A case of chronic hepatitis B merged with acute fatty liver of pregnancy with severe coagulopathy

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Abstract

Background: Acute fatty liver of pregnancy (AFLP) is a life-threatening disorder, and its relevance to viral hepatitis B (HB) remains unknown. This case presents an initial experience of treating a patient with HB progressing to AFLP throughout pregnancy; anesthesiologists should also recognize its clinical feature for perioperative management.

Case presentation: A 28-year-old parturient was diagnosed as chronic HB (CHB) at 21 weeks gestation. Liver and kidney dysfunction appeared rapidly at 34 weeks gestation, suspected as acute exacerbation of either CHB or AFLP. Emergency cesarean section was carried out, after which maternal disseminated intravascular coagulation and hypothermia persisted. With multidisciplinary management, the patient and infant were discharged on postpartum days 64 and 12, respectively.

Conclusions: Active CHB develops into AFLP. Antiviral therapy should be considered for parturient patients with CHB, particularly for those with high viral load. The most favorable outcome is prompt and accurate diagnosis to establish suitable termination method.

Keywords: Acute fatty liver of pregnancy, Hepatitis B, Parturient, Hypothermia
(Table 1). She was diagnosed with acute exacerbation of CHB and was started on 300 mg of oral tenofovir (300 mg, daily) and intravenous vitamin K (20 mg, daily). The next morning, she presented systemic edema. The Swansea Criteria, which defines AFLP at 6 points or more [1, 4, 7], scored at least 7 points at this time (abdominal pain, elevated bilirubin, ascites or bright liver on ultrasound scan, elevated transaminase, elevated ammonia, coagulopathy, and vomiting were positive; hypoglycemia, elevated uric acid, and liver biopsy were not examined; polydipsia or polyuria, encephalopathy, leukocytosis, and renal impairment were negative). To control coagulopathy, 24 units of fresh frozen plasma (FFP) and 3000 units of antithrombin were administered according to the obstetricians' estimations. Additionally, 20 units of platelet concentrate (PC) were given due to severe thrombocytopenia (Table 1; 35 5/7 weeks, 5 p.m.). The patient's vital signs following preoperative blood transfusions were blood pressure of 97/46 mmHg, pulse rate of 86 beats/min, body temperature of 36.0 °C, and peripheral oxygen saturation (SpO₂) of 97% in room air. The patient was classified as American Society of Anesthesiologists Physical Status Class 3E. The fetus showed reassuring status.

Table 1 Blood sampling data

|                  | Reference range | 21 weeks | 28 weeks | 35-4/7 weeks | 35-5/7/8 weeks | Pre-operative (35-6/7) | Post-operative | POD 4 | POD 7 | POD 62 | Post-operative 1 year |
|------------------|-----------------|----------|----------|--------------|----------------|------------------------|----------------|-------|-------|--------|----------------------|
| T-Bil (mg/dL)    | 0.2–1.2         | 1.2      | 1.3      | 4.6          | 5.7/NE         | NE                     | 3.6            | 13.5  | 19.0  | 4.6    | 0.9                  |
| ALT (U/L)        | 6–30            | 214      | 29       | 41           | 44/NE          | NE                     | 23             | 28    | 28    | 16     | 20                   |
| ALB (g/dL)       | 3.8–5.1         | 3.5      | NE       | NE           | 2.2/NE         | NE                     | 2.2            | 3.2   | 3.5   | 3.5    | 4.1                  |
| NH₃ (μg/dL)      | 12–66           | NE       | NE       | NE           | 132/NE         | NE                     | NE             | 70    | 65    | 56     | NE                   |
| Cre (mg/dL)      | 0.48–0.79       | 0.38     | 0.44     | 0.63         | 0.68/NE        | NE                     | 0.62           | 0.60  | 2.29  | 0.51   | 0.53                 |
| UA (mg/dL)       | 2.4–5.9         | 2.6      | NE       | NE           | NE/NE          | NE                     | 3.8            | 1.8   | NE    | 3.6    | NE                   |
| PT (%)           | 70–130          | 90.9     | NE       | 31.6         | 29.1/27.0      | 56.7                   | 47.3           | 29.3  | 37.0  | 56.0   | NE                   |
| APTT (sec)       | 25.5–39.5       | 34.6     | NE       | NE           | NE/64.2        | 42.0                   | 61.2           | >150  | 42.9  | NE     | NE                   |
| AT-III (%)       | 80–130          | NE       | NE       | NE           | NE/10          | 99                     | 60             | 52    | 88    | NE     | NE                   |
| Fib (mg/dL)      | 150–350         | NE       | NE       | NE           | NE/100         | 142                    | 146            | 199   | 185   | NE     | NE                   |
| WBC (μL)         | 4000–6000       | 8050     | 7950     | 9330         | 10,180/7310    | 6000                   | 5950           | 11,290| 18,480| 1880   | 2320                 |
| Hb (g/dL)        | 12.0–16.0       | 11.7     | 10.1     | 11.1         | 11.7/9.4       | 8.8                    | 7.4            | 9.1   | 9.3   | 10.5   | 8.4                  |
| PLT (K/μL)       | 150–350         | 167      | 165      | 62           | 59/50          | 37                     | 52             | 75    | 35    | 41     | 66                   |

NE: not examined; T-Bil: total bilirubin; ALB: albumin; NH₃: ammonia; Cre: creatinine; UA: uric acid; PT: prothrombin time; APTT: activated partial thromboplastin time; AT-III: antithrombin; Fib: fibrinogen; WBC: white blood cell; Hb: hemoglobin; PLT: platelet count.
with stable vital status. At one point, liver transplantation was planned, due to that the Model for End-stage Liver Damage score for acute disseminated intravascular coagulation (DIC) and liver dysfunction [8] on POD 4 was 24 points; however, 4 days of therapeutic plasma exchange (POD 3–6) and 6 days of hemodiafiltration (POD 3–8) were highly effective. Glycerin fructose was used for 9 days (on POD 2–10) because of cerebral edema, but she showed no neurological sequelae. Neither infection, sepsis, major respiratory complications, nor pancreatitis was remarked. Liver biopsy was not performed in consideration of coagulopathy. The patient was discharged from ICU and hospital on POD 13 and 64, respectively. HB virus vaccination and HB immunoglobulin given at birth prevented vertical transmission of HB, and the infant did not show any developmental delay. The infant was discharged from the hospital on postpartum day 12. For 1-year follow-up after discharge, ALT level of the patient has been kept in normal range and her HBV-DNA level as less than 3.0 Logcopies/mL (Table 1).

Discussion
Viral hepatitis patients generally have higher levels of serum transaminases, with values exceeding 1000 U/L. The level of uric acid is rarely elevated in FH patients, and signs of preeclampsia are absent in viral hepatitis [3]. Compared to AFLP, multiorgan failure is more likely to coexist with viral hepatitis. On the other hand, incidences of hypercreatinemia, DIC, and digestive tract hemorrhage are less common in patients with viral hepatitis than in those with AFLP [9]. It is also suggested that AFLP patients tend to show hypoglycemia [4]. These clinical features may be supportive in distinguishing between viral hepatitis, FH and AFLP. Termination is selected as a basic treatment for both AFLP and FH; however, especially in early preterm FH cases, careful observation with antiviral drug therapy may be an alternative in consideration of neonatal outcomes. In fact, as both AFLP and FH commonly reveal in the late pregnancy [1, 3, 6], accurate differential diagnosis is not always as important as it was for this case. Our judgment to carry out an urgent cesarean section, without accurate diagnosis, can be considered reasonable and necessary, given the sufficient gestational age, severity of liver dysfunction and reassuring fetal status. Moreover, antiviral agent therapy has been commonly utilized in pregnant cases. Tenofovir, a kind of nucleoside reverse transcriptase inhibitor that works by decreasing the amount of HB virus in the blood, has been confirmed as safe for use with fetuses, as evidenced by its level B status given by the Food and Drug Administration [10]. The latest report recommended the use of antiviral drugs to a pregnant patient with a high viral load (100,000–200,000 IU/mL) during their third trimester [10]. This treatment not only benefits the mother, but also the fetus by preventing mother-to-child transmission. In addition, HB virus vaccination and HB immunoglobulin are recommended for neonates as in this case [10]. More in-depth research is expected to determine if the levels of transaminase and HBV-DNA and virus genotype are related to AFLP and if antiviral agents are able to prevent AFLP onset.

Regarding anesthesia, some reports have shown the key to perioperative management of AFLP to be as follows: early diagnosis, prompt termination, strict fluid management, correct coagulopathy, and care for hypoglycemia [1, 3]. These warnings were of course applied for the current case, but body temperature proved difficult to control. There are few reports concerning perioperative body temperature in AFLP patients. Although mild hypothermia control of 32 to 35 °C is sometimes carried out in hepatic encephalopathy patients, hypothermia may cause coagulopathy [11, 12]. As the relationship between infection or hemorrhage and body temperature are still under investigation, we concluded normothermia to be acceptable, providing hepatic encephalopathy was not present. During surgery, we aimed to keep the patient’s body temperature over 36 °C; however, we failed to achieve this, despite using fluid-warming devices and a forced-air warmer. Preoperative temperature control would have been better as the massive transfusion prior to operation could be the cause of hypothermia. Close-knit integration and sufficient communication with obstetric and clinical staff on the ward are also required. It is sometimes difficult to keep core temperature in severe liver dysfunction status patients stable due to dilution of peripheral blood vessels.

Conclusions
Active CHB develops into AFLP. Antiviral therapy should be considered for pregnant patients with CHB, especially in the cases with high viral load. Prompt and accurate diagnosis is favorable in order to evaluate how urgent termination should be carried out. However, in cases of late preterm period without cervical dilatation, elected urgent cesarean section should be selected. If normothermia is to be maintained during surgery, perioperative management on the ward before admission to the operating room is necessary.

Abbreviations
AFLP: Acute fatty liver of pregnancy; ALT: Alanine aminotransferase; CHB: Chronic hepatitis B; DIC: Disseminated intravascular coagulation; FFP: Fresh frozen plasma; FH: Fulminant hepatitis; HB: Hepatitis B; ICU: Intensive care unit; PC: Platelet concentrate; POD: Postoperative day; RBC: Red blood cell; SpO2: Pulse oximetry

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Authors’ contributions
RF prepared the manuscript and obtained the written consent from the patient. KK managed anesthetic care of the patient and prepared the manuscript. FA and MY managed anesthetic care of the patient and helped to draft the manuscript. MN and MO also helped to draft the manuscript. All authors read and approved the final manuscript.

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Ethics approval and consent to participate
This report was approved by the institutional review board of the corresponding author’s institution.

Consent for publication
Informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

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