Spontaneously Ruptured Subcapsular Liver Hematoma Associated With Hemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) Syndrome

Pei-Yi Chou, Chen-Hsiang Yu*, Chien-Chin Chen[1], Wen-Tsung Chen[1]

Departments of Gynecology and Obstetrics and [1]Pathology, National Cheng Kung University Medical College and Hospital, Tainan, Taiwan.

Spontaneous subcapsular liver hemorrhage with or without rupture is an uncommon but potentially lethal complication of pregnancy [1]. It is often associated with severe preeclampsia or the HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome [1]. The maternal mortality rate is very high when hepatic rupture occurs, varying from 18% to 86% [2]. Early evaluation with imaging, appropriate diagnosis and prompt management are very important. Improved survival can be achieved through prompt recognition and a multidisciplinary approach [1]. To date, most cases have been managed with an aggressive operative approach, but surgery might not always be necessary if the patient is closely monitored [3]. We present a case of spontaneous rupture of subcapsular liver hematoma in association with HELLP syndrome, and the patient was successfully treated after surgical packing at laparotomy.

A 33-year-old pregnant woman, gravida 3, para 2, was transferred to our hospital from a local practitioner for lower abdominal pain, shock and intrauterine fetal demise at 26 weeks of gestation. She had suffered from intermittent lower abdominal pain for 2 days and visited a local clinic for assistance. Acute gastroenteritis was suspected by the local practitioner, and medication was given. However, the lower abdominal pain persisted. She then visited the local clinic again, and fetal demise was detected. Although her past medical history was unremarkable, she had no prenatal care. Her obstetric history included one normal term male and one stillborn fetus at 36 weeks; both were delivered by cesarean section. She denied any previous trauma history.

When she was sent to our emergency service, she was acutely ill with a pale face. Her blood pressure was 85/56 mmHg, with a pulse rate of 127 beats/min, a respiratory rate of 19/min and a body temperature of 36.3°C. Unfortunately, the patient had a rapid course of disease with deterioration and drowsiness emerging within 1 hour. Obstetric ultrasound revealed a dead fetus with a huge echo-free image in the peritoneal cavity. We made the clinical diagnosis of uterine rupture with a circulatory collapse. Therefore, emergency caesarean section was undertaken immediately. However, no uterine rupture was noted during the operation. The color of the amniotic fluid was clear. A dead female fetus was delivered, with a birth weight of 550 g. During laparotomy, massive intraperitoneal hemorrhage from a large ruptured subcapsular hepatic hematoma throughout the whole right lobe of the liver was observed. We used hemostasis with surgical packing around the liver to effectively arrest hemorrhage. Several indurations arising from the lateral side of the liver were prominent.

Liver biopsy was carried out, and pathology revealed portal inflammation by lymphocytes with fibrin deposition and hemorrhage. Prominent fibrin deposition and hemorrhage were observed around the portal area and periportal sinusoids. These findings are associated with toxemia of pregnancy.

Major laboratory findings at admission were a platelet count of 153,000/mL, an aspartate aminotransferase (AST) level of 315 U/L, an alanine aminotransferase (ALT) level of 448 U/L, a lactate dehydrogenase level of 652 U/L, and a hematocrit level of 32.8%. Other laboratory values included a serum urea nitrogen level of 27 mg/dL, serum potassium level of 6.5 mmol/L, creatinine level of 1.7 g/dL, and alkaline phosphatase

Correspondence to: Dr Chen-Hsiang Yu, Departments of Gynecology and Obstetrics, National Cheng Kung University Medical College and Hospital, 138 Victory Road, Tainan, Taiwan.
E-mail: mchydr@mail.ncku.edu.tw
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level of 148 U/L. Prothrombin time was 10.3 seconds (control, 12.4 seconds) and partial thrombin time was 29.0 seconds (control, 30.4 seconds); both were within normal limits. The indexes of urine routine examination were all normal except for proteinuria (3+).

Postsurgical supportive therapy included plasma, platelet and red blood cell transfusions. The patient was transfused with a total of four units of packed red blood cells, two units of fresh frozen plasma, and 12 units of platelets. Postoperatively, the blood pressure rose to 172/120 mmHg. On postoperative day 1, the hematocrit was 35.3%, platelet count was 70,000/mL, serum creatinine level was 1.1 mg/dL, serum AST level was 667 U/L, and serum ALT level was 732 U/L. Vital signs remained normal, and urine output was adequate. By the 11th day after delivery, ALT and AST levels declined to 36 U/L and 41 U/L, respectively. The patient had no complications and no evidence of further intra-abdominal bleeding. She was discharged on postoperative day 11 and was scheduled for outpatient follow-up.

At our outpatient clinic, her general condition, as well as platelet level and liver function tests, returned to normal in 2 weeks. An ultrasound image at 2 weeks post partum showed no residual hepatic hematoma or free peritoneal fluid. From the clinical presentation, abnormal laboratory findings and the pathologic report, HELLP syndrome with spontaneous ruptured subcapsular liver hematoma was confirmed. In the medical literature, the incidence of subcapsular hepatic hematoma formation with capsular rupture in pregnancies is extremely rare, and the incidence is approximately 1 per 45,000 live births [4]. Since this complication is rare, only a few large series analyzing this phenomenon have been reported to date and most of the reports have been case analyses.

The pathophysiology of HELLP syndrome with spontaneous ruptured subcapsular liver hematoma remains unknown. One hypothesis is that as fibrinogen is deposited, the obstruction causes liver distention and ultimately liver rupture, resulting in a massive extravasation of blood between the liver and Glisson capsule [5]. Fibrin deposition may also cause stimulation of platelets, formation of thrombi, and ultimately necrosis of hepatic tissue [5]. As blood accumulates, the capsule itself may rupture, causing hemoperitoneum.

Some reports have indicated that multiparous older women are at a higher risk of development of intrahepatic hemorrhage than younger or primiparous women [6]. In contrast, other studies have not indicated age as a risk factor [7]. A previous study reported that hepatic rupture occurred more often in multiparous women who were older than 40 years [2]. In addition, hepatic rupture and infarction often occur in the third trimester of pregnancy [8]. However, in our case, the patient was a multiparous young woman (33 years old), and the spontaneous hepatic rupture happened in the second trimester of pregnancy (26 weeks), which are different findings from the previous studies. We speculate that this difference between studies might be because the patient had hepatic lesions, such as adenoma, aneurysms, infection or chronic hypertension, before pregnancy. Since the patient's past medical history was unremarkable and the pathophysiology of this disease is unknown, the underlying etiology of this case remains unclear. Further studies are warranted.

Clinical presentation and laboratory findings of liver hematoma and rupture may be ambiguous [8]. Clinical presentation consists of nonspecific gastrointestinal symptoms, including right upper quadrant or epigastric pain, severe shoulder pain, nausea, vomiting, abdominal distention, and hypovolemic shock. Because of its variable presentation and low incidence, the diagnosis of subcapsular hematoma in HELLP syndrome is often delayed or missed, and medical and surgical treatments may be inappropriate [9]. Clinical presentations must be distinguished from other conditions, such as a ruptured uterus, abdominal pregnancy, fetal movements, rib pain, adnexal torsion, rupture of adnexal cyst, cholelithiasis, hepatitis, liver abscess, pancreatitis, gastritis, peptic ulcer, myocardial infarction, pulmonary embolus, pyelonephritis and nephrolithiasis [10]. In our case, the initial clinical presentations were hypovolemic shock and lower abdominal pain, not right upper quadrant pain. Because she did not receive any prenatal care at our hospital, there was no baseline blood pressure level and we did not know whether she had pregnancy-induced hypertension or severe preeclampsia before admission. Moreover, the patient had undergone two previous cesarean sections, which is a risk factor of uterine rupture. Thus, a clinical diagnosis of uterine rupture with a severe circulatory collapse was initially made and then proven to be false. Therefore, the diagnosis of a ruptured subcapsular liver hematoma should be always be considered.

Laboratory abnormalities of HELLP with liver hematoma include elevated AST and ALT values, a decreased hematocrit, and thrombocytopenia. Various modalities of diagnosis, including ultrasound imaging, computed tomography, peritoneal tab and arteriography, have been used to confirm subcapsular liver hematomas [11]. Rapid and accurate diagnosis, through imaging for example, may lead to appropriate treatment and prompt recovery [12]. However, too many examinations may delay an urgent laparotomy [11]. In our case, immediate emergency laparotomy was necessary and appropriate

because of unstable vital signs of the patient. If we had waited for further laboratory results and performed more imaging tests, our patient might have died from shock.

Notably, despite surgical efforts, approximately one-third of patients with liver rupture still die from hemorrhagic shock [6]. However, these figures should not underscore the fact that surgical control of hemorrhage is the most rapid measure in the treatment of this life-threatening condition. If liver rupture is strongly suspected, laparotomy must be carried out without delay, before secondary shock-related organic complications develop [6]. Our case is another successful example of surgical control of hemorrhage.

If vital signs are stable, blood transfusion under close observation may be undertaken. If vital signs are unstable, laparotomy should be considered. Packing is the first treatment step when laparotomy reveals a hepatic rupture with HELLP. If complete hemostasis has not been achieved, repacking of the liver becomes necessary [6]. Subsequently, portal vein ligation and hepatectomy may be considered and undertaken to control bleeding. If bleeding from a ruptured liver cannot be controlled by these "conventional surgical measures" or if extensive hemorrhagic necroses lead to progressive hepatic failure, a liver transplant (as a last resort measure) must be considered [6]. In our case, we could not use conservative management to control bleeding as a result of the patient's unstable vital signs, and emergency laparotomy was necessary. Fortunately, the patient did not develop disseminated intravascular coagulation and other secondary shock-related organic complications. The liver hematoma stopped bleeding by surgical packing applied around the liver, and portal vein ligation or liver transplantation was not needed in the patient. The findings in our case suggest that early surgical intervention may play a very important role in hepatic rupture with HELLP.

Recent studies have indicated the possible use of recombinant factor VIIa in the treatment of spontaneous subcapsular hematoma. Recombinant factor VIIa is a hemostatic agent approved by the US Food and Drug Administration for use in hemophilia patients with factor inhibitors [5]. Factor VIIa stimulates the formation of hemostatic plugs at points of hemorrhage. Merchant et al [5] used this treatment for three patients who developed hemodynamic instability after the formation of a subcapsular liver hematoma. Two patients responded well to the treatment of recombinant factor VIIa with hemostatic stability. The other patient responded homeostatically to treatment but later died of anoxic brain injury secondary to cardiac arrest, although hemodynamic control of the hematoma was established and documented before her death [5]. However, recombinant factor VIIa has not been used extensively because of the concerns about thrombosis and possible pulmonary embolism [5]. In addition, because many patients with HELLP syndrome develop disseminated intravascular coagulation, the use of factor VIIa can exacerbate this condition [5]. We did not use factor VIIa in our case, because the efficacy and safety of its use in pregnant patients have not been well documented. Its use merits further investigation before it can be safely used in patients [5].

In conclusion, ruptured subcapsular liver hematoma during pregnancy is associated with significant maternal and perinatal mortality and morbidity [1]. Diagnosis of hepatic rupture should be considered when there is a sudden onset of hypotension and acute anemia in patients with pregnancy-induced hypertension or HELLP. Early evaluation, appropriate diagnosis and prompt surgical intervention are crucial to deal with a life-threatening emergency. Management of such a situation requires close interdisciplinary cooperation between obstetricians and surgeons, and aggressive intensive care and surgical treatment [6]. At present, the underlying pathophysiology of hepatic rupture with HELLP is still not fully understood, and more advanced investigations are warranted.

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