Spontaneous clearance of hepatitis C virus during pregnancy

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Summary: Spontaneous clearance of hepatitis C virus (HCV) is expected to be unlikely in pregnancy due to the relative immunosuppression and increase in viraemia that occurs. We report the first case of spontaneous clearance of hepatitis C virus (HCV) occurring in pregnancy.

Keywords: hepatology, infection, infectious diseases, maternal-fetal medicine, high-risk pregnancy

CASE REPORT

A 20-year-old woman received regular HCV antibody testing as part of a methadone treatment program and tested negative for HCV antibody 12 months prior to conception. She presented late for antenatal care of her first pregnancy and was tested for HCV in her second trimester. Antibodies against HCV were detected and she was viraemic (as tested by HCV RNA polymerase chain reaction.) This was in the context of intravenous drug use and was consistent with recent HCV infection. She was asymptomatic at the time of testing. She was re-tested at 36 weeks gestation and HCV RNA was not detected in plasma consistent with spontaneous viral clearance. She went into spontaneous labour at term and delivered a healthy infant by normal vaginal delivery. She had further testing at 18 months after delivery and remained positive for HCV antibody with undetectable HCV RNA. (Figure 1) Her ALT was normal throughout. Her child was tested at age 18 months and was negative for HCV antibodies and HCV RNA.

DISCUSSION

The natural history of HCV in pregnancy sees a reduction in alanine aminotransferase (ALT) levels and an increase in viraemia.^{1,2} Gervais *et al.* reviewed 26 women with chronic hepatitis C and found that three quarters of women had normalisation of ALT and an increase in HCV RNA levels by more than 50% by the third trimester. These changes return to pre-pregnancy levels soon after delivery. There are exceptions to these general findings and both fulminant hepatitis and post partum hepatitis flares have been reported.^{1,3}

The maternal immune system undergoes complex changes believed to protect the antigenically foreign foetus. One mechanism is a shift in the T-helper response from a type 1 (Th1) to a type 2 (Th2) response. This is evident by improvement in Th1 associated conditions (e.g. rheumatoid arthritis) but worsening

of Th2 conditions (e.g. systemic lupus erythematosus).⁴ The mechanisms of HCV clearance are incompletely understood but the Th1 response is known to play a key role.⁵ The shift from the Th1 response may make the clearance of HCV infection less likely in pregnancy.

Although a strong Th1 response is an important factor in HCV clearance, paradoxically it is the persistent Th1 response that causes the ongoing hepatocyte destruction in chronic HCV. The Th1 cells secrete cytokines that stimulate cytotoxic CD8+ T-cells and cause hepatocyte lysis and subsequent fibrosis and cirrhosis.⁶ It is potentially this shift away from the Th1 response that reduces hepatocyte destruction in pregnancy, as reflected by normalization of the ALT.^{6,7} It is also known that progesterone and oestrogen affect T cell differentiation and the increase in these hormones during pregnancy may have a protective role.¹

HCV spontaneously clears in 15–50% of acute infections.^{3,5} The case presented here had host factors that in the non-pregnant population are associated with increased rates of viral clearance; she was young, female, negative for HIV and other hepatitis viruses, with low alcohol consumption.^{5,8} There is one other report of clearance of HCV in pregnancy, however in that case the seroconversion may have occurred post partum.⁹

Treatment for acute hepatitis has been shown to improve viral clearance with rates greater than those achieved by spontaneous clearance or treatment of chronic HCV.⁸ Current recommendations suggest waiting 8–12 weeks after diagnosing acute infection to allow for spontaneous clearance and then considering interferon-alpha therapy. In animal studies interferon-alpha has had abortifacient effects and should be avoided in pregnancy unless there are strong indications.¹⁰ The role of ribavirin in acute treatment is unclear, however it is contraindicated in pregnancy because of teratogenicity.^{8,11}

The risk of maternal-infant transmission in viraemic mothers is 5.6–12%.⁵ Risk factors for transmission include high maternal viral load, intravenous drug use and HIV co-infection.^{12,13,14} An undetectable viral load is associated with an almost negligible risk of transmission.^{14,15} Furthermore, there is no evidence

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Figure 1 Anti HCV = Hepatitis C Antibody; HCV RNA = Hepatitis C Virus RNA

that caesarean section or formula feeding reduce transmission in mothers with high viral loads.¹⁴ For future pregnancies our patient should have HCV re-infection excluded by re-testing for HCV RNA.

In summary, spontaneous clearance of hepatitis C virus is possible despite the immune modulation and increased viraemia that occurs during pregnancy.

DECLARATIONS

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