Case Report

A hepatitis B virus flare that led to hepatic decompensation and liver transplantation in a pregnant woman with chronic hepatitis B: a rare case report and literature review

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Abstract

Background: Acute viral hepatitis is the most common cause of jaundice during pregnancy. Distinct immunological changes during pregnancy and the postpartum period are possible crucial factors associated with flares of chronic hepatitis B. **Case**: We present the case of a healthy pregnant hepatitis B virus (HBV) carrier at 38 weeks of gestation. She underwent an emergent cesarean section due to acute hepatitis B flare, and ultimately underwent liver transplantation due to a decompensating liver based on an estimated Model for End-Stage Liver Disease score. **Conclusions**: For pregnant HBsAg positive women, close monitoring with serum HBV-DNA and spartate transaminase (AST)/alanine transaminase (ALT) levels every 3 months is highly recommended. According to the latest guidelines, prenatal antiviral therapy, postpartum HBV vaccination, and hepatitis B immunoglobulin should be administered to prevent mother-to-child transmission.

Keywords: Case report; Hepatitis B; Liver transplantation; Pregnancy

1. Introduction

According to World Health Organization (WHO) estimates, 257 million people were living with chronic hepatitis B virus (HBV) infection worldwide, and 900,000 people died from it in 2015 [1,2].

In pregnancy, acute exacerbation of chronic HBV infection can be life-threatening for both the mother and the fetus. Therefore, screening for high-risk groups and adequate management should be emphasized during prenatal visits.

2. Case presentation

Our case is that of a 33-year-old primigravida at 38 weeks gestation. She and her mother had chronic hepatitis B, but they had not received any routine care for hepatitis. She had undergone regular prenatal examinations in a local clinic. Her prenatal examinations revealed no abnormalities except that she was positive for HBsAg but negative for HBeAg. Her latest liver function tests (aspartate transaminase [AST]/alanine transaminase [ALT]) were within normal limits at 26+ weeks of gestation.

At 37 weeks and 3 days gestation, she began to have poor appetite, generalized weakness, upper abdomen discomfort, decreased urine output, and dysuria with dark colored urine. As her symptoms progressed, she visited her local obstetrician who found elevated ALT (901 IU/L), AST (677 IU/L), and total bilirubin (16.10 mg/dL) lev-

els. She was then transferred to our hospital after being diagnosed of an acute exacerbation of chronic hepatitis B infection. Prolonged prothrombin time/partial thromboplastin time (PT/PTT; 22.8/56.1 s) and thrombocytopenia (126,000/uL) was also noted. An emergent cesarean section was performed because of life-threatening decompensating liver disease.

She delivered a live female fetus who weighed 2520 g with normal appearance and Apgar scores of 7 and 9 in the 1st and 5th min, respectively. The fetus received hepatitis B immunoglobulin and the first vaccine dose of HBV after she was sent to the pediatric intensive care unit. The second dose vaccine was subsequently administered at the correct time at a Well-Baby clinic. The infant was tested negative for HBsAg and positive for Anti-HBs at age 12 months. No mother-to-child transmission was noted.

During the cesarean section, dark colored ascitic fluid (approximately 100 mL) was noted. The estimated blood loss was 250 mL. However, 500–1000 mL of a blood-tinged collection was drained from the Sil-Med drain daily for one week postoperatively. Therefore, we prescribed continuous blood transfusion with fresh frozen plasma, cryoprecipitate, platelets, and packed red blood cells to compensate for the blood loss. The patient's liver function kept deteriorating, the HBV-DNA viral load was 8,804,810 IU/mL. The Model for End-Stage Liver Disease (MELD) score was calculated at 28 points, which was used to predict that the

patient's 3-month mortality rate at 52.6%. In addition, persistent drowsiness was noted. Based on the findings above, liver transplantation was performed 10 days after cesarean section.

After receiving a liver allograft offer from her sister, the patient's condition improved gradually. Eventually, she was discharged 19 days after liver transplantation.

3. Discussion

The maternal immune system experiences modifications during pregnancy, in which cell-mediated immunity is suppressed. This state may be triggered by an increase in the level of adrenal corticosteroids, estrogens, and progesterone, in response to the fetus, which is semiallogeneic to the maternal immune system [1]. Certain alterations can lead to a relatively compromised immune status. In the present case, an acute exacerbation of HBV infection and further liver failure were induced in a pregnant woman.

Chronic HBV alone does not directly affect female infertility or pregnancy outcomes. However, when HBV induces acute hepatitis during pregnancy, it elicits coagulopathy, resulting in critical conditions for both the mother and child, thereby requiring emergent delivery [2].

3.1 Maternal screening program for inactive hepatitis B carriers

In regions with a high prevalence of HBV infection (Taiwan, Eastern Asia, and Western Africa), screening for pregnant women with HBsAg and HBe Ag is a routine practice. In these high-risk groups, it is essential to take precautions by performing periodic HBsAg and HBe Ag assay, as well as assays for AST and ALT levels. Predictors of HBV exacerbation during pregnancy have not been established, but a positive HBe Ag implies higher risk [2]. Although most hepatic flares were mild and resolved spontaneously, some reports have revealed that severe cases of liver failure could occur during pregnancy and the postpartum period [3]. A retrospective multicenter study of 113 pregnancies in the United States between 1997 and 2015 revealed that HBV-DNA flares occurred in 9% of pregnancies and in 4% of postpartum women. Based on this, the report recommended periodic monitoring of HBV-DNA and ALT levels are every 4–6 weeks during the first and second trimesters, and every 4 weeks during the third trimester [4].

According to the Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZCOG) guidelines (updated in 2019), all pregnant women should be screened using the HBsAg test (Grade A). If a woman is identified as HBsAg positive, further testing (HBeAg, anti-HBe, and HBV-DNA) should be performed (Grade A).

From the 2020 WHO guidelines for the prevention of mother-to-child transmission (PMTCT) of hepatitis B, it is recommended that HBe Ag testing be considered as an alternative to HBV-DNA testing to determine the patient's eligibility for tenofovir prophylaxis for HBV2 for PMTCT (conditional recommendation, moderate quality of evidence).

3.2 Necessity of antiviral therapy

According to available reports, newborn immunoprophylaxis can fail in up to 30% of infants, especially with high maternal HBV-DNA levels and HBe Ag positivity [5–7]. Therefore, judgment should be individualized according to the severity of infection [3]. Following the American Journal of Obstetrics and Gynecology (AJOG) recommendation, pregnant women with HBV-DNA >200,000 IU/mL should start with antiviral therapy at 28–30 weeks of gestation [2]. Tenofovir (TDF) and telbivudine are two antiviral regimens that can be used safely in pregnant women. Many studies have shown that antiviral therapy improves HBV suppression and reduces MTCT in women with chronic HBV infection and high viral load compared to the use of hepatitis B immunoglobulin and vaccination alone [8,9].

The 2020 WHO PMTCT guidelines for hepatitis B, recommends that pregnant women that test positive for HBV infection (HBsAg positive) with an HBV-DNA level of ≥ 5.3 log10 IU/mL ($\geq 200,000$ IU/mL) should receive tenofovir prophylaxis from the 28th week of pregnancy until birth. This should be coupled with three-dose hepatitis B vaccination in all infants, including a timely birth dose (conditional recommendation, moderate quality of evidence).

3.3 Vaccine and hepatitis B immunoglobulin for infants to prevent HBV infection

MTCT of HBV is more common in children born to women who have high viral loads and/or are positive for HBeAg [10]. To reduce MTCT rates of HBV, hepatitis B immunoglobulin (HBIG) should be administered to infants who are born to HBeAg-carrier mothers immediately after birth. This could reduce MTCT rates from 90% to 10% [11]. In Taiwan, since August 8, 2020 the Taiwan Centers for Disease Control offers free HBIG injections to children born to HBV-carrier mothers as soon as possible after birth. Furthermore, HBV vaccination is recommended for all newborns. Taiwan, which was once a region with a high prevalence of HBV infection, has successfully reduced the prevalence of HBV because it was the first country to establish and popularize HBV vaccination in infants; thus, it has become a global model regarding prevention of HBV infection in the world.

3.4 Liver transplantation for decompensated liver failure

Liver transplantation remains the only known treatment option for patients with end-stage liver disease [12]. The prognosis of chronic hepatitis B flare induced decompensated liver failure without liver transplantation is poor, with transplant-free survival rates ranging from 26% to 53% [5]. In contrast, liver transplantation strikingly improves survival with one- and five-year patient survival rates of 80% and 75%, respectively [11]. Otherwise, when

chronic hepatitis B flare complicates pregnancy, mortality approaches 40%, and the only way to ensure a better survival rate is liver transplantation [6]. In a recent study, the MELD score predicted prognosis better than the King College criteria with a lower false negative rate [7]. The patient we described in this had HBV infection-related liver failure with a MELD score of 28, and an estimated 3-month mortality rate of 19.6%. Therefore, liver transplantation was the only way to resolve her decompensated liver function and improve her survival.

4. Conclusions

Acute viral hepatitis-related liver transplantation in pregnancy is rare and difficult. This calls for attention to be paid to certain high-risk pregnant women. For HBsAg-positive pregnant women, close monitoring with serum HBV-DNA and AST/ALT levels every three months is highly recommended. According to the latest guidelines, prenatal antiviral therapy, postpartum HBV vaccination, and HBIG should be administered as early as possible after birth. Regarding irreversible liver failure, there are two critical determinants of prognosis: liver transplantation as early as possible and control of all underlying factors.

Author contributions

YHL conceived the idea of this research. CYH wrote the original manuscript. CCC, SEW, and PIK performed the literature review. All the authors discussed and commented on the manuscript. CHY, YLL, and CYH revised and edited the contents and formulated to the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

As this study is a retrospective case study, the need for informed consent was waived by the ethical committee. Written informed consent was provided by the patient for publication.

Conflict of interest

The authors declare no conflict of interest.

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