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HEPATITIS C VIRUS IN MONOZYGOTIC TWINS

Fernando L. GONÇALES JR(1), Raquel S. B. STUCCHI(1), Maria Helena P. PAVAN(1), Rodrigo N. ANGERAMI(1) & Neiva S. L. GONÇALES(2)

SUMMARY

A case of a pregnant patient with chronic hepatitis C who gave birth to monozygotic twins that were infected with HCV is reported. One of the newborns was positive for HCV-RNA in blood sample collected 12 hours after delivery. The other newborn was negative for HCV-RNA at birth, but was detected HCV viremia at three months of age. The results have led to the conclusion that one of the twins was probably contaminated in the intrauterine period, while the other acquired the infection in the perinatal period. Both were negative for HCV-RNA and for anti-HCV in the serum samples collected at nine months of age. The report describes the changes in the laboratory tests conducted in mother and twins until 29 months after delivery.

KEYWORDS: HCV Transmission; Monozygotic twins.

INTRODUCTION

The hepatitis C virus (HCV) is the main non-A, non-B hepatitis agent of parenteral transmission, usually by blood transfusions or by needle sharing among intravenous drug users (IVDU)[4,15]. These risk factors are absent in a large number of HCV patients. This indicated that there were other means of transmission such as vertical and perinatal, as observed in some cases of neonates born to HCV infected mothers[5]. The Centers for Disease Control of the United States Public Health Service estimated that the probability of HCV perinatal transmission is very low (5%-6%)[5]. This case report describes the intrauterine and perinatal infections of homozygotic twins born to an HCV infected mother.

CASE REPORT

A 39-year-old chronic HCV infected patient underwent a cesarean surgery to give birth to monozygotic twins having a single placenta. The mother had acute non-A, non-B hepatitis 7 years ago and the results for both, the anti-HCV-ELISA (EIA 3rd generation, Abbott Laboratories, Chicago, Illinois, USA) test as well as the HCV-RNA test (HCV AMPLICOR, Roche Diagnostic Systems, Nutley, New Jersey, USA), were positive. It was a confirmed genotype 1 (LIPA-Line Probe Assay-HCV/Innogenetics) infection. The results of a hepatic biopsy performed 5 years ago indicated chronic persistent hepatitis. The patient had never been subject to antiviral treatment because the AST (aspartate aminotransferase), ALT (alanine aminotransferase) and liver function test results were always normal. The patient denied blood transfusions, was not a drug addict and was seronegative for hepatitis A virus, hepatitis B virus and the HIV virus markers.

The twins were healthy at birth and when discharged from hospital on the third day after delivery, were in a very good condition. They were breastfed for 9 months. The first blood sample for HCV serological and virological testing was taken from a peripheral arm vein, 12 hours after birth. Over a period of 29 months the results obtained were normal for AST, ALT, alkaline phosphate, gamma glutamil transferase and liver function tests (LFT). In the table I were demonstrated the results of the anti-HCV, HCV-RNA tests (copies per mL) in both, mother and children, during follow-up.

In twins also was confirmed a infection by HCV genotype 1 (LIPA-Line Probe assay-HCV/Innogenetics).

DISCUSSION

HCV infection is thought to be transmitted by an HCV infected mother mainly at birth[4,14]. Although some authors have reported that the risk for infection is far higher in the case of children born of vaginal birth than in a cesarean section[6,12,14], not all studies show a link between vaginal delivery and perinatal HCV transmission[13]. HCV viremia was detected in the peripheral blood of twin 1 twelve hours after birth which could mean that is possible that the transmission must have occurred in the uterus and not by mucocutaneous exposure at the time of delivery. The mother too, had a detectable viremia, which may have helped to infect the newborn more easily[6]. Transmission is absent if the mother is not viremic[13,14] and it occurs more frequently when the mother's viral load is greater than 1 million copies/ml. The mother's viral load was quite low at delivery and probably this fact could explain the absence of transmission to both twins in the intrauterine period. In twin 2, viremia

(1) Disciplina de Doenças Transmissíveis da Faculdade de Ciências Médicas da UNICAMP, Campinas, São Paulo, Brasil.
(2) Hemocentro-Campinas, UNICAMP, Campinas, São Paulo, Brasil
Correspondence to: Fernando Lopes Gonçales Junior, MD.PhD, Av. Dr. Romeu Tortima 725, 13084-520 Campinas, SP, Brazil, Phone/Fax: (0-XX-19) 2894513. E-mail: flopes@correionet.com.br

Table 1
Results of laboratory tests conducted during 29 months of follow-up

	At Birth		6 Months		9 Months		18-29 Months	
	A-HCV[a]	RNA[b]	A-HCV[a]	RNA[b]	A-HCV[a]	RNA[b]	A-HCV[a]	RNA[b]
Mother	(+)	(+) 32.4 x 10^3	(+)	(+) ND[c]	(+)	(+)	(+)	(+)
Twin 1	(+)	(+) 6.2 x 10^3	(+)	(+) 38.5 x 10^3	(-)	(-)	(-)	(-)
Twin 2	(+)	(-) < DL[d]	(+)	(+) 5.0 x 10^3	(-)	(-)	(-)	(-)

a=Anti-HCV antibody using enzyme-linked immunosorbent assay (ELISA); b= HCV RNA detection by PCR - copies/ml (AMPLICOR HCV MONITOR™); c= Not Determined; d=Detection Limit

was absent at birth but an HCV-RNA was observed 6 months later. More likely, the infection occurred perinatally, as with HIV, by mucocutaneous exposure to HCV at the time of delivery. If viremia is detected in a 3-month-old child who was HCV-RNA negative at birth, it could be considered to be either due to a low viremic level at birth (false negative) or because the infection had taken place during the first few months[10].

Passively acquired HCV antibodies have also been found in uninfected infants[10]. In newborns the best manner to diagnose HCV infection is by the HCV-RNA detection using PCR method. The serum of an infected newborn may show persistent or intermittent HCV-RNA positive results, which could lead to a false negative PCR result[10]. This situation may have occurred in twin 2 at birth (HCV RNA negative). The transient presence of anti-HCV antibodies was clearly due to transplacental passage. In Japan, HCV-RNA positive children born to HCV infected mothers did not show an increase in ALT or were positive for anti-HCV[8] as shown by our children. Research conducted using quantitative PCR[11] and branched DNA signal amplification[15] studies have shown that higher viremic levels in HCV mothers increased the risk of vertical transmission. The same was observed in the case of anti-HCV reagent mothers co-infected with HIV[12,15], who had higher concentrations of HCV-RNA[15]. Material compiled from various studies have shown that 18% of the children born to HCV mothers co-infected with HIV developed HCV infection, while 4.5% of the children born to mothers infected only with HCV developed HCV[4].

Because mother's viral load at birth was quite low, one could suggest that the infection might have been installed after birth through breastfeeding. This transmission is a controversial subject and apparently is not associated with HCV infection of newborns. Using the PCR method, some researchers have found HCV particles in the mother's milk, however, it is not known if these particles could cause infections[7,9] though others have detected a high rate of transmission in children who have been breastfed[12]. Breastfeeding by HCV infected mothers has not been prohibited neither have cesarean births been stimulated[1,3].

A case of dizygotic twins born to HIV and HCV infected mothers was recently reported. One of the twins developed only an HIV infection while the other twin proved to be only HCV-RNA positive. This difference in transmission suggests that other viral, genetic or placental factors helped in increasing the child's susceptibility to these infections[2]. Although HCV-RNA detection may be transient in children born to HCV infected mothers, it remains unclear whether these infants have truly cleared infection or will have progressive disease.

The investigation conducted in our study suggests that HCV transmission was probably intrauterine in the case of twin 1 and perinatal in the case of twin 2. Although repeated HCV-RNA tests using the PCR method proved negative in the sample collected from twin 2 at birth, this could be due to false negative results. A follow-up of these twins would help evaluate the hepatic damage caused by the same HCV strain in individuals having the same genetic burden and help provide more extensive information on the natural history of the hepatitis C virus.

RESUMO

Hepatite pelo vírus C em gêmeos monozigóticos

É relatado o caso de paciente grávida, com hepatite C crônica que deu à luz dois gêmeos monozigóticos. Um recém-nascido apresentou positividade para o RNA do vírus da hepatite C (RNA-VHC), no sangue venoso, coletado de veia periférica doze horas após o parto. O outro recém-nascido apresentou-se negativo para o RNA-VHC logo após o nascimento, porém tornou-se RNA-VHC positivo na amostra coletada aos três meses de idade. Os resultados permitem supor que um dos gêmeos provavelmente foi contaminado no período intra-uterino, enquanto o outro adquiriu a infecção no período perinatal. Ambos foram negativos para a presença do RNA-VHC e para os anticorpos anti-HCV em todas as amostras séricas coletadas após os nove meses de idade. Os exames laboratoriais dos gêmeos não mostraram a presença de infecção crônica pelo VHC durante o acompanhamento de 29 meses .

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