

Good Outcome in HELLP Syndrome with Lobar Cerebral Hematomas

Mahmoud Rayes · Arkadiy Konyukhov ·

Victor Fayad · Seemant Chaturvedi ·

Gregory Norris

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Abstract

Background HELLP syndrome is associated with high morbidity and mortality which is attributed most commonly to intracranial hemorrhage (ICH) and/or stroke. The presence of other complications further worsens the prognosis.

Methods We present a rare case of HELLP syndrome which presented with ICH and further complicated by seizures, disseminated intravascular coagulation, and acute renal failure.

Results Aggressive surgical and medical management of her ICH, HELLP syndrome and associated complications resulted in good functional recovery. Hypothermia seems to be a good adjunctive in treatment.

Conclusion ICH associated with HELLP syndrome when managed aggressively can have meaningful neurological recovery.

Keywords HELLP · ICH · Hemorrhage · Craniectomy · Good outcome

Abbreviations

CT	Computed tomography
DIC	Disseminated intravascular coagulation
ICH	Intracranial hemorrhage
EVD	External ventricular drain
HTS	Hypertonic saline
INR	Prothrombin time-international normalized ratio

M. Rayes (✉) · A. Konyukhov · V. Fayad · S. Chaturvedi · G. Norris

Department of Neurology, Wayne State University,
Detroit, MI 48201, USA
e-mail: mrayes@med.wayne.edu

Introduction

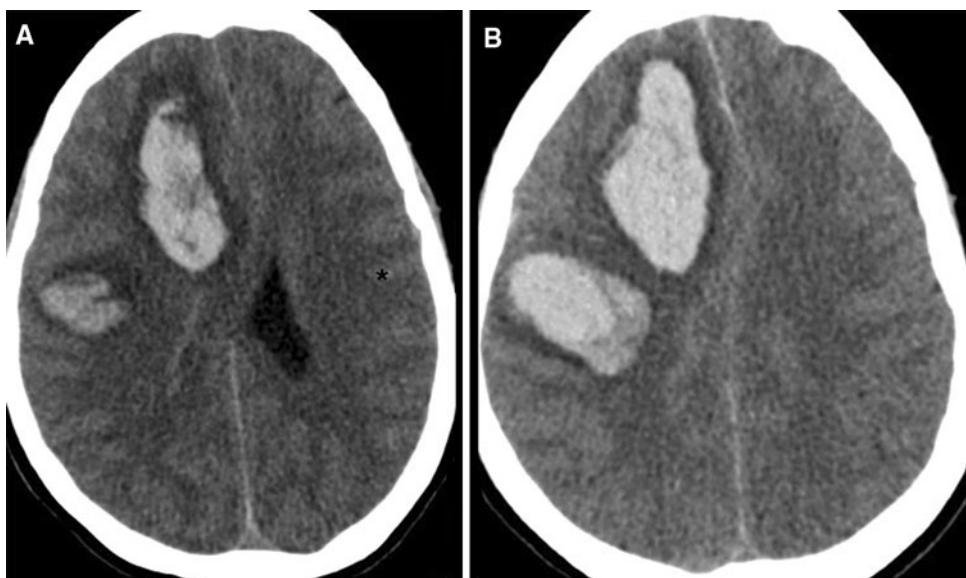
Intracerebral hemorrhage (ICH) is a devastating disease with annual incidence of 15.9 per 100,000 persons worldwide [1]. Common risk factors include: Hypertension, smoking, and diet [2]. Mortality has been reported to be as high as 50% at 30 days [1]. Thus, aggressive medical management is warranted and the underlying etiology should be addressed [3].

Pregnancy is associated with higher risk of spontaneous ICH when compared to non-pregnant females. The presence of HTN and coagulopathy were found to be independent risk factors for pregnancy-related ICH [4]. HELLP syndrome characterized by hemolysis (H), elevated liver enzymes (EL), and a low platelet count (LP) increases such risk dramatically [5]. We report a rare case of spontaneous ICH associated with HELLP syndrome and its complications in which aggressive surgical and medical management resulted in good outcome and provide literature review.

Case Report

A 38 years old Hispanic woman, at 30 weeks gestation (Gravida 6 Para 5) without prior medical history, was found to be difficult to arouse shortly after complaining of sudden onset excruciating generalized headache which was associated with nausea and vomiting. She was also noted to have slurred speech and decreased spontaneous movement of the left side of her body. She had routine prenatal care without any complications. However, her blood pressure was found to be high during the last prenatal visit 2 days ago.

Fig. 1 a, b Axial CT head at presentation showing right frontal hemorrhage measuring $5.2 \times 2.4 \times 3.9$ cm and $3.5 \times 1.9 \times 3.4$ cm with significant associated edema and mass effect causing effacement of the anterior portion of the frontal horn of the right lateral ventricle and 5 mm midline shift. *Subarachnoid hemorrhage



She was brought to the emergency room by ambulance and her blood pressure was elevated at 220/112 mmHg. She was intubated because she was not able to protect her airway and was started on propofol drip. She was obtunded and her Glasgow coma score was 6 (E1M4V₁) off the propofol drip. Neurologically, she had intact brainstem reflexes. However, there was no response to painful stimuli on supraorbital ridge or sternum. She only responded to painful pressure on the right hand nail bed by withdrawing her right upper extremity. ICH score was 2 (1 for GCS 6 and 1 for ICH volume of >30 cm³).

Emergent head CT W/O contrast showed two large foci of acute bleeding within the right frontal lobe ($5.2 \times 2.4 \times 3.9$ cm and $3.5 \times 1.9 \times 3.4$ cm) associated with significant edema, mass effect and 5 mm midline shift. A small amount of subarachnoid hemorrhage was also seen as shown in Fig. 1. Head CT angiogram and venogram (CTA/CTV) did not show any vascular malformation or venous thrombosis.

Abnormal laboratory data included: Platelets, 66,000/ μ l; aspartate aminotransferase (AST), 1210 U/l; alanine aminotransferase (ALT), 633 U/l; total bilirubin, 4.1 mg/dl; lactate dehydrogenase (LDH), 3790 U/l; D-Dimer 16.35 mg/L (normal <0.69); fibrinogen 278 mg/dL (range 158–474), prothrombin time-international normalized ratio (INR); 1.11.

Magnesium drip was started and 30 cc of 23% hypertonic saline (HTS) was bolused followed by 1 cc/kg drip of 3% HTS. Dexamethasone was given for fetal lung maturation. Four units of platelets were given and she was taken emergently to the operating room where an external ventricular drain (EVD) was placed followed by emergent cesarean section and then decompressive craniectomy, Fig. 2. Following surgery, temperature was kept at 35°C by



Fig. 2 Axial CT head (5 h after presentation) showing right frontal hemorrhage with midline shift and with surgical craniectomy changes

use of Arctic Sun (Medivance®) for 3 days and rewarmed over 2 days under sedation with midazolam.

Her hospital course was complicated by disseminated intravascular coagulation (DIC), acute renal failure, urinary tract infection and subsequent septic shock. She was managed aggressively with appropriate medical therapy (platelets, fresh frozen plasma, antibiotics, and hydration) and did recover from the prior mentioned complications. She also developed seizures evident clinically as well as on EEG which were controlled by Keppra. She was extubated successfully after 8 days and started to follow simple commands with her right upper extremity within 11 days. She started to use simple words within 18 days. She was transferred to the rehabilitation center where she stayed for

2 weeks. At discharge, she was functionally independent and required minimal assistance.

Discussion

Complications of pregnancy are diverse and CNS complications may be catastrophic. Some of these include but are not limited to: venous sinus thrombosis, eclamptic convulsions, brain edema, posterior reversible encephalopathy syndrome (PRES), acute cortical blindness, and ICH of which the last carries the worst prognosis [4, 6–9]. In general, ICH appears to be more frequent in the postpartum period than during gestation [4].

The term HELLP syndrome was introduced by *Weinstein* in 1982 to describe a group of pre-eclamptic women who had evidence of hemolysis, elevated liver enzymes and low platelet count [10]. It is a rare complication affecting 0.2–0.85% of all pregnancies and associated with a high perinatal mortality rate of 1–25% [5, 11].

Isler et al. [12], found that the most common primary cause of death as well as the most common contributing factor to death (45%) in patients with HELLP syndrome was intracranial hemorrhage (ICH) and/or stroke in 26.4 and 45% of cases, respectively. Thirty day mortality rate was found to be as high as 50% [1]. Further, the presence of a cerebrovascular malformation was higher in patients with pregnancy-related ICH compared to patients in the general delivering population but was still low [4].

The underlying mechanism of ICH in HELLP syndrome remains poorly understood. It has been postulated that increased cerebral perfusion pressure along with thrombocytopenia plays a major role. The intrapartum platelet count seems to be a good predictive of hemorrhagic complications. Thrombocytopenia in the setting of HELLP syndrome

is due to increased platelet consumption or destruction. In a retrospective study of 292 patients with HELLP syndrome, *Roberts et al.* [13], found a significantly higher incidence of postpartum hemorrhagic complications in patients with platelets count $<40,000/\text{m}^3$. Thus, platelets transfusion is recommended in females with HELLP syndrome in the presence of significant bleeding as well as all cases where platelets are less than $20,000/\text{m}^3$. Further, platelets should be kept $>40,000/\text{m}^3$ when emergent C section is planned [14]. Severe thrombocytopenia is a strong risk factor for ICH [15]. Thus, patient with severe thrombocytopenia resulting in spontaneous ICH should be treated by platelets transfusion [3]. In our case, the patient had ICH and underwent emergent C section so she was given platelets during her stay to keep platelets $>40,000/\text{m}^3$.

Bateman et al. [4], in their review, reported that women with ICH had significantly higher rates of hypertensive disorders, coagulopathy and thrombocytopenia. Further, cerebral blood flow velocity was reported to be significantly higher in pre-eclamptics compared to normotensive women as well as in the postpartum period [16]. This vasoconstrictive phenomenon might be related to increased concentrations of oxyhemoglobin derived from hemolysis [17, 18]. Another important explanation is the damage of blood–brain barrier as well as endothelial dysfunction which are usually associated with break-down of cerebral autoregulation and subsequent hyperperfusion.

In our case, the patient platelets were low at $69,000/\text{m}^3$ and continued to drop during her hospital course. Her neurological exam off sedation remained unchanged during her ICU course until she started to improve gradually. While there was no TCD or CTAs done during her stay to look for vasospasm, the absence of worsening of her neurological exam makes vasospasm unlikely. However, she had high blood pressure of 220/112 on admission. We believe that the

Table 1 Literature review of ICH in the setting of HELLP syndrome

Author	Age	Duration of pregnancy	Timing of ICH	Location/size	Vascular malformation	Intervention	Vasospasm	Outcome
Knopp et al. [21]	36 Y/O	39 W 6 D	Post-partum	IPH + IVH, 1.5 midline shift	–	Craniectomy, ICP monitor	+	Death
Hashigushi et al. [20]	37 Y/O	37 W 5 D	Pre-partum	IPH + IVH	+	Partial lobectomy, hypothermia	Cerebral swelling	Death
Gliemroth et al. [19]	36 Y/O	39 W 6 D	Post-partum	IPH + IVH, 1.5 midline shift	–	Evacuation + ICP monitor	+	Death
Yokota et al. [22]	32 Y/O	41 W	Pre-partum	SDH + IPH, midline shift	–	Craniectomy + hypothermia		Good recovery
Zeidman et al. [23]	34 Y/O	40 W 5 D	Pre-partum	IPH + IVH (pontine)	–	None		Death

Y/O years old, IPH intra-parenchymal hemorrhage, IVH intra-ventricular hemorrhage, SDH subdural hematoma, ICP intra-cranial pressure, W weeks, D days

Table 2 Comparison between our case and Yokota et al. [22]

Author	Age	Duration of pregnancy	Timing of ICH	Location	Size of ICH	Intervention	Hypothermia	Complication	Outcome
Yokota et al. [22]	32 Y/O	41 W	Pre-partum	SDH + L Occ/Par, midline shift	Unknown	Craniectomy	+34°C)	DIC	Good recovery
Rayes et al.	38 Y/O	30 W	Pre-partum	R Fro, SAH, midline shift 5 mm	5.2 × 2.4 × 3.9 cm, 3.5 × 1.9 × 3.4 cm	Craniectomy + EVD	+35°C)	DIC, ARF, seizures, UTI septic shock	Good recovery

Y/O years old, SDH subdural hematoma, ICP intra-cranial pressure, R right, L left, Occ occipital lobe, Fro frontal lobe, EVD ventricular drain, W weeks, D days

high blood pressure augmented by thrombocytopenia were the key contributing factors in our case to ICH.

A thorough review of the English literature was performed. The following search terms were entered into MEDLINE: [intracerebral hemorrhage OR intracerebral hemorrhage OR hemorrhagic stroke OR hemorrhagic stroke] AND [HELLP OR Pre-eclampsia]. Search was limited to English-language human studies. We screened the articles by text, abstract, and then full text. Only cases in which ICH was associated with HELLP were included. Reference lists were hand searched to identify additional relevant case reports. Only five cases were identified [19–23], Table 1. In all five cases ICH presented during the third trimester. Two patients had ICH in the ante-partum period compared to three post-partum. All except one case had intraventricular extension of their ICH. Surgical management including craniectomy (2), hematoma evacuation (2), and drainage of subdural hematoma (1) was utilized in all except in one case where the patient suffered from pontine hemorrhage. Further, hypothermia was used in only two cases. Despite aggressive management, the outcome was bleak. It should be mentioned that the cause of death in two cases was vasospasm which was not addressed aggressively in any of the cases. Only one case had good recovery. The patient had similar ICH score to our case of 2 (GCS 3), Table 2. However, their patient presented with acute subdural hematoma (SDH) along with smaller ICH size. Both cases were managed by emergent C section followed by craniectomy and were put under hypothermia. Both patients received appropriate aggressive medical treatment for DIC. However, in our case there were more complications including: septic shock, seizures, and acute renal failure. However, aggressive medical and surgical management resulted in good clinical outcome.

Conclusion

Despite severe comorbidities, ICH associated with HELLP syndrome when managed aggressively can have meaningful neurological recovery. Patients with ICH coexisting with HELPP should be managed in specialized neuro-critical care units.

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