Lethal Pontine Hemorrhage in Postpartum Syndrome of Hemolysis, Elevated Liver Enzyme Levels, and Low Platelet Count

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Background: HELLP syndrome (a combination of hemolysis, elevated liver enzyme levels, and low platelet count) is a severe variant of preeclampsia that generally occurs before delivery but can occur post partum. This syndrome is more common than eclampsia and frequently leads to devastating neurological consequences such as intracerebral hemorrhage.

Objective: Although mentioned in the obstetric literature, there has been sparse reporting in the neurology literature specifically regarding intracerebral hemorrhage in HELLP syndrome. We illustrate such a case and review the existing literature regarding this severe complication.

Setting: Obstetric unit at an academic medical center.

Patient: A 34-year-old primigravida experienced a pontine hemorrhage and subsequent respiratory arrest 22 hours after a normal delivery. This hemorrhage occurred 7 hours after the sudden onset of hypertension, severe headache, and intermittent abdominal pain.

Results: Laboratory and postmortem evidence suggested HELLP syndrome with disseminated intravascular coagulation as the cause of her intracerebral hemorrhage.

Conclusions: Our case suggests the importance of the neurology consultant’s familiarity with HELLP syndrome and the need for thorough laboratory testing and close monitoring in the puerperal patient with headache and hypertension.

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Hypertension in pregnancy consists of a broad spectrum of disorders manifested by mild or severe hypertension, along with various systemic dysfunctions. These include gestational hypertension, chronic hypertension, and preeclampsia. These disorders have an incidence of 5% to 10% in pregnancy, with gestational hypertension being the most frequently encountered. Hypertension is defined in these disorders as systolic blood pressure greater than or equal to 140 mm Hg or diastolic blood pressure greater than or equal to 90 mm Hg. The main differences between gestational hypertension, chronic hypertension, and preeclampsia are outlined in the Table.

Preeclampsia has been classically defined as the triad of hypertension, proteinuria, and edema, but more recently has been defined as gestational hypertension plus proteinuria, with edema being unnecessary for the diagnosis. Eclampsia is the new development of grand mal seizures not attributable to other causes in a patient with preeclampsia. The combination of hemolysis, elevated liver enzymes, and low platelet levels that constitutes HELLP syndrome occurs in 4% to 12% of women with preeclampsia or eclampsia and has been viewed as a variant of these conditions; however, HELLP syndrome can occur as an isolated condition with minimal or no signs of preeclampsia. In addition, severe preeclampsia/eclampsia can exhibit 1 or more laboratory features typical of HELLP syndrome without the full triad of features present. Preeclampsia occurs in 5% to 7% of all pregnancies, eclampsia in 0.1% to 0.2% of all pregnancies, and HELLP syndrome in approximately 0.2% to 0.6% of all pregnancies.

Although the etiology and pathogenesis are unknown in HELLP syndrome, vasoconstriction, coagulopathy, and abnormal vascular tone appear to be involved. Risk factors include prior HELLP syndrome (4%-27% recurrence rate), multiparity, maternal age greater than 25 years, white race, and a history of poor pregnancy outcome. Most HELLP syndrome cases oc-
cur ante partum, but up to 33% may occur post partum.\textsuperscript{2,4} Mortality due to eclampsia ranges from 0% to 14%, but mortality due to HELLP syndrome ranges from 1% to 25%,\textsuperscript{2,3} with complications such as disseminated intravascular coagulation (DIC), cerebral and hepatic hemorrhage, cardiopulmonary arrest, adult respiratory distress syndrome, renal failure, sepsis, and hypoxic-ischemic encephalopathy.\textsuperscript{5} In this report, we discuss a case of lethal pontine hemorrhage in a postpartum patient with HELLP syndrome.

<table>
<thead>
<tr>
<th>Features</th>
<th>Gestational Hypertension</th>
<th>Chronic Hypertension</th>
<th>Preeclampsia</th>
<th>Eclampsia</th>
<th>HELLP Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of disorder</td>
<td>&gt;20-wk gestation</td>
<td>&lt;20-wk gestation</td>
<td>≥20-wk gestation</td>
<td>≥20-wk gestation</td>
<td>≥20-wk gestation</td>
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<tr>
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<td>Mild or severe</td>
<td>Mild or severe</td>
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<tr>
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<td>Present sometimes†</td>
<td>Present sometimes†</td>
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<tr>
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<td>Absent</td>
<td>Present sometimes†</td>
<td>Present sometimes†</td>
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<tr>
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<tr>
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<td>Absent</td>
<td>Present sometimes†</td>
<td>Present, defining</td>
<td>Present sometimes†</td>
</tr>
</tbody>
</table>

Table. Comparison of Features Among Hypertension in Pregnancy Disorders

Abbreviation: HELLP, hemolysis, elevated liver enzyme levels, and low platelet levels.

*Defined as greater than 0.3 g of protein in a 24-hour urine specimen, or greater than 0.1 g/L of protein on 2 separate urine collections 4 hours apart.

†Associated with severe preeclampsia.

REPORT OF A CASE

A 34-year-old previously healthy primigravida was admitted to our hospital at 40 weeks and 5 days’ gestation for induction of labor owing to oligohydramnios. She had a remote history of migraine headaches. The night of her admission, she had a normal vaginal delivery. Fifteen hours after delivery, she complained of a severe headache that began with micturition. The headache was 10/10 in intensity, had a constant throbbing quality, affected her forehead equally on both sides, radiated to her temples, and was aggravated by movement. It was unrelieved by hydromorphone hydrochloride and lying supine. Nausea, emesis, photophobia, and mild diffuse abdominal pain began simultaneously with the headache. The patient denied phonophobia. There were no changes in vision or speech and no focal neurological symptoms. Blood pressure was 155/88 mm Hg. Results of her general and neurological examinations were normal. No meningism was present. Prenatal laboratory studies revealed a hemoglobin level of 12.5 g/dL and a platelet count of 291 10^3/µL.

Emergent non–contrast-enhanced computed tomography of the head showed unremarkable findings. Magnetic resonance (MR) imaging, MR angiography, and MR venography were ordered. Her headache improved slightly with the administration of more intravenous hydromorphone and oral phenobarbital sodium. Her blood pressure was still elevated (systolic, 154-179 mm Hg; diastolic, 82-99 mm Hg), and results of her physical examination now showed diffuse abdominal pain but were otherwise unremarkable. Because of hypertension, abdominal pain, and elevated liver enzyme levels (alanine aminotransferase, 743 U/L; aspartate aminotransferase, 893 U/L), she was presumed to have preeclampsia, and administration of a continuous intravenous magnesium sulfate drip was initiated. Her platelet count had now decreased to 113 10^3/µL, her hemoglobin level was 13.3 g/dL, and her prothrombin time was 9.6 seconds.

In the MR scanner 7 hours after the onset of symptoms, the patient suddenly became agitated and complained of a worsened headache. She became unresponsive and had pinpoint pupils and flaccid paralysis. Respiratory distress developed and she was intubated. Immediate non–contrast-enhanced computed tomography of the head showed a large pontine hemorrhage with intraventricular blood and hydrocephalus (Figure). In the intensive care unit, she was completely unresponsive to command or pain and had fixed and dilated pupils, absent gag or corneal reflex, no muscular tone, and

![Figure](Non-contrast-enhanced computed tomography of the head. A large pontine hemorrhage is seen 8 hours after symptom onset.)
bilateral retinal hemorrhages. The oculocephalic reflex was absent. An extraventricular drain was considered, but was deemed contraindicated by the neurosurgical consultant because of the size of the pontine hemorrhage and the severe neurological abnormalities.

At approximately 8 hours after the onset of symptoms, the platelet count had decreased to $51 \times 10^9/\mu L$, and by 13 hours, the laboratory studies reflected a clear picture of HELLP syndrome with DIC. The hemoglobin level was 5.6 g/dL; platelet count, $35 \times 10^9/\mu L$; indirect bilirubin level, 2.5 mg/dL (42.8 µmol/L); alanine aminotransferase level, 761 U/L; aspartate aminotransferase level, 1359 U/L; D dimer level, 8.0 µg/mL; fibrinogen level, 252 mg/dL (7.4 µmol/L); and prothrombin time, 12.6 seconds. Pressor drips and mechanical ventilation were initiated and continued for 11 hours.

Results of the postmortem examination revealed the origin of the hemorrhage to be 1 cm rostral to the pontomedullary junction. No vascular malformation or other structural lesion was identified on the gross or the microscopic examination. The hemorrhage extended into the midbrain and involved the distal portions of the internal capsule bilaterally and the entire ventricular system. There was diffuse cerebral edema and bilateral uncinal and cerebellar tonsillar herniation, presumably due to acute obstructive hydrocephalus and elevated intracranial pressure. There were multiple hepatic subcapsular and parenchymal hemorrhages that coalesced into a subcapsular hematoma and communicated with a large peritoneal hematoma. Also present were bilateral pulmonary alveolar hemorrhages, moderate pulmonary congestion and edema, and acute renal tubular necrosis.

**COMMENT**

Most of the aspects of this case are consistent with those described in the literature on HELLP syndrome. Symptomatically, 90% of patients with HELLP syndrome have malaise, 71% have epigastric pain or nausea and vomiting, 31% have a headache, and 12% have blurred vision or scotoma.2,4,3 Our patient had a headache with abdominal pain, nausea, and vomiting. On physical examination, hypertension and proteinuria are generally present but may be mild. Hypertension may be absent in 15% of patients. Edema may be present but is not a reliable indicator because it is present in 30% of normal gestations, and as many as 90% of patients will have right upper quadrant tenderness.2,4,3 Our patient had hypertension without proteinuria or edema, and she did not initially have abdominal tenderness but it developed later. Indeed, the absence of preeclampsia often leads to delayed diagnosis and treatment of HELLP syndrome.2 One study demonstrated delayed diagnosis in 51% of patients.

Laboratory diagnosis of HELLP syndrome consists of the following: evidence of hemolysis on peripheral blood smear with associated depression in serum haptoglobin levels, elevations of lactate dehydrogenase and indirect bilirubin levels, elevations of serum aminotransferase levels (>70 U/L, although levels may be as high as 4000 U/L), and a platelet count of less than $100 \times 10^9/\mu L$.3,4 After her cerebral hemorrhage, it was discovered that our patient had developed an indirect hyperbilirubinemia with severe anemia, further elevations in serum aminotransferase levels, and more severe thrombocytopenia. Elevated D dimer and lowered fibrinogen levels are often present in HELLP syndrome. The D dimer level may be elevated before HELLP syndrome develops and can be a predictive indicator, and fibrinogen levels below 300 mg/dL (<8.8 µmol/L) should lead one to suspect DIC.2,4 After our patient’s brain hemorrhage, it was discovered that she had both elevated D dimer and low fibrinogen levels, leading to the diagnosis of DIC in addition to HELLP syndrome. As in our case, the prothrombin time is usually normal until DIC develops.4

There has been an attempt to subclassify HELLP syndrome into partial and complete forms, with the partial form having only 1 or 2 components of the triad.6 Given the elevated serum aminotransferase levels and thrombocytopenia without evidence of hemolysis, along with headache, abdominal pain, and hypertension, our patient may have had a partial HELLP syndrome initially rather than severe preeclampsia. A more accurate term to describe our patient’s condition at the onset and shortly after the development of symptoms may be pre-HELLP syndrome (analogous to preeclampsia and eclampsia).2 Our patient experienced a fulminant course of HELLP syndrome over the course of only hours before a lethal pontine hemorrhage occurred. Postpartum HELLP syndrome typically occurs within hours to days after delivery, and in most cases the onset is within 48 hours of delivery.2 It is unclear whether DIC was present in addition to HELLP syndrome at the time of our patient’s pontine hemorrhage, or whether DIC developed after the hemorrhage and HELLP syndrome alone was responsible. The likely primary cause of death in our patient was compression of the brainstem respiratory center by the large pontine hemorrhage and hydrocephalus-induced herniation. The DIC may have contributed to her cerebral, pulmonary, and hepatic hemorrhages.

The most common primary cause of death (26.4%) and the most common contributing factor to death (45%) in patients with HELLP syndrome is intracranial hemorrhage (ICH) or stroke.5 In a population-based study of stroke in pregnancy and the puerperium by Sharshar et al,8 2 (12.5%) of 16 patients with ICH had HELLP syndrome. Hashiguchi et al9 reported a case of intrapartum HELLP syndrome complicated by frontal and occipital lobe hemorrhages and subsequent vasospasm. Their patient did not have DIC, and her condition progressed to a second cerebral hemorrhage and vasospasm despite frontal lobectomy to evacuate the first hemorrhage, corticosteroid therapy, and hypothermia. Knopp et al10 reported a case of antepartum HELLP syndrome with intrapartum occipital lobe hemorrhage, surgically evacuated with temporary recovery, and subsequent massive cerebral vasospasm and death. In general, ICH appears to occur more frequently in the postpartum period than during gestation. Kittern et al11 found the relative risk of puerperal ICH to be 28.3, compared with 2.5 during gestation. Kittern et al11 found preeclampsia/eclampsia in only 14% of women with ICH, whereas Sharshar et al9 found eclampsia in 44% of these women.
It is difficult to manage and treat HELLP-induced ICH, particularly in the brainstem, as evidenced in our case. Management was made even more difficult in our case because the diagnosis of HELLP syndrome and DIC was not possible until after the pontine hemorrhage had occurred. If the diagnosis of postpartum HELLP syndrome can be made before the ICH, certain therapeutic recommendations may lessen the risk of this devastating complication. As in all patients with preeclampsia, magnesium sulfate therapy should be started for seizure prophylaxis, and antihypertensive therapy and correction of coagulopathy should be initiated.1 In antepartum HELLP syndrome, delivery of the child is the mainstay of treatment, but postpartum HELLP management is challenging and controversial.2,4 Plasma exchange may be of benefit in isolated postpartum HELLP syndrome without multiorgan injury, but high-dose dexamethasone has demonstrated the most promise.12 By an uncertain mechanism, dexamethasone can rapidly normalize platelet counts and lactate dehydrogenase levels and significantly reduce bleeding-related morbidity.13

We have presented a case of HELLP syndrome–induced pontine hemorrhage. HELLP syndrome is rare, but it is more common than eclampsia and has received very little attention in the neurology literature. Because ICH may be one of the most frequent and devastating complications of this rare syndrome, neurologists should be aware of its presentation and management. A postpartum presentation may make the diagnosis challenging, but any puerperal patient with even mild hypertension, headache, and/or compelling abdominal pain should undergo the appropriate laboratory studies. Once the syndrome is suspected, serial measurement of hemolytic markers, liver function, platelet counts, and blood pressure may be helpful. Whether corticosteroid therapy or plasma exchange should be instituted in patients without a definite diagnosis is less clear.

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REFERENCES