td>
<td>WBC: 4000–9000 µL</td>
<td>AST = 101 U/L</td>
</tr>
<tr>
<td></td>
<td>Ceruloplasmin: 200–600 mg/L</td>
<td>ALT = 42 U/L</td>
</tr>
<tr>
<td></td>
<td>24-hour urine copper: 15–70 µg/dL</td>
<td>γGT = 16</td>
</tr>
<tr>
<td></td>
<td>Hb: 11.5–15.5</td>
<td>HCV Ab = +</td>
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<tr>
<td></td>
<td>Plt: 150–400 × 10³</td>
<td>HAV Ab = negative</td>
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<tr>
<td></td>
<td></td>
<td>HBS Ab = negative</td>
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<tr>
<td></td>
<td></td>
<td>HBS Ab = +</td>
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<tr>
<td>After ursobil treatment</td>
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<tr>
<td>After (sofosbuvir 400 mg/daclatasvir 60 mg) treatment</td>
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</tbody>
</table>

Abbreviations: α1At, α1-antitrypsin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ESR, erythrocyte sedimentation rate; γGT, gamma-glutamyl transferase; HAV Ab, hepatitis B virus antibody; Hb, hemoglobin; HBS Ab, hepatitis B surface antibody; HBS Ag, hepatitis B surface antigen; HCV Ab, hepatitis C virus antibody; IgA, immunoglobulin A; L, lymphocyte; M, monocyte; N, neutrophil; Plt, platelet; TSH, thyroid-stimulating hormone; TTG, tissue transglutaminase; WBC, white blood cell.

Due to the susceptibility of Ab HCV, the patient underwent polymerase chain reaction (PCR) examination for HCV RNA where, 5651000 copies of the virus genotype III were reported. The pathology of the liver examination is as follows:

Lymphoplasm cells were seen in portal spaces, with no interface: hepatitis or steatosis. Few eosinophils were observed in the portal and sinusoids, hepatic artery infusion = 3/18 along with different hydropic changes in hepatocytes with mild chronic hepatitis.

After consulting with gastroenterologists, sofosbuvir 400 mg and daclatasvir 60 mg tablets were prescribed, which improved the patient’s condition, after which the HCV RNA PCR became negative and WBCs were normalized (►Table 1).

The total duration of treatment was 3 months and the child consumed 2 pills per day. Complete eradication was achieved within 3 months of treatment. During the examinations, the child was found to have a history of dental procedures. We suspected that the infection was acquired during the course of dental treatment.

Furthermore, during the treatment, liver urea and creatinine tests were performed once every month for drug control.
for 3 months. We report 24 months of sustained virologic response (SVR) characterized by HCV RNA below lower limit of quantitation of 25 IU/mL. The patient reported minor diarrhea and nausea as a result of the drug side effect for the first 2 weeks only.

The methods are reported in accordance with the Surgical Case Report 2020 guidelines.8

Discussion

DAA drugs are well-tolerated class of drugs for the treatment of HCV infection. In addition to mono-infection, it is also well suited for the treatment of human immunodeficiency virus (HIV)/HCV individuals, marked by a high sustained viral response.9 These are the inhibitors of viral RNA polymerase.

Daclatasvir and velpatasvir are used for the treatment of nearly all genotypes. However, in cases where the duration of treatment is longer, ribavirin is prescribed along with DAA.

A recent clinical report has also suggested that the short-term treatment of sofosbuvir and daclatasvir is effective against genotype II HCV infection in adults.10 In a single-arm trial, 77 patients with genotype I or IV HCV and HIV were treated with sofosbuvir and an inhibitor of NS5A (ledipasvir). The outcomes showed that efficacy of the treatment was similar to that of interferon (INF)-based treatment; however, the course of the treatment was shorter and safer.11 Similarly, daclatasvir and sofosbuvir, with or without ribavirin, also have safer and more efficient outcomes where SVR was 12 weeks.12 Ghaffar et al13 reported that sofosbuvir/daclatasvir for the treatment of HCV genotype IV in children aged 8 to 18 years is effective and safe. Note that 100% SVR were reported in children who completed the treated regime of 12 weeks. Similar findings were reported in 3 adolescent patients treated for chronic HCV infection.14,15 However, side effects such as increase creatinine levels, gastroenteritis, and diarrhea can be reported with the treatment.7

The present study shows the efficacy of a combination of 400 mg of sofosbuvir and 60 mg of daclatasvir for the treatment of acute viral infection of hepatitis C in a pediatric patient. It has been found to be a cost-effective treatment and it halts the progression of virus to chronic invasion stages. We also suggest that the adverse effects of the drug should be closely monitored, particularly in comorbid patients. Our patient did not have a history of any other liver disease such as hepatocellular carcinoma or cirrhosis, and therefore, the safety of this drug in these patients cannot be concluded through this case report.

Conclusion

This case report suggests the efficacy of 400 mg of sofosbuvir and 60 mg of daclatasvir, manufactured in Iran, for the treatment of HCV mono-infection in a pediatric patient. Two-years of follow-up showed complete absence of viral RNA and patient turned out to be a healthy individual, with no side effects.

Note

Consent was not obtained to publish the case report. This report does not contain any personal information that could lead to the identification of the patient.

Availability of Data and Material

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Conflict of Interest

None declared.

Authors’ Contributions

F.F.: Conceptualized and designed the study, drafted the initial manuscript, and revised the manuscript.

P.R.: Designed the data collection instruments, collected data, performed the initial analyses, and reviewed and revised the manuscript.

G.H.: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

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