Case Report

Complete recovery after antepartum massive intracerebral hemorrhage in an atypical case of sudden eclampsia

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Abstract

**Background:** Intracerebral hemorrhage is an infrequent but severe complication in pregnant women with hypertension.

**Case Description:** We describe an atypical case of a patient with no risk factors who developed sudden eclampsia and spontaneous intracerebral hemorrhage during the 34th week of pregnancy. She underwent successful emergent Cesarean section followed by craniotomy. Both intraoperative surveillance and postoperative magnetic resonance angiographic examination of the cerebral vessels failed to identify an aneurysm, arteriovenous malformation, tumor, or leptomeningeal disease.

**Conclusion:** We discuss the management of this case and review the literature regarding the threshold for which initiation of antihypertensive treatment is indicated in pregnant patients.

**Key Words:** Eclampsia, intracerebral hemorrhage, pregnancy

INTRODUCTION

The incidence of preeclampsia–eclampsia in the USA is 7–10%.18 Preeclampsia is defined as the *de novo* appearance of hypertension (systolic BP of ≥140 mmHg or diastolic BP of ≥90 mmHg), accompanied by new-onset proteinuria (defined as ≥300 mg/day) developing after the 20th week of pregnancy.22 The incidence of stroke in women who are younger than 50 years of age is <5%.2 Stroke contributes to 12% of all maternal deaths,16 and in patients with preeclampsia when the stroke is present, it accounts for 50% of all deaths related to cerebral complications in this group.20

We present a unique case of sudden eclampsia and intracerebral hemorrhage (ICH) during an otherwise normal pregnancy.

CASE REPORT

A 32-year-old female, G2P1 at 34 weeks of gestational age, with regular prenatal care, and with no history of headache, proteinuria, or hypertension on previous visits presented to the OB clinic for a routine follow-up visit. On the day of the visit, her BP was 150/90 mmHg, thought to be due to anxiety, and she was admitted to the OB ward for observation. Hypertension was considered borderline and was intermittently treated by IV labetalol, but without resolution. Approximately 10 h after admission, she started to complain of diffuse
headache, nausea, vomiting, and epigastric pain. The work-up was negative for other findings of preeclampsia (liver function test, proteinuria, uric acid). During the course of the admission, the BP ranged between 150/90 and 180/110 mmHg, and her headache symptoms increased. The patient’s condition progressed to a sudden onset of a focal seizure on the left side, which progressed to generalized tonic–clonic seizures, and she suddenly became unresponsive. At that point, magnesium sulfate was administered (4 g loading dose over 20–30 minutes) with a maintenance dose of 1 g/h. One gram of phenytoin was administered to control the seizure. Immediate blood analysis showed the following: a drop in platelets to 116,000/µl; elevated liver function tests alanine transaminase (ALT; 866 units/L) and aspartate transaminase (AST; 971 units/L); uric acid of 6.2 mg/dl; and alkaline phosphatase of 169 mg/dl. Arterial blood gases showed a metabolic acidosis (pH = 7.1, base deficit = -14). The diagnosis of eclampsia was made and the decision to deliver the fetus by an emergency Cesarean section was determined. The airway was secured using a rapid sequence technique, and a healthy infant was delivered under general anesthesia with Apgar scores of 8 and 10 at 1 and 5 minutes, respectively. Postoperatively, the patient remained comatose, and the Glasgow Coma Scale (GCS) revealed a score of 4 (1 + 2 + 1), 1 h after the Cesarean section. Ninety minutes later, she demonstrated a decerebrate posture with non-reactive pupils (3 mm diameter). At this point, the OB team considered it to be a structural brain injury. A non-contrast computed tomography (CT) scan revealed an intracerebral hematoma [Figure 1]. Emergency neurosurgery consultation was ordered. The patient was rushed to the operating room with mannitol 1 g/kg and furosemide 20 mg IV infusion, while maintaining a mean arterial BP of 80 mmHg and a PaCO₂ of 30 mmHg. Disseminated intravascular coagulopathy (DIC) was treated by administering two packed RBC units to elevate the Hg to 10 g/dl. Twenty units of platelets and 4 units of fresh frozen plasma were given to correct the coagulopathy. Right frontotemporal craniotomy was performed, with evacuation of an intracerebral hematoma and insertion of right frontal external ventricular drain. Intraoperatively, there was no evidence of an aneurysm or any tumor-like tissue. A postoperative CT scan confirmed the resolution of the ICH [Figure 2]. Pathology report indicated no malignant cells, atypia, arteriovenous malformation, or leptomeningeal disease. The magnetic resonance imaging (MRI) and MRI-angiography revealed after surgery no gross anomaly other than postoperative changes [Figure 5].

In the ICU, the intracranial pressure (ICP) was normalized to less than 10 mmHg, and supported hemodynamic and ventilatory measures were weaned off over the next couple of days. The patient opened her eyes and started responding to commands by the third postoperative day. Liver function tests and the coagulopathy normalized by postoperative day 5. Postoperatively, the pupils were increasingly reactive over the next 7 days. The GCS was 9 (1 + 3 + 5), and platelet transfusions were required to maintain the platelet count to ≥100,000/µl. The trachea was extubated on postoperative day 7. In less than 3 weeks, the patient was transferred to rehabilitation services where physical, occupational, and speech therapies were conducted for 4 weeks. In the outpatient clinic, all antihypertensive medications (angiotensin-converting-enzyme [ACE] inhibitor, calcium channel blocker, and vasodilator) were weaned off within 2 months. The patient regained all
her intellectual functions, personality, and various social activities within 6 months. She was also weaned off all seizure medication, and 3 years later she was deemed to have regained a full cognitive recovery.

**DISCUSSION**

This case illustrates an atypical presentation of a patient with uneventful prenatal care for the first 34 weeks, who developed a sudden onset of hypertension and rapid progression within hours to seizure and ICH. Ideally, CT scan should have been ordered and concomitant Cesarean section and craniotomy performed. However, the differential diagnosis of ICH was not in the armamentarium of the OB team at that time. The elevation of BP was considered borderline by the OB team and the seizure was underplayed early, until the patient did not awaken from anesthesia and the anesthesia team examined the pupils and decided to get a CT scan. This case is unique because the patient had a complete recovery by employing aggressive medical and surgical intervention for the ICH, despite a poor preoperative neurological status (GCS 4) and a 7-h delay of definitive diagnosis and decompression.

Eclampsia is the most common cause of ICH associated with pregnancy, and it is responsible for 5–12% of maternal deaths during pregnancy. Contrary to what is published, our patient did not have any of the known risk factors for ICH, such as maternal age >35, African American race, tobacco dependence, substance abuse, coagulopathy, or previous preeclampsia/eclampsia. However, our patient was from India, and there are some reports indicating a higher incidence of hemorrhagic stroke in Asian women compared to Caucasian patients, most commonly occurring in the prepartum stage (58%).

Cerebrovascular malformations are evident in 20–67% of patients with pregnancy-related ICH. In our case, no underlying vascular malformation or aneurysm was found by either intraoperative surveillance or postoperative MRI. The vascular tissue structure of the brain, the changing of coagulation status during pregnancy, and the pathological state of preeclampsia-eclampsia, such as endothelial dysfunction, could have contributed in our case to the ICH.

To the best of our knowledge, ICH in this case was due to the escalation in the BP, with no other preeclampsia findings and normal prenatal care. The brief BP rise led the OB team to believe that the rise of BP was related to anxiety. The sequence of events began with hypertension, followed shortly thereafter by development of severe preeclampsia, eclampsia, and ICH. A sudden increase in BP can lead to hypertensive encephalopathy in pregnant women without a history of hypertension, even with a diastolic BP around 100 mmHg. Clinical manifestations of severe headache, visual disturbances, seizure, and coma may rapidly follow. Eclampsia may be seen with BPs below the range that produces encephalopathy, and there is no correlation between BP and electroencephalographic abnormalities in preeclamptic-eclamptic patients. There are no findings that suggest any direct relation between the degree of hypertension and eclamptic convulsions.

Additional studies in patients with preeclampsia/eclampsia found a moderate decrease in cerebrovascular resistance together with increased cerebral blood flow velocities, causing cerebral hyperperfusion, losses of autoregulatory mechanisms, and eclampsia with ICH. Even though there are two reports in the literature, with similar clinical presentations, our case is unique because the patient developed ICH only a couple of hours after the first recordings of elevated BP. In one case, the patient had preeclampsia superimposed on chronic hypertension, where at 34 weeks of pregnancy she presented with a BP of 165/100 mmHg. She received nifedipine and magnesium sulfate to control the event. The second case is a patient at 36 weeks of pregnancy with 10 days of induced hypertension and 3 days of neurological symptoms. In this case, the authors did not use magnesium sulfate, which could have had a favorable effect on hemodynamic stability. Our case is a prime example supporting early initiation of therapy with magnesium sulfate. It has been proposed that magnesium sulfate may prevent vasospasm by acting as a calcium antagonist.

Hypomagnesemia causes increased cerebral vascular resistance and is therefore a competitive antagonist of Ca$^{2+}$, having opposing effects on vascular tone. Increased Ca$^{2+}$ concentration has been shown to induce vasospasm in isolated cerebral arteries. The effect of vasospasm is amplified by lowering the concentration of Mg$^{2+}$ and is alleviated by increasing the concentration of Mg$^{2+}$. Hypomagnesemia causes increased cerebral vascular...
During ischemia, the calcium influx is through ion channels linked to the N-methyl-D-aspartate (NMDA) subtype of glutamate receptor. The increase of Mg$^{2+}$ concentration can block the effects on inward current flow through these channels. It has been suggested that a large part of the magnesium sulfate effect in eclampsia may be exerted by blocking NMDA receptors, especially since their involvement in epileptiform bursting has been demonstrated. In cases like ours, the rapid increase in the BP made it difficult to realize the benefits of initiating magnesium sulfate to prevent the complications of severe preeclampsia and to reduce the rate of eclampsia. Even in cases with mild preeclampsia, due to few studies and the limited enrolment of patients, it is difficult to draw conclusions.

Even though there are reports of simultaneous Cesarean section and craniotomy, there are cases of differed intervention because either the patient needed to be transported to the facility with a neurosurgery team or, in our case, due to delayed diagnosis. However, even with a delay of diagnosis, it is never too late to do neurosurgery and achieve complete brain recovery. Previous reports support our efforts. Wiltin has reported six patients with ICH with delayed diagnosis from 1 to 4 days. The mortality was 66%, but remarkably one patient with ICH in the right caudate nucleus survived. In our case, young age and hormonal changes of pregnancy with increased levels of estrogens may have played a neuroprotective role. Estradiol seems to protect the cerebral tissue, at least through three different mechanisms. The first mechanism is a non-estrogen receptor (ER)-mediated effect, which reduces the level of NMDA currents and the calcium influx that might decrease cell death during ischemia. The second mechanism is through estrogens’ influence on the nitric oxide synthase family to induce vasodilation and improve the blood flow to compromised brain regions. The third mechanism of estrogens is the role as antioxidants inhibiting lipid peroxidation via the C3 hydroxyl group located on the phenolic A-ring of steroids. These findings may be the key to understanding the excellent outcome in our patient.

This case emphasizes that even short time hypertension should be treated aggressively to prevent ICH. Even though eclampsia can cause seizures with no ICH, OB and family practitioners should be suspicious about ICH. The prompt intervention of a multidisciplinary team (obstetric, neurosurgery, and anesthesiology) is required to ameliorate the devastating effects of eclampsia and ICH.

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