Case Report

HELLP Syndrome in Pregnancy as a Cause of Sudden Unexpected Death and Spontaneous Hepatic Rupture: A Medico-Legal Autopsy Case Report

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This is the first reported medico-legal autopsy case in Thailand. It is a case of a 26-year-old Thai female with primigravida and 34 weeks gestational age that had sudden unexpected death. The laboratory investigations before death revealed evidence of hemolysis, which is decreased hematocrit, elevated lactate dehydrogenase (865 U/L), and low platelet count (8.7 x 10^9 cells/L). These findings were compatible with HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) syndrome. The autopsy findings showed two ruptures of the right lobe of the liver, hepatic subcapsular hematoma, rupture of Glisson's capsule, and massive hemoperitoneum with abruptio placentae. Histological features of liver and kidneys revealed specific characteristics that can assist the forensic pathologist to diagnose HELLP syndrome when laboratory examinations are not available.

Keywords: *HELLP syndrome, Spontaneous rupture liver, Sudden and unexpected death, Medico-legal autopsy*

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Spontaneous rupture of liver in pregnancy is a very unusual condition that was first reported in 1844 by Abercrombie[1]. Later, it was found that this condition frequently occurs in pre-eclampsia/eclampsia or HELLP syndrome (Hemolysis, Elevated Liver enzymes and Low Platelets)[2]. In 1982, this syndrome was first reported by Weinstein[3]. The prevalence of HELLP syndrome is 1/40,000 to 1/250,000 deliveries[4] and this syndrome found in 4 to 18.9% of pre-eclampsia or eclampsia cases[5,6]. Hepatic subcapsular hematoma is found in 2 to 3% of this syndrome in pregnancy and is life threatening because it has maternal mortality of 56 to 61% and perinatal mortality of 62 to 77%[6,7]. Sudden unexpected death due to spontaneous hepatic rupture due to HELLP syndrome in pregnancy with medico-legal autopsy is first reported in Thailand in the present study.

Case Report

A 26-year-old female patient with primigravida and 34 weeks gestational age had occasional labor pain for one and a half hours with no fetal movement for one day. She had six times of antenatal care and the laboratory examinations were normal. Abnormality was not detected in both mother and fetus.

Admission physical examinations revealed body temperature 36.5°C, heart rate 104 beats per minute, blood pressure 127/89 mmHg and no physical abnormality except increasing uterine contraction and undetectable fetal heart sound. Pelvic examination revealed 50% cervical effacement and 1-centimeter cervical os. The fetus was cephalic presentation without ruptured amniotic membrane. Dead fetus in utero was diagnosed then the patient was admitted to the hospital. The laboratory examinations showed a hemoglobin level of 9.5 g/dl, a hematocrit of 27%, a white blood cell count of 22.9 x 10^9 cells/L (89% neutrophils and 11% lymphocytes), a platelets count of 8.7 x 10^9 cells/L, and no protein in urine. Liver function tests revealed 865 U/L lactate dehydrogenase, 164 U/L alkaline phosphatase, and normal levels of aspartate aminotransferase, alanine aminotransferase, and bilirubin. Blood urea nitrogen, creatinine, and uric acid were in normal levels. Coagulation blood tests showed prolonged prothrombin time (16.1 seconds) and prolonged partial thromboplastin time (44.8 seconds). Thickening of the placenta by ultrasound indicated that there was abruptio placentae. Approximately

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two hours after admission, the patient developed dyspnea with underwent hypovolemic shock. The patient was treated by symptoms but did not recover. She died approximately four hours after admission and autopsy was performed.

Autopsy findings

The autopsy confirmed a Thai female body that had moderately hypersthenic build, weight of 72 kilograms, and height of 150 centimeters. The uterus was 34 x 24 x 15 centimeters in size. There was abruptio placentae that had approximately 1.6 liters of hematoma between placenta and uterine wall. There was a male fetus with body weight of 2,280 grams and crown-heel length of 47 centimeters in the uterus. External congenital abnormality was not detected. The placenta and umbilical cord also had no gross abnormality.

There were two ruptures of the liver at the right anterior lobe that had 4 x 0.5 cm in size with 1.5 cm in depth and 2.5 x 0.5 cm in size with 1 cm in depth. Hemorrhage spread through the surface of the right anterior lobe of the liver under Glisson's capsule until the capsule was torn at the upper area of the right lobe. In addition, 2.5 liters of hemoperitoneum and 100 ml of pleural effusion in each pleural cavity were observed. Gross abnormality was not found in other internal organs such as brain, heart, lung, spleen, pancreas, kidneys, and adrenal glands.

Histopathological appearances of the liver showed multifocal of periportal coagulation necrosis and hemorrhage, few foci of leukostasis in liver sinusoids, swelling of Kupffer's cells and no inflammatory cell infiltration in liver cell cords. The microscopic examinations of the kidneys revealed bloodless glomeruli, swollen and few vaculated intracapillary cells, cigar-shaped capillary loops, enlarged glomerular tuft with foci of capillary loop herniation into proximal convoluted tubules, and swelling of mesangial cells.

Discussion

HELLP syndrome was first reported by Weinstein in 1982[3]. The modified Tennessee classification system separated HELLP syndrome into full and partial HELLP syndrome. The criteria for full HELLP syndrome diagnosis are lactate dehydrogenase (LDH) > 600 U/L, total bilirubin > 20.5 μmol/L, aspartate aminotransferase > 70 U/L, and platelet count < 10 x 10^9 cells/L. Two of the above criteria are used to diagnose partial HELLP syndrome[5,8,9]. HELLP syndrome may be classified by platelet count into three classes, *i.e.*, Class 1, 2, and 3 by perinatal platelet count of < 5 x 10^9 cells/L, 5-10 x 10^9 cells/L, and 10-15 x 10^9 cells/L, respectively[9,10].

HELLP syndrome is found in 1/40,000 to 1/250,000 of deliveries[4] and 4 to 18.9% of patients with pre-eclampsia or eclampsia[5,6]. The most common cause of maternal death was intracranial hemorrhage or stroke while the less common causes of death were cardiopulmonary arrest, adult respiratory distress syndrome, hepatic hemorrhage, hypoxic ischemic encephalopathy, and disseminated intravascular coagulopathy[10]. Abruptio placentae occurred in 16% of HELLP syndrome cases[5].

Subcapsular liver hemorrhage rarely occurs that has an incidence of approximately 2 to 3% in HELLP syndrome in pregnancy. However, it is a cause of death with 56 to 61% maternal mortality and 62 to 77% perinatal mortality[6,7]. In addition, it frequently occurs in multiparous women with age of more than 30 years especially during third trimester of pregnancy and within the first 24 hours postpartum[11]. Principal clinical manifestations occur such as epigastric pain, hypovolemic shock, nausea, vomiting and shoulder pain[5,10,12]. Liver rupture mostly occurs at right lobe, the frequency was found to be 75%, 11%, and 14% in right, left and both lobes, respectively[6]. Ultrasound scan or computerized tomography is a rapid diagnosis method. Other histopathological features in the liver may be periportal coagulation necrosis and hemorrhage, fibrin network from surrounding unaffected liver parenchyma, focal leukostasis in liver sinusoids, swelling of Kupffer's cells, absence of inflammatory cell infiltration in liver plates and no fatty metamorphosis of liver cells. Histopathological features in the kidneys are bloodless glomeruli with swollen and vacuolated intracapillary cell, cigar-shaped capillary loops, enlarged glomerular tufts with herniation of capillary loops into the proximal convoluted tubules, and swelling of mesangial cells. These histopathological features are the characteristics for HELLP Syndrome that can help forensic pathologists to diagnose the disease from autopsy when laboratory examination is not available[13]. The consequent mechanism of periportal necrosis of liver is parenchymal destruction rendering to subcapsular hemorrhage, rupture of Glisson's capsule with massive intraperitoneal hemorrhage[14].

There are various treatments[15] from simple to complicated that are observation, immediate interruption of pregnancy, hepatic compression, hepatic

artery tying, selective transarterial embolization, argon beam electrocoagulation[16], Factor VIIa administration, liver resection, and emergency liver transplantation.

The present study reported a 26-year-old female with primigravida and 34 weeks gestational age. It was an unusual clinical case of abruptio placentae because there was no tetanic and pain from uterine contraction. The physical examination and ultrasound investigation suggested that abruptio placentae probably occurred already before the patient was admitted to the hospital. This phenomenon will cause death of fetus in utero and abnormal coagulogram. While hypovolemic shock frequently occurs in spontaneous rupture of liver in pregnancy[5,10,12] probably was the cause of death in this patient. The histopathological examination will confirm the progression process of the present case. No inflammatory reaction was detected in ruptured site will interpret that rupture liver had recently occurred. In addition, rupture liver was not caused by external injury because tear of Glisson's capsule was found in a different position as rupture position and necrosis of hepatocytes at ruptured site was found. Furthermore, ruptured position in the present case was in the right lobe area that is commonly found in HELLP syndrome[6].

The result from laboratory examination before death showed evidence of hemolysis that was low hematocrit. In addition, impairment of liver enzymes, *i.e.*, increase serum lactate dehydrogenase (865 U/L) and low platelet count (8.7 x 10^9 cells/L) including histopathological features of liver and kidney, *i.e.*, periportal necrosis with hemorrhage, focal leukostasis in liver sinusoids, swelling of Kupffer's cells, bloodless glomeruli of kidneys with cigar-shaped capillary loops, enlarged glomerular tufts and swelling of mesangial cells. These observations are compatible with the criteria of diagnosis of HELLP syndrome Class 2 that was previously mentioned. The summarized circumstances of HELLP syndrome Class 2 consist of hemolysis, increased lactate dehydrogenase (> 600 U/L), low platelet count (5-10 x 10^9 cells/L), and additional histopathological features.

Conclusion

A medico-legal autopsy of sudden and unexpected death due to spontaneous hepatic rupture due to HELLP syndrome in pregnancy in Thailand is first reported in the present study. The diagnosis was made by using previously described HELLP syndrome criteria that consist of a group of abnormalities as evidence of hemolysis, elevated serum lactate dehydrogenase (> 600 U/L), and low platelet count (< 10 x 10^9 cells/L). The additional histopathological features in the present case and previously reports[13] will assist forensic pathologists to diagnose HELLP syndrome in pregnancy easier.

Potential conflicts of interest

None.

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กลุ่มอาการ HELLP ในภาวะตั้งครรภ์กับการเสียชีวิตแบบกะทันหันและไม่คาดคิดเนื่องจากภาวะแทรกซ้อนจากตับฉีกขาดเอง: รายงานการตรวจศพทางนิติเวชศาสตร์

กาญจนา สุจิรชาโต, สมิทธิ์ ศรีสนธิ์, วิชาญ เปี้ยวนิ่ม

การศึกษานี้ได้รายงานการตรวจศพทางนิติเวชศาสตร์รายแรกในประเทศไทย ในกรณีที่หญิงไทยอายุ 26 ปี ซึ่งอยู่ระหว่างการตั้งครรภ์ ครรภ์แรกและมีอายุครรภ์ประมาณ 34 สัปดาห์ ได้เสียชีวิตอย่างกะทันหันและไม่คาดคิด ผลการตรวจทางห้องปฏิบัติการก่อนเสียชีวิต พบมีภาวะการแตกของเม็ดเลือดแดง (hemolysis) โดยตรวจพบปริมาณของฮีโมโกลบิน และฮีมาโตคริตต่ำ มีระดับ lactate dehydrogenase สูง (865 ยูนิตต่อลิตร) และจำนวนเกล็ดเลือดต่ำ (8.7×10^9 เซลล์ต่อลิตร) ซึ่งผลดังกล่าวเข้าได้กับกลุ่มอาการ HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) ผลการผ่าตรวจศพ พบตับกลีบขวาฉีกขาดสองแห่ง เลือดออกกระจายใต้เยื่อหุ้มตับ เยื่อหุ้มตับฉีกขาด และเลือดออกจำนวนมากภายในช่องท้อง รวมทั้งพบภาวะรกลอกตัวก่อนกำหนด (abruptio placentae) ด้วย ผลการตรวจทางจุลพยาธิวิทยาของตับและไต พบลักษณะพยาธิสภาพเฉพาะที่ช่วยให้นิติพยาธิแพทย์วินิจฉัยกลุ่มอาการ HELLP กรณีไม่ทราบผลการตรวจทางห้องปฏิบัติการได้