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Recurrent spontaneous hepatic rupture in pregnancy
A case report

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Abstract

Rationale: Spontaneous and repeated hepatic ruptures caused by hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome are uncommon but life-threatening conditions that rarely occur early in the second trimester of pregnancy.

Patient concerns: We describe a patient who experienced spontaneous hepatic ruptures in the absence of hypertension during the early second trimesters of both her first and second pregnancies.

Diagnoses: A 34-year-old multiparous woman without hypertension was admitted at 21 weeks' gestation because of a spontaneous hepatic rupture with hemoperitoneum. Four years previously, the patient had undergone an exploratory laparotomy during her first pregnancy that involved the ligation of bleeders, because a hepatic capsule rupture had caused hemoperitoneum development.

Interventions: Unlike the first pregnancy, she was managed nonsurgically and conservatively during the second pregnancy, and she underwent frequent laboratory analyses and magnetic resonance imaging follow-up. On day 11 of the patient's hospital admission, we decided to deliver the baby at 23 weeks' gestation, because her condition had deteriorated.

Outcomes: Non-surgical management improved the patient's outcome, and the baby was born alive, even though the pregnancy was in the early second trimester and the maternal condition was deteriorating rapidly.

Lessons: HELLP syndrome without hypertension and the recurrence of an intrahepatic rupture at an extremely premature gestational age are rare. This patient's findings suggested HELLP syndrome, which was subsequently diagnosed. This patient's clinical course highlights the difficult decisions made by clinicians for mothers and fetuses.

Abbreviations: CRP = C-reactive protein, CT = computed tomography, HELLP = hemolysis, elevated liver enzymes, and low platelets, ICU = intensive care unit, MRI = magnetic resonance imaging.

Keywords: atypical preeclampsia, HELLP syndrome, hepatic rupture

1. Introduction

Spontaneous hepatic rupture during pregnancy is a rare, but life-threatening complication of preeclampsia. It is frequently associated with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.[1] HELLP syndrome develops in approximately 1% of all pregnancies, and hepatic hematomas occur in approximately 0.39% to 1.6% of patients who develop HELLP syndrome.[2] Spontaneous hepatic ruptures occur during 1 in 45,000 pregnancies and 1 in 225,000 deliveries overall, and they are associated with increases in maternal and perinatal morbidity and mortality.[3]

Here, we describe a woman who during the early second trimesters of her first and second pregnancies, experienced hypovolemic shock followed by hepatic hematomas and capsular ruptures without any of the significant signs and symptoms associated with preeclampsia.

2. Case presentation

This study was approved by Gangnam Severance Hospital's Ethics Committee, and written informed consent was obtained from the patient. A 30-year-old nulliparous woman presented with pain in her right upper quadrant and nausea at 18 2/7 weeks' gestation in September 2013. She looked acutely ill, and the fetal heart rate was appropriate for the gestational age. Her medical and family histories were unremarkable. She had no complications during the antenatal visits. On presentation, her blood pressure was 72/47 mm Hg with a sinus tachycardia rate of 111 beats/min. The major laboratory findings showed that the patient's serum hemoglobin level was 9.0 g/dL, hematocrit level was 26.0%, platelet count was 98,000/µL, serum aspartate aminotransferase level was 529 IU/L, and her serum alanine aminotransferase level was 709 IU/L. Other laboratory tests showed that her proteinuria level was 3+. Since the abdominal ultrasonography findings had confirmed a moderate hemoperitoneum, an abdominal computed tomography (CT) scan was

Figure 1. Initial noncontrast abdominal computed tomography images of the first pregnancy showing an inhomogeneous parenchymal hemorrhagic necrosis that was about 16-cm wide (arrowheads), which replaced the medial segment, and the right hemiliver with internally preserved lobal and segmental portal tracts. (A) Sagittal view, (B) Coronal view.

performed (Fig. 1A and B), and it showed the hemoperitoneum and a perihepatic hematoma from a hepatic rupture that was associated with extensive hemorrhagic necrosis of the liver parenchyma. The patient was admitted to the intensive care unit (ICU). After admission, her clinical condition deteriorated rapidly, her vital signs were unstable, and her hemoglobin level declined abruptly, even though packed red blood cells and fresh frozen plasma were transfused continuously. After an interdisciplinary consultation, we determined that the patient should undergo an emergency laparotomy. During the exploratory laparotomy, an extensive capsular rupture and a hematoma near

the right lower segment of the liver were identified. The bleeding emanated from a ragged laceration of the right lower segment that had been caused by the capsule rupture. After ligating the bleeders, packing with gauze, and performing a cholecystectomy, the operation was completed, and the patient's estimated blood loss was 3500 mL. She returned to the ICU, and remained intubated and mechanically ventilated. She required ongoing vasopressor support, continuous transfusions with blood products to maintain hemodynamic stability, and the administration of broad-spectrum antibiotics. The pathologic findings from the liver biopsy performed during the laparotomy showed recent hemorrhages in the subcapsular spaces, portal tract, and sinusoidal spaces. Three days after admission, ultrasonography showed an intrauterine fetal death. The pregnancy was terminated using a prostaglandin analog, and a 195-g stillborn male infant was delivered. A second-look laparotomy was conducted on postoperative day 3, during which the gauze packing was removed, and there was no evidence of continuous bleeding and the patient's vital signs were stable. After the second-look laparotomy, the intubation was maintained, because pleural effusion was present. On day 18 after admission, the patient was extubated and her laboratory test results showed a gradual recovery. The patient's hemoglobin level remained at 10 g/dL, and her liver function test results declined and reached normal levels without increasing the level of drainage. The abdominal CT scan undertaken before discharge showed that the extensive hepatic parenchymal hemorrhagic necrosis and perihepatic hematoma had mostly resolved. At 2 months after discharge, abdominal ultrasonography showed that the liver parenchyma on the right side was regenerating. The patient underwent counseling for contraception for over 1 year to ensure a complete recovery. Ultrasonography performed 2 years after the patient's hospital admission, showed a distorted liver margin, which was probably caused by previous liver diseases, but the findings were otherwise unremarkable. No significant complications occurred, except an incisional hernia, which was observed.

In October 2017, the patient became pregnant again after careful prepregnancy counseling. Low-dose aspirin (100 mg/tablet) was prescribed from 8 weeks' gestation. The patient's immunoglobulin M and immunoglobulin G cardiolipin antibodies were negative, and no significant abnormalities were evident until 21 weeks' gestation. Her prenatal course had been uneventful, with no evidence of hypertension and proteinuria. However, the patient was admitted at 21 5/7 weeks' gestation, because she was experiencing right upper quadrant and epigastric pain, and sharp pains on inspiration, but no tenderness or rigidity. The fetal movement was reactive. The patient's initial vital signs were a blood pressure of 113/82 mm Hg and a pulse rate of 94 beats/min, and her proteinuria level was 1+. Abdominal magnetic resonance imaging (MRI) without contrast confirmed the presence of an extensive subcapsular hematoma and an intraparenchymal hemorrhage in the right hemiliver with small amount of hemoperitoneum (Fig. 2A and B). Since coagulopathy had not occurred, the patient's vital signs were stable, and there was no severe pain, nonsurgical management of the hepatic rupture was considered. On day 6 post-admission, abdominal MRI was performed, because the patient's hemoglobin level had suddenly declined and she was tachycardic, and an extension of the hemoperitoneum into the right subphrenic area was detected (Fig. 3A and B). The patient's abdomen was also distended, and she had dyspnea, thoracic pain, and a dry cough. Finally, respiratory failure led to endotracheal intubation. After a
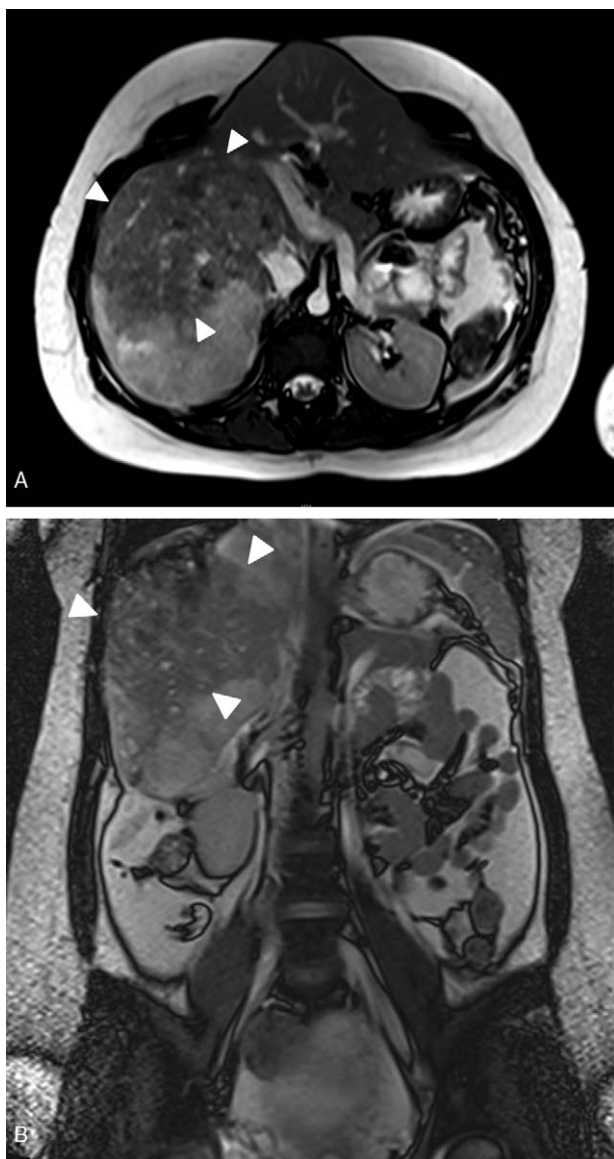
Figure 2. Abdominal magnetic resonance imaging on the day of admission during the second pregnancy. An extensive subcapsular hematoma and intraparenchymal hemorrhage are present (arrowheads) in the right hemiliver with hemoperitoneum. (A) Sagittal view, (B) Coronal view.
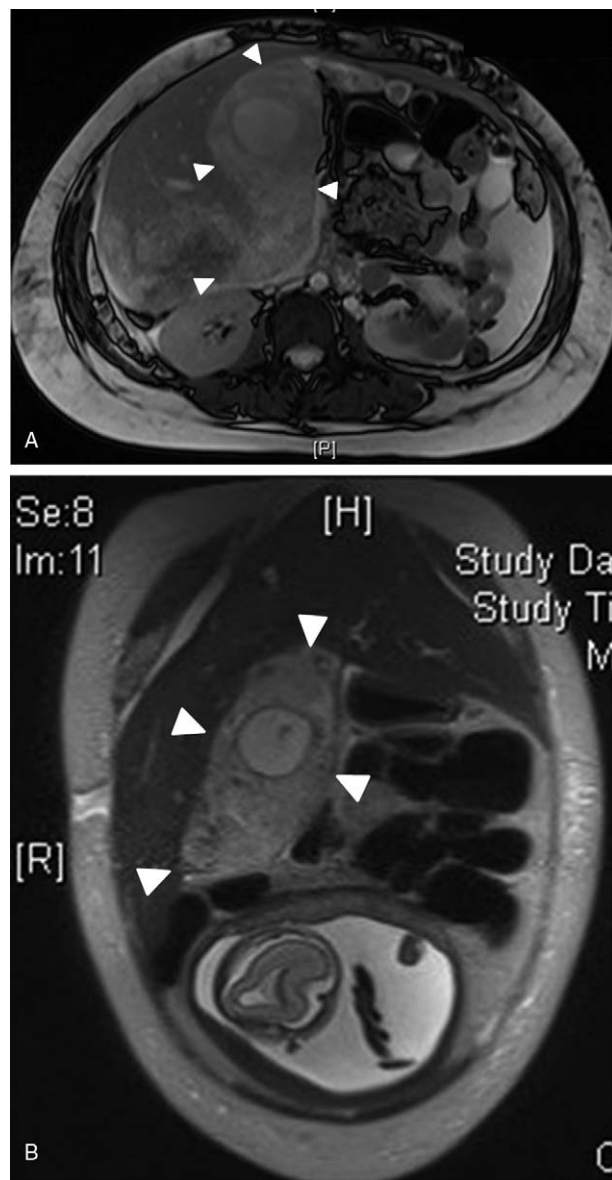

Figure 3. Abdominal magnetic resonance imaging on day 6 post-admission during the second pregnancy. An extension of the subcapsular hematoma and an intraparenchymal hemorrhage are present (arrowheads) in the right hemiliver with hemoperitoneum. (A) Sagittal view, (B) Coronal view.

multidisciplinary consultation, conservative treatment that included a massive transfusion and the administration of broad-spectrum antibiotics, was implemented to preserve the viability of the fetus. Thereafter, the patient's condition remained stable, and conservative treatment continued with regular laboratory tests. However, the delivery was induced on day 11 post-admission, because the patient's urinary output had declined to <40 cc/h, level of pleural effusion had increased, white blood cell count had risen, and her C-reactive protein (CRP) level had increased, all of which indicated the deterioration of the mother's condition. At a gestational age of 23 1/7 weeks, a 620-g male infant with Apgar scores of 3 and 6 at 1 minutes and 5 minutes, respectively, was born via a vaginal delivery and was admitted to the neonatal ICU. The mother was extubated 4 days later, and her vital signs were stable; there were no further complications. Given the patient's high CRP level, pleural effusion, and right

subhepatic, perihepatic, and subphrenic hematomas without active bleeding, empirical antibiotic therapy was administered, and follow-up MRI was performed. The MRI showed that the right subphrenic and perihepatic hematomas had decreased in size. During the postpartum period, the patient's vital signs did not show any changes, her laboratory test results were almost within the normal ranges, and she was discharged at 17 days post-delivery. The male infant is alive and receiving conservative treatment that is appropriate for premature babies, including ventilatory support.

3. Discussion

Spontaneous hepatic rupture in pregnancy is a rare, life-threatening complication, and its etiology is relatively unknown. It occurs mainly in patients with HELLP syndrome and in

association with an underlying pathology, including acute fatty liver, adenomas, malignancies, and hemangiomas.[4] During pregnancy, the incidence of a spontaneous hepatic rupture in patients with preeclampsia and HELLP syndrome is <1% to 2%. The recurrent HELLP syndrome rate ranges from 2% to 19%. The pathogenesis of spontaneous hepatic rupture associated with HELLP syndrome is unclear.[4] In relation to hypertensive disorders, the most likely explanation is that microvascular thrombus formation caused by clotting abnormalities leads to subcapsular hematomas. The pathogenesis of spontaneous hepatic rupture without hypertension is yet to be elucidated. In 1997, Schwartz and Lien described 10 cases of spontaneous liver hematoma or rupture in pregnancy that were not clearly associated with preeclampsia that occurred between 1983 and 1995, and only 10 cases were additionally reported between 1995 and 2008.[4,5]

Hypertension is the main characteristic of women with preeclampsia, but this may be absent in 12% to 18% of cases.[2] HELLP syndrome can manifest without hypertension or proteinuria, and while these symptoms support the diagnosis if they are present, they do not exclude the diagnosis when they are absent. When a hepatic rupture occurs without the classic laboratory findings associated with preeclampsia, but the platelet count is low and the aspartate aminotransferase level is elevated, it is difficult to determine whether the abnormal findings are being caused by atypical preeclampsia, HELLP syndrome, or a massive blood loss caused by a large liver hematoma.[6] Schwartz and Lien reported that 10 of 68 cases (14.7%) of spontaneous hepatic rupture in pregnancy were not clearly associated with preeclampsia.[4]

The common clinical symptoms and signs of a spontaneous hepatic rupture are right upper quadrant pain, epigastric pain, severe right shoulder pain, nausea, vomiting, abdominal distension, and hypovolemic shock, which occur in 30% to 90% of patients; hence, physicians can easily confuse these symptoms with those associated with nonspecific gastrointestinal problems, including acute fatty liver of pregnancy.[5] The

laboratory findings associated with HELLP syndrome with a liver hematoma include elevated aspartate aminotransferase and alanine aminotransferase levels, a reduced hematocrit level, and thrombocytopenia. During its early stages, it is difficult to differentiate between acute fatty liver of pregnancy and HELLP syndrome. The patient in the current case was diagnosed with atypical preeclampsia. Her blood pressure was not elevated, but she had proteinuria and laboratory findings of preeclampsia. Patients with acute fatty liver of pregnancy may display very similar symptoms to those present in patients with preeclampsia, including nausea, vomiting, and abdominal pain accompanied by hypertension and proteinuria. Furthermore, there can be variable degrees of moderate-to-severe liver dysfunction that manifest as moderately elevated aminotransferase levels, which may increasingly mimic preeclampsia and eclampsia.

The recurrent episodes of hepatic hemorrhage were of considerable importance for attaining the current patient's diagnosis, even though they occur infrequently during subsequent pregnancies.[4] During the first and second pregnancies, spontaneous hepatic ruptures were diagnosed at 18 weeks' and 21 weeks' gestation, respectively. At extremely early gestational ages, severe preeclampsia and HELLP syndrome are uncommon, and, when present, delivery is the only choice of treatment, but when the fetus is extremely premature, there are high risks of neonatal mortality and morbidity.[3] While prolonging a pregnancy may improve the fetal outcomes, it may compromise the maternal outcomes. Our patient received 2 different forms of treatment. Table 1 compares the clinical presentations and laboratory findings during the first and second pregnancies to provide a better understanding of the decision-making processes. During the first pregnancy, the patient's initial vital signs were unstable, and continuous hydration for volume expansion was not effective. Her hemoglobin level declined from 9.0 to 5.9 g/dL in 5 hours, which suggested continuous active bleeding. The radiologic findings (Fig. 1) showed that the largest hematoma was 16 cm. During the second pregnancy, the

Table 1

Comparison of the first and second pregnancies in relation to the vital signs, and laboratory and radiographic findings.

Parameters (Normal range)	First pregnancy		Second pregnancy	
	Initial findings	Follow-up 5 h later	Initial findings	Follow-up 24 h later
Vital signs				
SBP/DBP, mm Hg	72/46	97/52	113/82	106/66
Pulse, bpm	111	119	94	97
Laboratory findings				
Hemoglobin level, g/dL (12–16 g/dL)	9.0	5.9	9.9	7.8
White blood cell count, $\times 10^3/\mu L$ (4.0–10.8 $\times 10^3/\mu L$)	12.8	12.86	13.92	11.28
Platelet count, $\times 10^3/\mu L$ (150–400 $\times 10^3/\mu L$)	98	106	166	107
PT, s (10.6–13.1 s)	12.6	–	11.7	12.5
aPTT, INR (0.92–1.13 INR)	28.0	–	25.9	26.8
Creatinine, mg/dL (0.55–1.02 mg/dL)	0.51	–	0.37	0.40
Total bilirubin, mg/dL (0.2–1.2 mg/dL)	1.5	–	0.8	0.9
Aspartate aminotransferase, IU/L (14–30 IU/L)	529	–	304	460
Alanine aminotransferase, IU/L (6–33 IU/L)	709	–	410	585
Radiographic findings at admission				
CT or MRI	Perihepatic hematoma size of 16.3 × 7.8 × 13.2 cm from hepatic rupture related to extensive hemorrhagic necrosis of liver parenchyma with moderate amount of hemoperitoneum		Intraparenchymal hemorrhage and subcapsular hematoma size of 11.3 × 6.8 × 12.4 cm with small amount of hemoperitoneum	

aPTT = activated partial thromboplastin time, bpm = beats per minute, CT = computed tomography, DBP = diastolic blood pressure, INR = international normalized ratio, MRI = magnetic resonance imaging, PT = prothrombin time, SBP = systolic blood pressure.

patient's vital signs remained stable without any medical management, involving, for example, inotropic agents, and her hemoglobin level declined from 9.9 g/dL to 7.8 g/dL in 24 hours, which could be managed with transfusions. The radiologic findings (Figs. 2 and 3) revealed lower hematoma volumes.

During the first pregnancy, the patient was hemodynamically unstable because she had a ruptured subcapsular hematoma, and immediate operative measures, including perihepatic packing, partial liver resection, hepatic artery interruption, and hepatic transplantation, should be considered for these cases. For stable patients, close inpatient observation may be all that is required, and when associated with HELLP syndrome, a regimen of magnesium sulfate and evaluations of fetal wellbeing are necessary.[7] Van Oostwaard et al[8] reported that pregnancies in women with severe early onset preeclampsia were prolonged by a median of 5 days, and they concluded that prolongation should not be considered as routine management. However, we prolonged the current patient's pregnancy by >11 days and the delivery was induced, because the maternal laboratory test results indicated that her condition was deteriorating. During the 11 days of admission, there were no reassuring fetal heart rate patterns. Thus, when considering prolonging a pregnancy, the fetus and the mother must be closely monitored. If the fetus is vulnerable, the mother's condition is the main concern that will guide decision making. Also, when labor is indicated and there are no indications for a cesarean delivery, the first-choice treatments based on the maternal laboratory findings at any gestational age are an oxytocin infusion or the administration of prostaglandin.

In summary, it is important to emphasize that spontaneous hepatic rupture during pregnancy is not always associated with a hypertensive disorder, it can be diagnosed at an extremely premature gestational age, and it is a rare and serious condition that is associated with high rates of maternal and neonatal complications. Although an extremely rare event, hepatic rupture during pregnancy is not exclusively associated with hypertensive disorders; hence, a hepatic rupture during pregnancy should be considered when assessing pregnant women with acute abdominal pain.

4. Conclusion

HELLP syndrome without a hypertensive disorder and the recurrence of an intrahepatic rupture at an extremely premature gestational age is a rare and serious condition that is associated with maternal and neonatal mortality and morbidity. Prolonging the pregnancy may be considered, depending on the conditions of the mother and fetus; however, according to the consensus in the international literature, prolonging the pregnancy should not be offered routinely. Given the high risks of maternal and fetal morbidity, laboratory and imaging examinations should be undertaken serially while considering the limits surrounding neonatal survival, and the fetus' extreme prematurity and its sequelae.

Author contributions

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