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A rare and catastrophic finding of HELLP syndrome: subcapsular hematoma and/or hepatic rupture

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Abstract

Objective: It was aimed to present cases which developed subcapsular hematoma and/or hepatic rupture associated with hemolysis, increased liver enzymes and thrombocytopenia (HELLP) syndrome in a tertiary center.

Methods: The data of patients who applied to the Department of Obstetrics and Gynecology, Faculty of Medicine, Dicle University between January 1995 and December 2012 and whose laboratory parameters were compatible with the diagnosis criteria of HELLP syndrome (platelet count <100 billion/L, aspartate aminotransferase >70 unit/L, lactate dehydrogenase >600 unit/L) were evaluated retrospectively. Patients whose clinical symptoms and radiological view were in favor of subcapsular hematoma and/or hepatic rupture were included in the study. Demographic data of patients such as age, gravida and parity, weeks of gestation, antenatal care history, laboratory parameters (full blood, biochemistry), gynecologic and obstetric histories, systolic-diastolic blood pressures, delivery types, postoperative complications, diagnostic imaging finding, medical and surgical treatments applied and similar data were provided from archive files and electronic database of the hospital.

Results: It was found out that 53,217 deliveries were carried out at our clinic during the study (1995-2012). It was seen that there were 6637 (12.47%) deliveries due to pregnancy-induced hypertensive diseases, and among them, 5412 (10.17%) deliveries were preeclampsia, 347 (0.65%) deliveries were eclampsia and 878 (1.65%) deliveries were carried out due to the indication of HELLP syndrome. While the incidence of subcapsular hematoma and/or hepatic rupture in all deliveries was 0.015% (8/53.217), this rate was found 0.91% among the pregnants with HELLP syndrome. Four (50%) of the patients included in our series died. Two of them were reported to die due to intraoperative bleeding after hepatic rupture, and other two cases due to disseminated intravascular coagulation.

Conclusion: Subcapsular hematoma and/or hepatic rupture is a life-threatening catastrophic complication. Life-saving surgical and medical treatment support may be provided such patients with an early diagnosis and multidisciplinary approach in the tertiary centers where they are provided healthcare.

Keywords: HELLP syndrome, subcapsular hematoma, hepatic rupture, pregnancy.

Özet: HELLP sendromunun nadir görülen katastrofik bir bulgusu: Subkapsüler hematom ve/veya hepatik rüptür

Amaç: Tersiyer bir merkezde hemoliz, artmış karaciğer enzimleri, trombositopeni (HELLP) sendromuna bağlı subkapsüler hematom ve/veya hepatik rüptür gelişen hastaların sunumu amaçlanmıştır.

Yöntem: Çalışmamızda Dicle Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Servisine Ocak 1995-Aralık 2012 tarihleri arasında başvuran ve laboratuvar parametreleri HELLP sendromu tanı kriterlerine (trombosit sayısı <100 milyar/Litre, aspartat aminotransferaz >70 Ünite/Litre, laktat dehidrogenaz >600 Ünite/Litre) uygun hastaların verileri retrospektif olarak incelendi. Çalışmaya klinik semptomları ve radyolojik görüntüleri subkapsüler hematom ve/veya hepatik rüptür lehine olan hastalar dahil edildi. Hastalara ait yaş, gravida, parite gibi demografik veriler, gebelik haftaları, antenatal bakım öyküsü, laboratuvar parametreleri (tam kan, biyokimya), jinekolojik ve obstetrik öyküleri, sistolik-diastolik kan basınçları, doğum şekli, post-operatif gelişen komplikasyonlar, tanısal görüntüleme bulguları ve uygulanan medikal ve cerrahi tedaviler gibi veriler hastane arşiv dosyalarından ve elektronik veri tabanından temin edildi.

Bulgular: Çalışma süresince (1995-2012 yılları) kliniğimizde 53.217 doğum olduğu tespit edildi. Gebeliğe bağlı hipertansif hastalıklar nedeniyle 6.637 (%12.47) doğumun olduğu, bunlardan 5.412 doğumun (%10.17) preeklampsi, 347 doğumun (%0.65) eklampsi, 878 doğumun (%1.65) HELLP sendromu endikasyonuyla gerçekleştiği görüldü. Tüm doğumlara bağlı subkapsüler hematom ve/veya hepatik rüptür insidansı (8/53.217) %0.015 iken HELLP sendromlu gebelerde bu oran %0.91 olarak bulundu. Serimize dahil edilen hastalarımızdan dördü (%50) ex oldu. Hastaların ikisinin intraoperatif, hepatik rüptür sonrası kanamaya, diğer iki hastanın ise dissemine intravasküler koagülasyona bağlı ex olduğu bildirilmiştir.

Sonuç: Subkapsüler hematom ve/veya hepatik rüptür gebeliğin hayatı tehdit edici katastrofik bir komplikasyonudur. Bu hastalara üçüncü basamak sağlık hizmetlerinin sunulduğu merkezlerde erken tanı ve multidisipliner yaklaşımla hayat kurtarıcı cerrahi ve medikal tedavi desteği sağlanabilir.

Anahtar sözcükler: HELLP sendromu, subkapsüler hematom, hepatik rüptür, gebelik.

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Introduction

HELLP syndrome characterized with a catastrophic form of pregnancy-induced hypertension reveals itself together with hemolysis, increased liver enzymes and thrombocytopenia.[1] It is considered that the basic mechanism in the pathophysiology of HELLP syndrome develops depending on the microangiopathy. While HELLP syndrome is seen frequently at the end of second trimester or at the third trimester, and mostly at 32-34 weeks of gestation, it is seen in one third of the patients during postpartum period.[2,3] On referral, serious maternal morbidities such as disseminated intravascular coagulation (DIC), intracranial hemorrhage, ablatio placenta, acute renal failure (ARF), pulmonary edema, retinal detachment, subcapsular hematoma or hepatic rupture may develop.[4,5]

Subcapsular hematoma or hepatic rupture which is a rare but rapidly developing complication progressing with high mortality was first defined by Abercrombie in 1884, and it was Weinstein who described its development associated with HELLP syndrome for the first time in 1982.[6,7] The incidence of subcapsular hematoma or hepatic rupture during pregnancy is 1/45,000-225,000.[8,9] This rate is less than 2% of the patients with HELLP syndrome.[10] While preeclampsia or HELLP syndrome is frequently seen in young primigravida patients, hepatic rupture is observed mostly in multipara patients with advanced ages.[11]

The most common clinical findings observed in the patients are pain in right upper quadrant or epigastric region, severe right upper shoulder pain, nausea-emesis, abdominal distention and hypovolemic shock.[12] Maternal and fetal mortality rates associated with hepatic rupture are reported between 60 and 86% in the literature.[13] In the cases with hepatic rupture, there are two main approaches. These are conservative approach where hepatic artery embolization or medical treatment support is provided, and surgical approach where hepatic packing, hemihepatectomy and/or liver transplantation.[2]

In our study, it was aimed to present patients with HELLP syndrome who developed subcapsular hematoma or hepatic rupture at a tertiary center.

Methods

The data of patients who applied to the Department of Obstetrics and Gynecology, Faculty of Medicine, Dicle University between January 1995 and December 2012 and whose laboratory parameters were compatible with the diagnosis criteria of HELLP syndrome (platelet count < 100 billion/L [$\times 10^9$/L], aspartate aminotransferase [AST] >70 unit/L [U/L], lactate dehydrogenase [LDH] >600 unit/L) were evaluated retrospectively. Patients with HELLP syndrome whose clinical symptoms and radiological view were in favor of subcapsular hematoma and/or hepatic rupture were included in the study. Clinical data of patients such as age, gravida and parity, weeks of gestation, antenatal care history, laboratory parameters (full blood, liver function tests), gynecologic and obstetric histories, systolic-diastolic blood pressures, delivery types, postoperative complications, diagnostic imaging finding, medical and surgical treatments applied and similar data were provided from archive files and electronic database of the hospital. The approval of the Ethics Committee of Dicle University was received before the study.

The statistical analysis of the study was carried out by SPSS 11.0 software (SPSS Inc, Chicago, IL, USA). Percentages and mean values were used.

Results

It was found out that 53,217 deliveries were carried out at our clinic during the study (between January 1995 and December 2012).

It was seen in the patients followed up in the high-risk pregnancy service that there were 6637 (12.47%) deliveries due to pregnancy-induced hypertensive diseases, and among them, 5412 (10.17%) deliveries were preeclampsia, 347 (0.65%) deliveries were eclampsia and 878 (1.65%) deliveries were carried out due to the indication of HELLP syndrome. Eight patients who applied to our clinic and diagnosed as HELLP syndrome which had clinical symptoms and findings and radiological images compatible with subcapsular hematoma and/or hepatic rupture were included in our series. While the incidence of subcapsular hematoma and/or hepatic rupture in all deliveries was 0.015% (8/53.217), this rate was found 0.91% among the pregnants with HELLP syndrome. Clinical characteristics, weeks of gestation during referral, delivery types and diagnosis types of liver pathologies of the patients are given in **Table 1**.

Mean age of our patient was 32.75 and mean parity value was 3.25. While only two of our patients were primigravida, remaining six patients were multipara. When we analyzed their weeks of gestation, we found

Table 1. Characteristics of the patients complicated with subcapsular hematoma and/or hepatic rupture induced by HELLP syndrome.

Case	Age	Gravida	Parity	Week of gestation	Antenatal care	Delivery type	Diagnosis method
1	35	3	1	35	Yes	Cesarean	During cesarean
2	28	3	2	40	No	Cesarean	Abdominal ultrasonography
3	27	3	2	37	No	Cesarean	During cesarean
4	22	1	0	37	No	Cesarean	During cesarean
5	42	12	9	40	No	Cesarean	Abdominal ultrasonography
6	42	9	8	26	No	Cesarean	During cesarean
7	38	5	4	21	No	Cesarean	Abdominal computed tomography
8	28	1	0	30	No	Cesarean	During cesarean

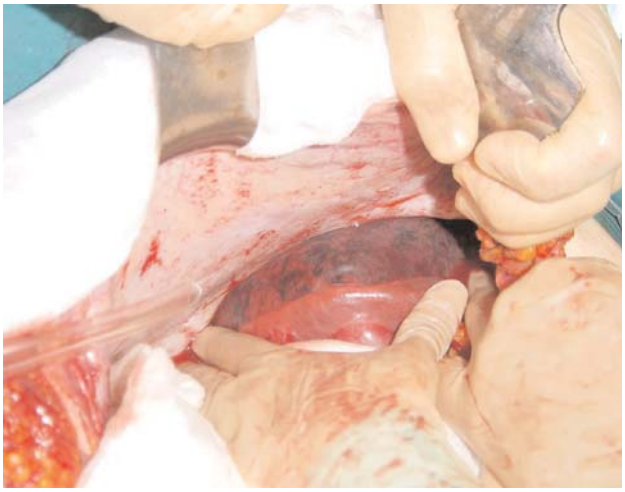

Fig. 1. Hepatic subcapsular hematoma and the rupture during laparotomy.

that two patients were at second trimester (21 and 26 weeks of gestation), and six patients were at third trimester. Subcapsular hematoma or hepatic rupture diagnoses of our patients were established by ultrasonography, during laparotomy and by computed tomography (CT) (**Figs. 1-3**). We found that only one of our patients had hypertension history in her previous pregnancy. Except that patient, none of the patients had hypertension, chronic kidney disease or cardiac disease during or before the pregnancy. Arterial blood pressure and pulse values, and full blood count and liver function parameters of the patients on referral are given in **Table 2**.

All of the patients in our series were compatible with the diagnosis criteria of HELLP syndrome (platelet count <100×10^9/L, AST >70 U/L, LDH >600 U/L). Mean platelet count of our cases was 52.3×10^9/L and it was <100×10^9/L for all the patients. Referral symptoms

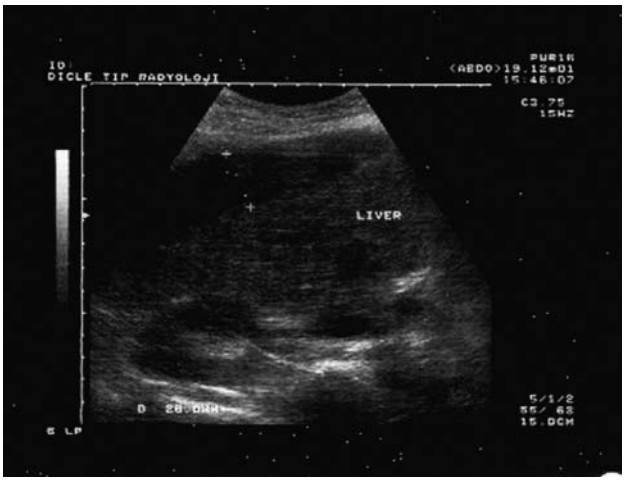

Fig. 2. The view of hepatic subcapsular rupture in abdominal ultrasonography.

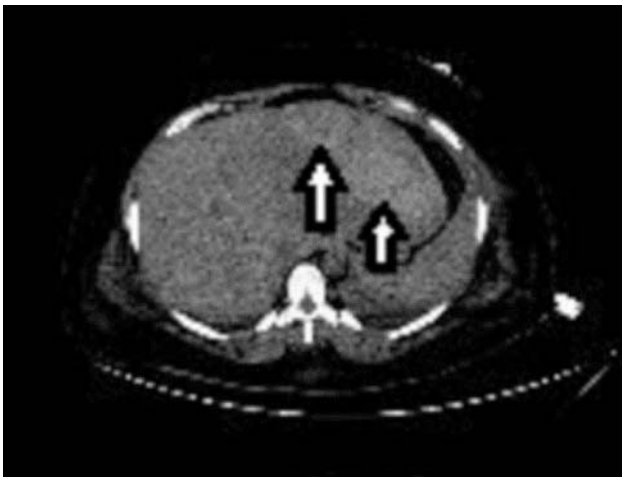

Fig. 3. Subcapsular hematoma and rupture (arrows) in computed tomography.

Table 2. Blood pressure, pulse and laboratory findings on referral.

Case	Blood pressure (mmHg)	Pulse /min	Htc (%)	Hb (g/dl)	Platelet ($\times10^9$/L)	Leucocyte ($\times10^3$/µl)	Albumin (g/dl)	ALT (U/L)	AST (U/L)	T. bil. (mg/dl)	LDH (U/L)
1	140/90	96	25.8	8.6	48	7.8	3.1	486	309	2.1	595
2	150/100	86	39.5	14.6	76.6	9.2	2.7	189	257	3.2	874
3	150/100	110	35.5	12	62	1.96	2.4	470	109	1.6	978
4	70/30	150	12.6	4.3	43	15.3	1.9	1050	870	4.3	2247
5	140/100	120	15.9	5.58	64	14.5	1.73	132	235	4.65	1767
6	170/100	114	24.1	8.45	40.5	17.6	2.02	154	226	2.9	>1995
7	160/100	96	43.8	15.6	36.6	14.1	2.3	419	782	33.7	>1995
8	150/80	92	34.9	11.7	47.7	11.3	2.51	847	914	3.9	>1995

ALT: alanine aminotransferase, **AST:** aspartate aminotransferase, **Hb:** hemoglobin, **Htc:** hematocrit, **LDH:** lactate dehydrogenase, **T. bil.:** total bilirubin.

of the patients, the duration of their hospitalization in the intensive care, maternal mortality, surgical treatments applied and the amount of blood and blood products given are listed in **Table 3**. The most common clinical finding seen in our patients was epigastric and right upper quadrant pain.

Four of the patients included in our series died and our maternal mortality rate was found 50%. Two of them were reported to die due to intraoperative bleeding after hepatic rupture, and other two cases due to disseminated intravascular coagulation. Our fetal mortality rate was found 37.5%.

Discussion

Subcapsular hematoma and/or hepatic rupture is a rare life-threatening catastrophic complication of gestational hypertensive diseases (preeclampsia, eclampsia, HELLP).[1,12] The pathophysiology of this clinical condition progressing with high morbidity and mortality cannot be fully revealed yet. On the other hand, in the histopathological examinations, it is seen that vascular microthrombi and intravascular fibrine deposits cause sinusoidal obstruction and vascular congestion, and it is considered therefore that necrosis in hepatic parenchyma, subcapsular bleeding and in advanced stages, subcapsular rupture and hemoperitoneum occur.[14]

The incidence of hepatic rupture varies between 1/45,000 and 1/225,000.[15] In our study, the incidence of hepatic rupture was found high compared to other studies in the literature. The reason for high rate in our study is considered that our hospital is the biggest tertiary health center in the region, serving 11 cities in east and southeast Turkey and where high-risk pregnant women are directly referred. In the study of Rinehart et al. compiled from various series, it was reported that mean platelet count of the patients was 83×10^9/L and it was $<100\times10^9$/L in 77.5% of the patients.[13] In our study, mean platelet count was found 52.3×10^9/L and it was $<100\times10^9$/L for all patients which was consistent with

Table 3. Referral symptoms of the patients, treatments and complications.

Case	Referral symptom	Intense case (Day)	Treatment duration	Maternal mortality	Blood transfusion (Unit)
1	Mild epigastric pain	8	Primary repair + omental patch	No	8
2	Escalating epigastric pain and distention	12	Primary repair	No	15
3	Acute abdomen	6	Perihepatic packing	Yes	47
4	Shock status	0	Primary repair	Yes (intraoperative)	1
5	Convulsion, escalating epigastric pain and distention	15	Perihepatic packing	No	51
6	Intraoperative cardiac arrest	0	Primary repair	Yes (intraoperative)	13
7	Escalating jaundice, right upper quadrant and epigastric pain	3	Hepatic transplantation	No	18
8	Shock status	52	Conservative treatment	Yes	32

the literature. In a study performed on ten series of patients by Araujo et al., the multiparity (4.5±5.5) and advanced age (42.5±5.9) were reported as the factors increasing hepatic rupture risk in the patients with HELLP.[16] Reck et al. reported that intrahepatic bleeding risk increased in older and multipara patients compared to younger and primipara patients.[17] In the study carried out by Sheikh et al., age was not considered as a risk factor.[18] In a review published by Grand'Maison et al., it was shown that parity and age vary according to regional differences.[2] The ages of the patients in our study varied between 22 and 42. Mean age of our patients was 32.75 and parity value was 3.25, and these rates were including risk factors such as advanced age and increased multiparity given in the literature.[2]

In cases with hepatic rupture, early diagnosis and rapid surgical intervention are very significant to decrease high fetal and maternal mortality rates.[19] The most common clinical findings seen in the patients are right upper quadrant pain, suddenly developing hypotension without any external blood loss, nausea-emesis and epigastric pain. Abdominal pain seen in the patients with severe preeclampsia and HELLP syndrome should make clinician worried, and lead to screening methods (USG, CT, arteriography etc.) in terms of the diagnosis and elimination of hepatic lesion development.[17] On the other hand, in case that aminotransferase levels draw a curve at postpartum period or at its suspected increase, liver lesion should certainly be ruled out. In cases where organ integrity cannot be seen in the liver after radiological examination and in hematoma cases, early surgical intervention is very significant for decreasing mortality. In the patients in our series, the most common clinical finding was epigastric and right upper quadrant pain. In the intraoperative evaluation of our two patients, common hemoperitoneum was observed. Cardiac arrest developed in both cases and they were considered as died when no response to cardiopulmonary resuscitation (CPR) was received. When maternal and fetal mortality rate associated with hepatic rupture was analyzed from past up to now, Bis et al. reported maternal and fetal mortality rates in 1976 as 59 and 62%, respectively; Rinehart et al. reported these rates as 32 and 51%, respectively for the cases between 1960 and 1997; Grand'Maison et al. reported these rates as 17 and 38%, respectively for the cases between 2000 and 2010.[2,13,20] According to the data of Grand'Maison et al., no maternal mortality was observed due to hepatic rupture. If hepatic rupture develops in patients with HELLP syndrome, fetal death risk increases.[4] Four of eight patients in our study died, and maternal mortality rate was found 50% and fetal mortality rate was found 37.5%. While our maternal mortality rate is higher than the studies in the literature, fetal mortality rate seems consistent with the literature. We attribute our high maternal mortality rate to patients being at terminal period on referral and insufficiency of our intense care conditions.

The treatment of cases with subcapsular hematoma or hepatic rupture varies from conservative treatment to various surgical treatments. The first thing to do in the treatment of patients with HELLP syndrome diagnosed as hepatic rupture is to deliver by emergency cesarean and to carry out bleeding control. In the presence of hepatic bleeding, it is preferred to do packing with gauze first, and to do lobectomy after bleeding is brought under control. On the other hand, as alternatives to lobectomy, collagen patches with fibrin adhesives, electrocoagulation, methacrylate use, gel foam use, omental patches and suture may be used on rupture and bleeding areas in liver parenchyma.[4,21] As an alternative to surgical treatment, hepatic artery embolization seems to be a common method recently preferred in the conservative approach.[22] While the success rate of hepatic artery embolization is high in blunt traumas of liver, it is limited with only the case reports in cases with hepatic rupture and bleeding. All of the patients in our series delivered by cesarean section. Nevertheless, when two patients who were evaluated by intraoperative general surgery and died were excluded, primary repair was applied to one patient, primary repair and omental patch were applied to one patient, hepatic packing was applied to three patients by gauzes and conservative treatment was applied to one patient. When liver failure developed in one patient who was applied hepatic packing, the patient was transferred to another center for emergency transplantation. No effective method has been found yet for early diagnosis and prevention of HELLP syndrome.

Conclusion

Subcapsular hematoma or hepatic rupture is a catastrophic finding of pregnancy in patients with HELLP syndrome. It is difficult to diagnosis since findings and symptoms are non-specific. Clinicians should always pay attention to pregnant women referring with the com-

plaints of hypertension or shock findings, epigastrium or shoulder pain, including patients at postpartum early period, in terms of liver rupture which is a rare complication of HELLP syndrome, and they should be capable of rapid intervention for such conditions. By considering the high rate of maternal and fetal mortality, patients are needed to be transported to centers with experience where multidisciplinary approach and advanced surgical interventions can be practiced, and which have good intensive care conditions.

Conflicts of Interest: No conflicts declared.

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