Missed opportunities: Peripartum hepatic failure in a Chinese immigrant

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Abstract

Hepatitis B surface antigen (HBsAg) positivity presents unique management challenges in pregnancy. We present the case of a 26-year-old HBsAg-positive woman who presented at 35 weeks gestational age with nausea, vomiting, and abdominal pain with markedly elevated liver enzymes. An elevated alpha-feto-protein on antenatal screening had been misconstrued as fetal in origin. Magnetic resonance imaging and liver biopsy confirmed hepatocellular carcinoma. She died of fulminant hepatic failure two weeks after emergent delivery. This case highlights the importance of adequate evaluation and management of pregnant patients testing positive for HBsAg on routine antenatal testing.

Keywords

Gastroenterology, hepatology, high-risk pregnancy, infectious diseases, neoplasm

Case presentation

A 26-year-old primigravid woman was transferred to our tertiary care centre for the evaluation of liver dysfunction. She presented to a local hospital at 35 weeks gestational age with a 4-day history of nausea, vomiting, abdominal pain, and dyspnoea. She had cough and malaise three weeks earlier, treated with an unknown Chinese herb. Review of systems was otherwise negative.

Her pregnancy was otherwise uncomplicated. Antenatal screening showed an elevated alpha-feto-protein (AFP), which had prompted an amniocentesis (normal). Fetal ultrasounds were normal. Hepatitis B surface antigen (HBsAg) screen was positive, with known prior naturopathic treatment in China. She had immigrated to Toronto, Canada, two years earlier and had never seen a hepatologist.

On arrival, her heart rate was 119 beats/minute, respiratory rate 40 breaths/minute, and blood pressure 110/75 with normal oxygen saturation and temperature. She had marked scleral icterus, jaundice, and 1+ oedema to mid-shin. A systolic flow murmur was present. Respiratory examination was normal. She was tender to palpation of the right upper quadrant; she had hepatomegaly with a hard mass palpable 10 cm below the costal margin.

Investigations revealed a hemoglobin of 92 g/L, white blood cell count of 13.1×10^9 cells/ μ L, and platelet count of 289×10^9 cells/ μ L. Liver transaminases were elevated: aspartate aminotransferase (AST) 279 U/L, alanine transaminase (ALT) 95 U/L, and alkaline phosphatase (ALP) 227 U/L. Bilirubin was elevated at 146 μ mol/L (direct 117 μ mol/L). International normalized ratio was 1.2. Arterial blood gas showed metabolic acidosis with pH 7.25, pCO₂ 18 mmHg, HCO₃ 8 mmol/L, and anion gap of 22. Lactate was 9.7 mmol/L. Fibrinogen and D-dimer were elevated, and haptoglobin was undetectable. She was hypoglycemic (2.4 mmol/L). Urinalysis showed 1+ protein and 1+ blood, while creatinine was 43 μ mol/L. HBsAg, Hepatitis B e antigen (HBeAg), and Hepatitis B viral (HBV) core IgG and IgM were positive. Hepatitis D and HIV serology was negative. HBV DNA was sent but not done due to logistical reasons. An abdominal ultrasound showed a coarse, 19-cm liver with innumerable nodules and an enlarged spleen.

She became progressively acidotic over the next 12 h. Labour was induced to prevent fetal compromise. She delivered a 2360-g infant with Apgar scores of 9 after 1, 5, and 10 min. She was transferred to the intensive care unit.

Urgent abdominal magnetic resonance imaging was done (Figure 1). Infiltrative hepatocellular carcinoma (HCC) was confirmed by percutaneous liver biopsy. The tumor size and the presence of vascular invasion precluded resection or transplantation. Sadly, she died two

weeks later of progressive hepatic failure. Her infant received HBV vaccination and HBV immunoglobulin (HBIG). After one-year follow-up, the infant was well.

Discussion

Liver disease in pregnancy can be classified as preexisting, coincidental, or unique to pregnancy.¹ As signs and symptoms can be nonspecific, the timing of hepatic dysfunction is key to forming a differential diagnosis. Coincidental entities, such as pancreatitis, cholelithiasis, or cholangitis, can occur in any trimester. Hyperemesis gravidarum occurs mostly in the first trimester. Pre-eclampsia, eclampsia, and HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome can occur in the second and third trimesters, while acute fatty liver of pregnancy (AFLP) and intrahepatic cholestasis of pregnancy are typically third trimester concerns.¹ Given our patient's elevated AST (>ALT) and proteinuria, several potential diagnoses were initially considered: pregnancy-induced hypertension/pre-eclampsia, partial HELLP syndrome, AFLP, toxin-mediated hepatitis from the unknown herbs she had recently ingested, decompensation of chronic liver disease, HBV flare, and HCC.

Our patient likely acquired HBV vertically. Regions of high endemicity include Southeast Asia and Africa. Universal HBsAg screening of pregnant women is recommended to identify infants requiring prophylaxis. Immunoprophylaxis with HBV vaccination plus HBIG significantly reduces perinatal transmission, without which 90% of exposed infants with HBsAg- and HBeAg-positive mothers develop chronic infection at the age of 6 years.² Pregnancy category B antivirals telbivudine and especially tenofovir are used in late second or third trimester to lower maternal viral load and further reduce vertical transmission risk, particularly among highly viremic, HBeAg-positive mothers.³ Breastfeeding (in the absence of cracked or bleeding nipples) has not been found to increase the risk of HBV maternal to child

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Figure 1. Magnetic resonance imaging (MRI) findings. Multiplanar multisequence MRI taken with and without contrast demonstrates a diffuse infiltrative process predominantly involving, and almost completely replacing, the left lobe of the liver with extension into the right lobe. Internal hypovascular areas within the infiltrative process are suggestive of necrosis. Marked heterogeneity and nodularity of the liver are noted. The left portal and hepatic veins are thrombosed.

transmission, although transmission and medication safety-related concerns persist.⁴

The evidence on the management of HBV infection for maternal indications is less established. Acute HBV infection in pregnancy has been associated with low birth weight and prematurity but not teratogenicity or increased maternal mortality. Chronic HBV is usually mild in pregnancy but can flare postpartum due to a decrease in immune tolerance. Acute flares of chronic active HBV in pregnancy can be treated with lamivudine, though tenofovir is preferred for its superior resistance profile.⁵

HCC in pregnancy is rare. Most cases are associated with good fetal outcomes but high maternal mortality. Tumor growth may be accelerated by estrogen and immunosuppression.⁶ HCC has been associated with paraneoplastic phenomena, including hypoglycemia secondary to insulin-like growth factor-1 production. Our patient's early hypoglycemia in the absence of other synthetic dysfunction is suggestive of paraneoplastic phenomenon, which is more likely in patients with HBV-associated HCC and large tumor burden.⁶

Curative options for HCC depend on early detection, though evidence is lacking as to whether screening measures confer a survival benefit.⁷ Surveillance ultrasonography for every six months is recommended for certain HBV-positive populations, including Asian men over age 40, Asian women over age 50, African or North American black individuals over age 25, those with a family history of HCC, those with cirrhosis, or those without cirrhosis but evidence of active hepatitis.^{7,8} AFP should not be used for surveillance unless ultrasonography is unavailable.⁷

All pregnant women found to be HBsAg-positive should undergo a thorough history of the duration and previous treatment of HBV infection, an evaluation of viral replication (through measurement of HBeAg and HBV DNA), liver enzymes, and an ultrasound looking for evidence of cirrhosis and HCC, if viral replication is high.

HBsAg-positive pregnant women should be referred to gastroenterology in first trimester to discuss antiviral therapy in pregnancy to reduce immunoprophylaxis failure, particularly if viral replication remains high ($>6-7 \log 10$ copies/mL) at 28 weeks gestation or if there is a history of vertical transmission to a child. Postpartum, they can manage potential flares and provide long-term follow-up, as some women may be able to stop antiviral therapy post-partum if they do not require therapy based on their degree of liver disease. In addition, although an elevated AFP in pregnancy is usually interpreted as fetal in origin, hepatocellular origin should be entertained in patients with risk factors for HCC. Efforts should be made to address broader systemic issues that contribute to the fragmentation of care and delays in diagnosis and treatment, such as our patient's limited access to primary care and translation services.

Conclusion

This case demonstrates the importance of a broad, systematic approach to the pregnant patient with liver failure, particularly in the context of pre-existing liver disease. Pregnancy presents a unique opportunity to care for patients who may otherwise not come to medical attention, stressing the importance of early and appropriate referral and highlighting the importance of thorough evaluation of HBsAg-positive pregnant patients, for better outcomes of both mother and the fetus.

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Declaration of conflicting interests

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Ethical approval

Written consent was obtained from the patient's family for publication.

Guarantor

SG guarantees the authenticity of this clinical case and original report.

Contributorship

MS wrote the first draft of this manuscript. MS and SG contributed to content and reviewed the final draft.

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