Recurrence Seizures in Pregnancy—Epilepsy or Eclampsia: A Diagnostic Dilemma?
A Case Report

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Peripartum seizure is a serious disease with substantial morbidity and mortality for the mother and fetus. Among various causes of such seizures, sometimes 2 causative factors can occur, simultaneously creating a dilemma in pharmacotherapeutic management. We describe a 34-weeks-pregnant woman with a history of epilepsy (receiving antiepileptic drugs) who had eclampsia and recurrent seizures in the peripartum period. Seizure control required multiple medications, including benzodiazepine, valproate, phenytoin, and magnesium sulfate. She underwent emergent cesarean delivery under general anesthesia to rescue the baby. Blood pressure control was achieved using \( \alpha \)-methyldopa, labetalol, nitroglycerine, and amlodipine. Maximum vigilance is required for such patients, and therapy needs to be titrated according to patient’s response, keeping in mind its impact on the fetus.

Keywords: Eclampsia, epilepsy, pharmacotherapy, pregnancy, recurrent seizures.

Peripartum seizure is a serious disease with substantial morbidity and mortality for the mother and her fetus. Apart from idiopathic cause, the various other causes of seizures in pregnancy include antiphospholipid syndrome, eclampsia, cerebral vein thrombosis, thrombotic thrombocytopenic purpura, cerebral infarction, drug and alcohol withdrawal, and hypoglycemia.\(^1\)

Peripartum seizure is a common manifestation of epilepsy and eclampsia. Epilepsy is a chronic neurologic disorder that may complicate pregnancy, affecting about 0.5% of pregnancies.\(^2\) The main concern in pregnancies complicated by epilepsy includes the increased risk of congenital abnormalities associated with antiepileptic drugs. The risk of seizures increases at delivery, with 1% to 2% of women with epilepsy having a seizure during labor or in the first 24 hours postpartum.\(^2\)

On the other hand, eclampsia is a hypertensive disorder of pregnancy associated with edema, proteinuria, and convulsion. Eclampsia has been reported to be associated with various neurologic problems, such as cerebrovascular accidents and blindness.\(^3\) In severe preeclampsia and eclampsia, immediate delivery of a viable baby and maintenance of maternal health are the therapeutic goals.

Uncontrolled seizures during pregnancy are dangerous to both the mother and fetus. Tonic-clonic seizures can cause physical injury and abruptio placentae in the mother and hypoxia, acidosis, intracranial hemorrhage, and death in the fetus.\(^4\) The pregnant patient may aspirate, causing aspiration pneumonitis during seizure episodes. Fetal bradycardias have been reported during and after maternal convulsions.

It should, however, be kept in mind that it is difficult to distinguish eclamptic seizures from an epileptic seizure. Cesarean delivery is required if there are recurrent seizures in labor.\(^2\) We herein report the perianesthetic management of a pregnant woman with eclampsia and epilepsy who underwent emergency cesarean delivery.

Case Summary
A 41-year-old pregnant woman (34 weeks’ gestation), weighing 73 kg, was referred to our tertiary-level hospital from a peripheral primary care hospital, with the chief complaints of recurrent seizures and hypertension. On a review of the medical history, she had known epilepsy for 15 years and was being managed on a regimen of oral phenytoin (200 mg) twice daily and valproate (400 mg) 3 times daily. Results of her laboratory investigation, including hemogram, liver and kidney function tests, and electrocardiogram, were normal. Her blood pressure was maintained at approximately 140/90 mm Hg during follow-up with her obstetrician. At the 34th week of pregnancy, she had an episode of seizures and received intravenous diazepam (10 mg), following which seizures subsided.
After 5 hours, the seizure recurred, and an injection of diazepam (10 mg) and a loading dose of phenytoin were administered intravenously. She was then referred to our institute.

At our institute, she again had an episode of seizures. Midazolam (2 mg) was administered intravenously. Five minutes later, another dose of midazolam (1 mg) was required to control the seizures fully. A loading dose of valproate (1,500 mg) was administered over 30 minutes, followed by 400 mg 3 times daily. On examination, she had pedal edema, a pulse rate of 92/min, and blood pressure of 194/114 mm Hg. Laboratory investigation showed the following values: platelets, 50,000/mm³; aspartate aminotransferase, 190 IU/L; alanine aminotransferase, 98 IU/L; alkaline phosphatase, 332 IU/L; serum bilirubin, 3.7 mg/dL; serum total protein, 5.1 g/dL; serum albumin, 2.2 g/dL; serum globulin, 2.9 g/dL; and urine protein and red blood cells, 2+. Mild epistaxis was present. Fundus examination revealed no papilledema.

A diagnosis of eclampsia with HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) and epilepsy was made. An injection of magnesium sulfate, 10 g, was administered intramuscularly, followed by 5 g every 4 hours. It was determined that the patient required emergency cesarean delivery. Written informed high-risk consent was obtained. In the operating room, routine monitors (electrocardiogram, automated noninvasive blood pressure, and pulse oximeter) were attached. The radial artery cannula and peripherally inserted central venous catheter via the left cubital vein were placed. The blood pressure (198/112 mm Hg) was managed with bolus intravenous administration of labetalol (10, 10, and 5 mg) over 15 minutes, and the blood pressure decreased to 140/88 mm Hg.

After preoxygenation, anesthesia was induced with thiopental sodium (300 mg), succinylcholine (100 mg) along with cricoid pressure, and preservative-free lidocaine (80 mg) intravenously. The trachea was intubated with a cuffed orotracheal tube (7-mm internal diameter). Anesthesia was maintained with 0.5% sevoflurane in oxygen and nitrous oxide (50:50). Neuromuscular blockade was maintained with neuromuscular monitor-guided administration of atracurium, in an initial dose of 30 mg, followed by boluses of 7.5 mg each. Hydration was maintained with central venous pressure–guided intravenous fluid (Ringer’s lactate).

Intravenous fentanyl (120 μg) was administered after the delivery of the baby. The neonate had an Apgar score of 6 (blue appearance, pulse rate of 120/min, grimace, some activity, irregular respiration) at birth and had poor respiratory efforts, which recovered after about 40 seconds of bag and mask ventilation. The Apgar score improved to 7 at 2 minutes (blue appearance, pulse rate of 132/min, grimace, some activity, regular respiration) and 9 (peripheral blue appearance, pulse rate of 144/min, active cry, good activity, regular respiration) at 5 minutes. The neonate was taken to the neonatal intensive care unit for further management under the supervision of a neonatologist.

The rest of the intraoperative procedures remained uneventful. Intraoperatively, the pulse rate ranged from 72/min to 98/min, and blood pressure ranged from 132 to 158 mm Hg systolic and 78 to 92 mm Hg diastolic. After completion of surgery, the residual neuromuscular blockade was reversed with neostigmine and glycopyrrolate, and the trachea was extubated.

She was transferred to the intensive care unit for observation. Monitors, including electrocardiogram, pulse oximeter, invasive blood pressure, and central venous pressure, were attached. Her pulse rate was 84/min, blood pressure was 138/88 mm Hg, and oxygen saturation was 98%. Oxygen was supplemented via face mask. Analgesia was provided with fentanyl infusion (20 μg/h).

After 2 hours, her oxygen saturation started decreasing (86%), and blood pressure increased to 210/126 mm Hg. Continuous positive airway pressure (CPAP) of 5 mm Hg was applied via a noninvasive ventilation mask, following which oxygen saturation improved to 98%. Titrated nitroglycerin infusion (4 to 5 μg/kg/min) was started, and blood pressure was maintained at around 140/90 mm Hg. Two hours later, the patient had an episode of seizures and was managed with 2 boluses of midazolam (2 mg). One hour later, she had a recurrence of seizures and was managed with a 2-mg injection of midazolam. A loading dose of phenytoin (1,500 mg) was administered intravenously over 30 minutes, followed by 100 mg 3 times daily. A second platelet count was 35,000/mm³. Four units of platelets were transfused. The patient remained hemodynamically stable. Twelve hours later treatment with amlodipine tablets, 5 mg twice daily, was started, and the nitroglycerin dosage was tapered and stopped over 5 to 6 hours. The platelet count was 41,000/mm³. In view of persistent thrombocytopenia, valproate therapy was stopped and treatment with syrup levetiracetam, 750 mg twice daily, was started after a loading dose of 2,000 mg intravenously over 30 minutes. Gradually hematuria cleared, and no episode of epistaxis was observed. The platelet count improved to 65,000/mm³, 140,000/mm³, and 160,000/mm³ on the first, second, and third postoperative day, respectively.

The patient was transferred to a medical-surgical ward and continued treatment with phenytoin tablets and syrup levetiracetam. She remained seizure free and hemodynamically stable. She was discharged 8 days later with advice to schedule follow-up visits in the neurology and gynecology departments.

She continued receiving antiepileptic drugs (phenytoin tablets and syrup levetiracetam), and seizures did not recur. Her blood pressure was controlled with oral amlodipine (5 mg) twice daily. Results of repeated inves-
tigations at 6 weeks, including complete hemogram and liver and kidney function tests, were normal.

Discussion
The initial management of patients presenting with active seizure in pregnancy should include maintenance of the airway, oxygenation, and support of adequate perfusion. Immediate attention must also be applied to the fetus, particularly if it has reached a viable gestational age. While an ongoing evaluation is in progress to investigate the organic causes, administration of a parenteral benzodiazepine, followed by intravenous phencytoin at conventional doses, is a reasonable approach. A computed tomographic (CT) scan of the brain is required to differentiate the central organic cause of seizures from that of eclampsia, but concern for safety of the mother and her fetus because of radiation exposure remains.

Our patient had recurrent generalized tonic-clonic seizures with features suggestive of eclampsia along with a history of epilepsy. We were in a dilemma regarding the pharmacotherapeutic management of seizures in this scenario.

Epilepsy disorder may improve or even deteriorate during pregnancy. Reasons for deterioration during pregnancy include poor compliance, nausea and vomiting, increased volume of distribution, changes in protein binding, increased drug clearance, lack of sleep, reduction of absorption of antiepileptic drugs from the gastrointestinal tract, hyperventilation during labor, and hormonal changes. In practice it is useful to have a baseline blood level of antiepileptic drugs early in pregnancy to confirm compliance and to guide any increases that may be necessary. Measurement of the plasma levels for antiepileptic drugs was not feasible in our patient because of the emergency scenario, and levels were not obtained in early pregnancy.

Our patient responded to conventional antiepileptic agents, but there was recurrence of seizures, which later subsided only after the initiation of magnesium therapy. This implies the generally accepted dictum that if the seizures occur in pregnancy, they should be evaluated as eclampsia until proved otherwise and should be treated as such until the attending physician can perform a proper evaluation. Emergency cesarean delivery is required if there are recurrent generalized seizures, to avoid any maternal and fetal morbidity. Thus, evaluation of the cause of seizures remains a limitation in an emergency scenario.

The other concern in our patient was persistent thrombocytopenia, which was attributed to HELLP syndrome and later found to be associated with valproate. This may lead to derangement in coagulation and thus the possibility of central nervous system bleeding, which may be further aggravated by uncontrolled blood pressure. In our case, thrombocytopenia subsided only after valproate therapy was stopped.

The use of polypharmacy in the management of patients with recurrent seizures has an impact on the fetus, as was seen in our patient. The baby had a poor Apgar score at delivery, which improved only after adequate resuscitation. Thus, in the perioperative management of such patients, a pediatrician's presence and resuscitation equipment must be available.

We conclude that maximum vigilance is required for a patient with concomitant diseases such as epilepsy and a high-risk pregnancy with eclampsia. Therapy needs to be titrated according to the patient's response, keeping in mind its impact on the fetus.

REFERENCES

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