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Vertical genotype 1 HCV infection treated successfully in the second year of life: A case report

Authors' Contribution:

- A** Study Design
- B** Data Collection
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- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

Małgorzata Pawłowska^{ACDEFI}, Waldemar Halota^{GD}, Ewa Smukalska^{BGD}

Chair of Infectious Diseases and Hepatology, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland

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Summary

Background:

Perinatal HCV transmission appears to be an important cause of HCV in children. Treatment of chronic hepatitis C in young children is controversial because of spontaneous HCV clearance and possible adverse events.

Case Report:

Vertical HCV genotype 1 infection was diagnosed in a 3-month-old infant. In the subsequent clinical examination we still observed hepatomegaly, fluctuations of ALT, AST and GGT activity, with the highest values 2206 U/L, 1319 U/L, and 297 U/L, respectively. In qPCR, HCV RNA was >700.000 IU/ml. In the 42nd week of observation, liver biopsy was performed with Grade 1 grading and Grade 1 staging. At age 12 months, interferon-alpha2b (1.5 MU 3 times a week) and ribavirin (2x80 mg daily) were administered for 48 weeks. At the beginning of the treatment we observed fever after IFN injection. In the 12th week of therapy, HCV RNA disappeared followed by SVR, and it was sustained for 6 years. To our knowledge, this is the first report of a pediatric (1-year-old) patient treated with combined IFN alpha-2b and ribavirin therapy.

Conclusions:

This case report confirms the possibility of successful anti-HCV treatment in a young child, with 6-year sustained virological response without significant adverse events.

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vertical HCV infection • genotype 1 • treatment

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Author's address:

Małgorzata Pawłowska, Chair of Infectious Diseases and Hepatology, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland, e-mail: mpawlowska@cm.umk.pl

BACKGROUND

In Poland the number of persons with chronic HCV infection is estimated at 700 000. HCV infection is the most frequent cause of chronic hepatitis in children [1].

While parenteral transmission is still common in Polish patients, perinatal transmission now seems to be the leading cause of HCV transmission in children. Maternal factors cited as playing a significant role in HCV vertical transmission include: high HCV viral load, HIV/HCV coinfection, intravenous drug use, certain HLA types, and the presence of HCV RNA in maternal peripheral blood mononuclear cells and advanced HCV-liver disease in the mother [2–4].

The natural history of HCV infection in children is different from that in adults. It commonly is an asymptomatic chronic infection, with normal alanine aminotransferase (ALT) activity and minor abnormalities of liver histology, most often diagnosed incidentally or as a result of epidemiological investigation. Spontaneous HCV clearance can occur in up to 25–30% of children, especially those infected with genotype 3 HCV, and the rate of clearance is independent of the mode of HCV transmission [5]. It appears that the probability of persistent viremia and development of end-stage liver disease is relatively higher in children infected with genotype 1 HCV and in those who have acquired disease via vertical transmission [6].

Treatment of chronic hepatitis C in young children is controversial because of spontaneous HCV clearance and possible adverse events.

We report a case of vertical HCV genotype 1 infection successfully treated in the second year of life, with sustained response for 6 years.

CASE REPORT

A 3-month-old infant, who was born in 40 HBd, second pregnancy, with weight 3200g, was hospitalized because of diarrhea and vomiting. Past medical history revealed that his mother was admitted to the hospital because of acute hepatitis C 5 days after delivery.

His general condition at admission was rated as quite good. Physical examination revealed hepatosplenomegaly, with enlarged liver (4 cm) and spleen (1 cm). In laboratory testing we detected elevated aminotransferases activity (ALT 82 U/l, AST 92 U/l). Serum levels of bilirubin, GGT, and prothrombin ratio were within normal limits. The child was vaccinated against HBV and the anti-HBc total test result was negative. Serologic testing revealed the presence of anti-HCV antibodies, and hepatitis C was confirmed by detection of HCV RNA with PCR method. In the differential diagnosis of hepatitis we excluded HAV, EBV, and CMV infections and *Toxoplasma gondii*, as well as Wilson's disease, alpha-1 antitrypsin deficiency, and amino acids metabolic disorders. Parallel to hematological diagnostics, we looked for the diarrhea etiology and found rotaviruses in stool. Bacteriological cultures of blood, urine, and stool were negative. The infant was diagnosed with vertical HCV infection and rotavirus diarrhea.

Table 1. Liver test results during observation.

Weeks	AIAT (U/l)	AspAT (U/l)	GGT (U/l)
2	46	73	28
6	559	451	58
7	188	155	47
8	1226	438	297
10	337	247	90
11	1200	600	124
16	684	351	57
20	2206	1319	85
22	498	266	68
27	1284	617	73
33	750	432	42
41	254	179	23

In the first days of hospitalization, we observed vomiting and loose stools without disorders of water balance or electrolyte and acid-alkaline equilibrium. After 4 days the patient was discharged in good clinical condition with recommendation for systematic follow-up at the Hepatology Clinic. During the following 40 weeks he was systematically evaluated in clinical examination and biochemical tests (Table 1).

Postnatal psychomotor development was normal, as well weight and height.

In clinical examination we still observed hepatomegaly. In laboratory results, fluctuations of ALT, AST, and GGT activity showed highest values of 2206 U/L, 1319 U/L and 297 U/L, respectively. In quantitative HCV RNA test (PCR), the value of viral load was >700 000 IU/mL (> upper limit of detection), and HCV genotype 1b with INNO-LIPA test was detected. At the same time, investigations performed in his mother revealed similar results, confirming diagnosis of vertical HCV infection in the infant. In the 42nd week of observation, liver biopsy was performed. Histological diagnosis of chronic hepatitis C was established, with Grade 1 inflammatory activity (grading), and Grade 1 fibrosis (staging) according to the modified Scheuer's scale [7].

In the 12th month of life, treatment with interferon-alpha2b (1.5 MU 3 times a week) and ribavirin (2×80 mg daily) was administered. The patient was treated with this combined therapy for 48 weeks. At the beginning of the treatment we observed fever after IFN injection. No other adverse events were observed during treatment. In the 12th week of therapy we observed the disappearance of HCV RNA followed by SVR and it has been sustained for 6 years (Table 2).

In that year, IL28B single nucleotide polymorphism rs12979860 and rs8099917 were determined in the child and his mother, and the analysis revealed in both of them the presence of CC, and TT polymorphism, respectively, with favorable response to treatment.

Table 2. Liver tests and HCV viral load during treatment and follow-up.

Weeks	AIAT (U/I)	HCV RNA (IU/ml)	Years after the end of treatment	AIAT (U/I)	HCV RNA (IU/ml)
Before treatment	180	>700 000	0.5	25	negative
4	110		2	21	negative
8	185		3	21	negative
12	1600	<600	4	33	negative
14	177		5	25	negative
20	108				
24	186				
48	107				

Anti-HCV treatment helps prevent unfavorable clinical consequences like liver cirrhosis or hepatocellular carcinoma.

DISCUSSION

We have described a patient with vertically transmitted HCV genotype 1 infection. To our knowledge this is the first report of a pediatric (1-year-old) patient treated with combined IFN alpha-2b and ribavirin therapy.

Some authors believe that interferon therapy should not be given to children younger than 3 years of age because of the high rate of spontaneous viral clearance and possible adverse events, especially potential neurotoxicity and growth inhibition [8–11]. Spontaneous clearance of HCV can occur in up to 25–30% of children; younger age at follow-up and ALT within normal limits favor HCV clearance [12]. On the other hand, Farmand et al, on the basis of ALT activity dynamics, suggested that in vertically HCV-infected children a potent inflammatory response in the liver precedes viral clearance and temporarily elevated liver function tests, followed by a decline of viral load, may be indicative of a near viral clearance in early childhood [13]. Ruiz-Extremera et al showed that IL28B CC child polymorphism is independently associated with the spontaneous clearance of HCV genotype-1 among infected children [14]. In the presented case, the decision about treatment was based on elevated LFTs, still HCV RNA serum presence and histological changes in the liver suggested chronic hepatitis C. It was maintained by the analysis of hepatitis C treatment efficacy, which revealed higher SVR rates and fewer adverse events reported in children compared to adults [8,15]. Now, after 6 years, our decision turned out to have been correct, confirmed by sustained viral response and the lack of late adverse events of interferon therapy as growth disorders. This child's mental development is normal and his weight and height are between the 50th and 75th percentiles.

Despite a generally asymptomatic course of HCV infection in children with mild histological changes in the liver, chronic hepatitis C may lead to liver fibrosis, cirrhosis, and even HCC in children and adolescents [16,17]. Bortolotti et al described end-stage liver disease in 1.8% of analyzed children, who were mainly infected perinatally with HCV genotype 1 [6]. According to Wirth et al, about 5% of affected children develop significant liver disease in childhood [18].

CONCLUSIONS

This case report confirms the possibility of successful anti-HCV treatment in a young child, with a 6-year sustained virological response without significant adverse events.

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