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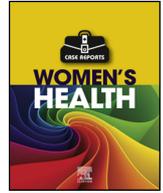
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Sexually acquired acute hepatitis C infection diagnosed during pregnancy: a case report of successful postpartum treatment

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ABSTRACT

Background: Infection with the hepatitis C virus (HCV) during pregnancy has emerged as an increasingly recognized and prevalent condition among women of reproductive age in the United States. While screening recommendations exist for pregnant women at high risk of HCV infection, pregnant women with HCV are often under-screened, not diagnosed, or do not receive adequate follow-up, thereby increasing the risk of suboptimal maternal and infant outcomes (including in future pregnancies).

Case: A pregnant woman living with HIV presented with intrahepatic cholestasis of pregnancy. She had tested negative for HCV earlier in pregnancy as part of routine screening recommended for women living with HIV. She was found to have sexually acquired a new HCV infection from her partner during pregnancy. She successfully completed treatment postpartum.

Conclusion: With the rise in HCV infection among pregnant patients, physicians should be diligent in assessing pregnant women and their partners for HCV risk factors, testing for HCV when risk is identified, and arranging follow-up testing and treatment for HCV-positive mothers and their infants.

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1. Introduction

The incidence of infection with the hepatitis C virus (HCV) among women of reproductive age in the United States increased from 781 new cases in 2009 to 2194 new cases in 2014. In fact, the number of women of reproductive age living with hepatitis C recently surpassed that of women aged 45–64 years [1]. This trend in reported rates has been attributed to increases in intravenous (IV) drug use as well as more available screening [2]. Approximately 1–2.5% of pregnant women in the United States have HCV infection, which can lead to adverse outcomes for the mother and fetus, including intrahepatic cholestasis of pregnancy (ICP), preterm birth, low fetal birthweight, and fetal distress, as well as long-term complications of chronic HCV infection in mothers and children [3].

HCV acquisition in women usually occurs through blood exposure, and HCV is not efficiently transmitted sexually, particularly across the female genital tract. Data suggest no difference or only a minimally higher risk of HCV infection in individuals who have sexual partners with hepatitis C compared with those with partners without hepatitis C. However, the risk of acquiring hepatitis C sexually increases with the number of sex partners, HIV co-infection, and in the context of

high-risk and traumatic sexual practices [4]. While clinical guidelines recommend risk-based screening for HCV infection of pregnant women, many women, their partners and their infants are not screened due to underestimated risk, and new cases of HCV infection are often missed [5]. We report a rare case of sexually acquired hepatitis C diagnosed during late pregnancy in a patient with HIV; she was successfully treated for hepatitis C after delivery.

2. Case presentation

A 33-year-old HIV-positive woman, gravida 3 para 2 + 0, at 34 weeks and 3 days of pregnancy presented with acute onset of severe pruritus consistent with intrahepatic cholestasis of pregnancy (ICP). This was confirmed by her elevated level of bile acids and transaminitis. She had had a negative hepatitis C antibody test at 20 weeks and 4 days of gestation as part of the routine prenatal evaluation of pregnant women living with HIV. Given her new diagnosis of ICP and increased risk given her HIV status, she was re-tested for HCV and was diagnosed with active infection based on positive HCV antibody and HCV polymerase chain reaction (PCR) testing.

The patient had been followed closely from 14 weeks and 3 days of gestation in a high-risk HIV in pregnancy clinic. Her HIV infection had been diagnosed 11 years previously, and her CD4 count at time of initiating pregnancy care was 901 cells/mm³. Her nadir CD4 count was 280

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cells/mm³ and she had been on suppressive antiretroviral therapy for over 5 years; her HIV viral load was <40 copies/mL at the estimated time of conception. During the first 3 months of pregnancy, the patient stopped antiretroviral therapy (tenofovir disoproxil fumarate/emtricitabine with ritonavir-boosted atazanavir) due to hyperemesis and she had a HIV viral load of 32,470 at 16 weeks and 4 days of gestation. She was restarted on a single-tablet regimen of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate with good reported adherence and had an undetectable viral load by 20 weeks and 4 days of gestation, which continued throughout her pregnancy and postpartum.

She also had a history of excess alcohol use and depression, which was treated with supportive psychotherapy during pregnancy. Her prenatal course was unremarkable. However, at 34 weeks and 4 days, she reported severe itching for 2–3 weeks with no associated rash or pain in the right upper quadrant. Her alanine transaminase (ALT) and aspartate transaminase (AST) levels were 254 u/L and 300 u/L, respectively, and she had an elevated level of bile acids, at 57 umol/L.

In light of her symptoms and laboratory test results, she was diagnosed with ICP. Her biophysical profile was normal and she was started on oral ursodiol three times daily with a plan for delivery at 36 weeks. Pruritus continued and at 35 weeks and 4 days of gestation her bile acid level rose to 168 umol/L, and her transaminase levels were persistently elevated (AST 246 u/L, ALT 217 u/L). An HCV antibody test at that time was positive. The patient was not treated for HCV infection, however, as the standard treatment is contraindicated in pregnancy. Re-testing postpartum was planned, as this would determine whether she had cleared the infection without intervention [6].

She delivered via an uncomplicated lower-transverse cesarean section at 36 weeks and 3 days of gestation due to severe ICP. This was a repeat cesarean section; her first had been performed due to her high HIV viral load during her first pregnancy. Membranes were intact prior to delivery, no meconium was observed, and APGAR scores were 8 and 9. HCV RNA PCR for the mother was positive, with a viral load of 58,158 IU/mL; her transaminase levels had somewhat improved (AST 194 u/L, ALT 178 u/L) by postpartum day 1. Her pruritus had also improved, and she was discharged on postpartum day 2 with the recommendation to continue oral ursodiol dose for 1 week. Her HCV viral load at 3 weeks postpartum was 12,052 IU/mL and genotyping revealed HCV 1b.

At her 6-week postpartum follow-up office visit, the patient reported that her pruritus had resolved. Her transaminase levels had significantly decreased but remained above normal (AST 56 u/L, ALT 73 u/L). Hepatitis B surface antigen was negative and surface antibody was positive. Treatment options for HCV were deferred to 6 months postpartum in order to allow time for possible clearance of HCV infection.

The patient denied any history of intravenous (IV) drug use or other opiate or cocaine use. During follow-up care, the patient learned that her male partner, who was HIV negative but who had a history of IV drug use, had recently started antiviral treatment for chronic HCV infection and had not disclosed this diagnosis to her prior to the pregnancy. In addition to the negative second-trimester HCV antibody test noted above, she had had a negative HCV antibody test approximately 9 months before she became pregnant.

At 6 months postpartum, her HCV viral load was 90,068 IU/mL and her transaminase levels were unchanged. At 1 year postpartum, she presented for re-evaluation for treatment of her chronic HCV infection and her HCV viral load was 72,414 IU/mL. Antiretroviral therapy was changed to dolutegravir, tenofovir alafenamide, and emtricitabine to avoid drug interactions and to allow for initiation of a 12-week course of elbasvir/grazoprevir. At the time of initiation of treatment, a liver ultrasound scan was normal. She successfully completed this treatment for 12 weeks with minimal side-effects and reported full adherence. She had evidence of rapid virologic response within 1 month of treatment and her end-of-treatment HCV viral load was undetectable (the last result available at the time of writing).

Her child tested negative for HIV and HCV, and the patient did not breastfeed due to her HIV status.

3. Discussion

Sexually acquired HCV infection is rarely detected during the third trimester of pregnancy after negative HCV testing earlier in pregnancy. Negative HCV antibody testing before pregnancy and in early pregnancy followed by positive testing in the third trimester suggests acquisition of HCV infection during pregnancy. Fewer than 12 such cases have been reported in the literature [6]. For our patient, risk factors for HCV acquisition include HIV infection and a sexual partner with a history of intravenous (IV) drug use and HCV infection. Initial testing on the basis of the patient's risk profile and repeat testing prompted by her presentation with ICP identified a new HCV infection and generated appropriate follow-up for the patient and her child. With the increasing prevalence of HCV among women of reproductive age, re-assessing risk factors for HCV infection in the pre-conception and antenatal periods, as demonstrated by this case, is critical for identifying HCV infection and the providing follow-up care.

The increasing prevalence of HCV infection in pregnant women reflects the general rise of HCV infection in the United States due to opioid use. In a sample of pregnant women receiving pharmacotherapy for opioid addiction, more than half had been exposed to HCV and nearly 40% had chronic HCV [7,8]. The transmission of HCV is primarily parenteral, typically via shared needles during IV drug use. Although sexual transmission of HCV is possible, it is more common with rectal exposure and is rare without the presence of traumatic sex and/or pre-existing proctitis or ulcerative disease. HIV infection may increase the risk of HCV transmission, but the relevant data are mostly derived in the context of transmission in men who have sex with men [4]. While male-to-female sexual transmission of HCV is rare, the increasing rates of HCV infection, particularly in areas with high HCV prevalence or with other factors that modify the risk of transmission, warrants clinical suspicion for all types of HCV transmission in the routine evaluation of a pregnant patient.

The Centers for Disease Control and Prevention recommend universal HCV testing in adults born from 1945 through 1965 and screening for other populations based on risk of exposure or infection [4]. Clinical guidelines recommend risk-based screening of pregnant women, and pregnancy offers an opportunity for HCV diagnosis, testing of infants at risk, and referral for treatment after delivery [9]. Prenatal HCV screening is recommended for women who have certain HCV risk characteristics, including women who have ever injected illegal drugs, used intranasal illicit drugs, were ever on long-term hemodialysis, have had percutaneous and/or parenteral exposures in an unregulated setting (such as tattooing), have a history of incarceration, sought evaluation or care for a sexually transmitted infection, including HIV, or have an unexplained liver disease [10–12]. Repeat screening later in pregnancy is recommended for women with persistent or new risk factors for HCV infection. However, under-screening for HCV is widespread. In a survey of obstetric providers asking about screening protocols in their practices, over 80% of respondents indicated that they asked patients about IV drug use but fewer than 50% said they offered routine HCV testing [13]. In addition, under-screening, under-reporting, and lack of knowledge of partner risk factors likely contribute to a pregnant woman's risk of HCV acquisition.

Another reason for diligent HCV screening among pregnant patients is to identify vertical HCV transmission risk during the present as well as subsequent pregnancies, and thereby reduce incidental HCV infection in children. Vertical transmission is the most common cause of HCV infection in children and occurs in approximately 6 in 100 pregnancies of women with HCV infection [14,15]. The risk of vertical transmission is doubled for infants of women with HIV/HCV co-infection, possibly due to increased HCV viral load secondary to immunosuppression from HIV [10,15]. Many infants who are at risk of vertical transmission lack

follow-up care. A study from Philadelphia found that 84% of children born to mothers with HCV infection did not receive adequate follow-up testing, which highlights a nationwide gap in screening practices and follow-up care [16].

The advent of direct-acting antiviral medications has emphasized the need for more vigilant screening of mothers and infants at risk of HCV infection. Current HCV treatment regimens have fewer side-effects, usually avoid the use of ribavirin (a known teratogen), and result in cure rates exceeding 90%. Despite high efficacy and minimal adverse fetal effects in animal studies, no HCV treatment regimen is currently approved for pregnant women. Furthermore, there is no approved intervention for the prevention of HCV transmission from mother to infant, though at least one clinical trial is under way [14,17]. Nonetheless, pregnancy is associated with increased healthcare engagement and provides an opportunity for appropriate linkage to treatment after delivery.

Our patient had a thorough work-up which identified new HCV infection and she was referred to appropriate follow-up care postpartum. Even in the absence of approved treatment during pregnancy, broadened screening for HCV in pregnant women would provide more opportunity to promptly identify those with hepatitis C and ensure appropriate maternal follow-up treatment and testing of the exposed infants. Both the rising prevalence of HCV infection in women of reproductive age and the system-wide shortfalls in the follow-up of affected mothers and infants suggest that general obstetricians should ensure appropriate HCV risk assessment and testing in pregnancy and postpartum linkage to care.

Contributors

All authors contributed equally to the preparation of this case report and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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