Late Postpartum Eclampsia with Posterior Reversible Encephalopathy Syndrome

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Eclampsia is the development of generalized convulsions in a pregnant or puerperal woman, usually between 20 weeks' gestation and the first 48 hours postpartum.[1] In classic eclampsia, the onset of seizures is preceded by the preeclamptic syndrome of proteinuria and hypertension during the antepartum or intrapartum periods. In contrast, late postpartum encephalopathy (LPE) occurs between 48 hours and 1 month postpartum,[1,2] frequently in women who have had a normal pregnancy and delivery and have no signs of a preeclamptic syndrome.[1–5] These features can make LPE difficult to recognize and can delay diagnosis. Prompt diagnosis and treatment of eclampsia are important as cerebrovascular damage caused by eclampsia may result in permanent neurologic sequelae. This article reports 2 cases that illustrate common presentations of LPE, reviews the management of LPE, and discusses the diagnosis of posterior reversible encephalopathy syndrome (PRES), a clinicoradiologic condition associated with eclampsia.

CASE PRESENTATION 1

Initial Presentation and History

A 30-year-old woman gravida 2, para 2 presented to the emergency department (ED) 8 days postpartum after she experienced severe headaches, nausea, and a seizure. During pregnancy, she had 1 recorded episode of high blood pressure that resolved by the time it was rechecked during the same office visit. Her medical history was significant for migraines during pregnancy. She had a normal pregnancy and an uncomplicated vaginal delivery. After delivery, she received hydrocodone/acetaminophen for her headaches. She took 1 tablet in the morning on the day she presented to the ED.

Physical Examination

On admission to the ED, the patient was afebrile and tachycardic to 111 bpm, with a blood pressure of 135/79 mm Hg. During evaluation in the ED, her blood pressure was measured as high as 176/96 mm Hg. Her physical examination was normal, including a full neurologic examination. During the examination, she suddenly became dazed and had a generalized tonic-clonic seizure, which resolved spontaneously after 1 minute.

Further Evaluation and Hospital Course

Following the seizure, the patient was given 2 mg lorazepam intravenously (IV) and 1 g phenytoin IV and was admitted to the medical floor. The etiology of the seizure was unclear on admission. The differential diagnosis included: subarachnoid hemorrhage; intracranial mass, hemorrhage, or thrombosis; hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome; and substance abuse. A review of of the literature regarding HELLP syndrome discussed LPE, and after reviewing the information on LPE, it became a likely diagnosis.

Computed tomography (CT) scan of the head, lumbar puncture, complete blood count (CBC), and a metabolic panel were performed to work-up the witnessed seizure, and all results were normal. Urine dipstick showed trace protein. Magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and magnetic resonance venography (MRV) were ordered to rule out thrombosis and masses not detected by CT.

While awaiting the results of the imaging studies, the patient was started on magnesium sulfate IV at 2 g per hour for 48 hours with close monitoring of her magnesium level. Her blood pressure returned to the normal range after the seizure without treatment. The patient received 100 mg of phenytoin IV 3 times daily throughout the hospital course. MRI (**Figure**) showed mild bilateral parieto-occipital T2 hyperintensity, a finding consistent with PRES. The results of MRA and

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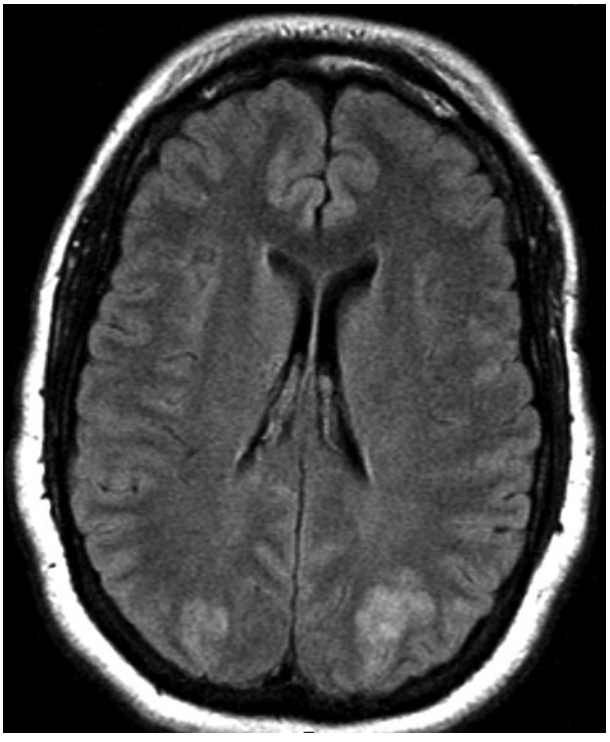

Figure. T2-Weighted magnetic resonance image obtained following case patient 1's seizure. The image shows bilateral parieto-occipital hyperintensity consistent with posterior reversible encephalopathy syndrome.

MRV were normal. The diagnosis of LPE was confirmed by imaging and clinical course as well as by ruling out other etiologies. The patient had no further seizures, fully recovered, and was discharged on hospital day 3.

CASE PRESENTATION 2

Initial Presentation and History

A 30-year-old woman gravida 1, para 1 presented to the ED complaining of severe headaches for 3 days, nausea and vomiting, and blurry vision. She reported having peripheral edema since a normal vaginal delivery 12 days prior. At the time of delivery, the patient had borderline elevated blood pressures (140–152/54–85 mm Hg) but no other signs or symptoms of preeclampsia. The patient was previously healthy and took no medications.

Physical Examination

On admission to the ED, the patient was febrile to 38.0°C and had a heart rate of 55 bpm and a blood pressure up to 191/101 mm Hg. The physical examination was normal, including a full neurologic exam, except for trace pedal edema.

Laboratory Evaluation and Computed Tomography

The results of a CT scan of the head and a lumbar puncture were normal. CBC revealed a slightly elevated white blood cell count ($18 \times 10^3/\mu L$ [normal, $4.5–11 \times 10^3/\mu L$]) and slightly elevated platelet count ($473 \times 10^3/\mu L$ [normal, $150–400 \times 10^3/\mu L$]). A chemistry panel showed hypernatremia (152 mEq/L [normal, 135–145 mEq/L]). Urine dipstick showed 1+ protein. During evaluation in the ED, the patient had a generalized seizure. She was treated with 2 mg lorazepam IV and was started on magnesium sulfate IV 4 g load then 2 g per hour for 24 hours for presumed LPE. An MRI, MRV, and MRA were ordered. Her blood pressure was controlled with hydralazine, labetalol, enalapril, and clonidine.

Further Treatment and Hospital Course

The patient was admitted to the medical intensive care unit and her blood pressure was stabilized on labetalol and enalapril. MRI showed bilateral symmetric frontal-parietal cortical abnormalities with mild swelling, results consistent with PRES. The results of MRA and MRV were normal. The patient had no further seizures, slowly recovered, and was discharged on hospital day 7. The patient was discharged on phenytoin 300 mg daily and metoprolol 25 mg twice a day.

DISCUSSION

These cases illustrate the difficulty that is frequently encountered in recognizing and diagnosing LPE. If the case patients had presented antepartum when suspicion for eclampsia is high, the diagnosis likely would have been made easily. In both cases, when the patients manifested some classic symptoms of imminent eclampsia—headache, blurred vision, nausea—the diagnosis went unrecognized and the patients ended up seizing.[1] The etiology remained unclear until other common conditions in the differential had been ruled out (**Table**).[6–22] Another reason for the difficulty in diagnosis was the lack of any preceding classic symptoms of preeclampsia (eg, hypertension and proteinuria) during or after the pregnancy. In a review of 14 reported cases of LPE, only 5 showed at least 1 symptom of preeclampsia.[3,4,13,23–26]

LATE POSTPARTUM ECLAMPSIA

Clinical Features

Eclampsia occurs in approximately 3 to 5 of every 10,000 live births.[1] LPE accounts for 5% to 26% of eclampsia cases. It occurs between 48 hours and 1 month after delivery and has a clinical picture that is different from classic eclampsia.[1,2] In classic eclampsia,

the preeclamptic syndrome of proteinuria and hypertension precedes the onset of seizures. In LPE, the pregnancy and delivery often are completely normal and without signs of a preeclamptic syndrome.[1–5] LPE manifests instead after a prodrome that appears clinically like hypertensive encephalopathy and most often begins abruptly with headaches of increasing severity days to weeks after delivery (50%–75% of cases).[1,2,23] Other common symptoms include vision changes (19%–32% of cases), nausea/vomiting, and generalized or focal neurologic deficits.[1,5,23] LPE convulsions begin within hours to days of onset.[1,2] Once the convulsive phase of LPE has begun, T2-weighted MRI often demonstrates findings consistent with PRES.[1,3]

Posterior Reversible Encephalopathy Syndrome

PRES is a recently described clinicoradiologic syndrome that is associated with several medical conditions, including hypertensive encephalopathy and eclampsia. It has been described as clinical findings of headache, visual changes, altered mental status, and seizures[13] in conjunction with radiologic findings of posterior cerebral white matter edema.[26,27] Most evident on T2-weighted MRI images, the lesions are hyperintense and located at the gray-white junction, and most often involve the parieto-occipital regions bilaterally. Less frequently the lesions involve the frontal, temporal, and cerebellar regions bilaterally.[13] More severe radiologic findings have been associated with more severe clinical findings in PRES.[23] It is unknown, however, whether imaging before seizure onset would reveal evidence of PRES.

PRES is usually reversible with appropriate treatment.[23,26–29] However, it is important to recognize and treat the etiology responsible for PRES, as PRES has been shown to progress from reversible vasogenic edema to irreversible ischemic damage if appropriate treatment is not promptly initiated. Ischemic damage can cause irreversible neurologic sequelae, such as epilepsy, as well as death.[25,28,29]

The reversibility of PRES is due to its underlying pathophysiology, which has been attributed to failure of cerebral autoregulation and endothelial dysfunction. The leading pathophysiologic hypothesis for PRES involves a breakdown of brain vascular autoregulation due to an increase in blood pressure above the patient's baseline level. It is believed that the posterior brain is at greater risk for autoregulation breakdown because it is less extensively innervated, rendering it less able to adjust to blood pressure fluctuations.[26,27] The failure of autoregulation results in vasogenic edema.[26,27,30] The presence of endothelial dysfunction decreases the threshold blood pressure at which vasogenic edema occurs.[26,27] For this reason, vasogenic edema may occur with mildly elevated or normal blood pressure. Blood pressure in eclamptic patients varies, with 20% to 54% of patients having severe hypertension (systolic blood pressure [SBP] > 160 mm Hg or diastolic blood pressure [DBP] > 110 mm Hg), 30% to 60% having mild hypertension (SBP 140–160 mm Hg or DBP 90–110 mm Hg), and 16% having no hypertension.[1]

Table. Differential Diagnosis for Late Postpartum Eclampsia with and without Posterior Reversible Encephalopathy Syndrome (PRES)

With PRES
Hypertensive encephalopathy
Immunosuppressants,[6–8] chemotherapeutics,[9–12] other drugs[13–18]
Reaction to contrast dye or blood transfusion[19–21]
Cerebral vasculitis[22]
Metabolic disorders
Without PRES
Meningitis
Encephalitis
Cerebral hemorrhage
Arterial or venous thrombosis
Epilepsy
Amphetamine or cocaine use
Space-occupying brain lesions
Cerebral vasculitis
Metabolic disorders

Evaluation and Diagnosis

The work-up for suspected LPE should include serial blood pressure measurements because in many cases blood pressure was elevated only intermittently.[3,4,13,23–26] A basic metabolic panel, CBC, urine toxicology screen, lumbar puncture, and cerebral imaging help to differentiate LPE from other possible diagnoses (Table).[1] T2-weighted MRI is the test of choice for LPE with PRES.[26,27] Magnetic resonance diffusion-weighted images (DWI) and apparent diffusion coefficients (ADC) can distinguish between vasogenic and cytotoxic edema.[24,29,30] In vasogenic edema, DWI shows moderately increased signal intensity and the ADC is isointense or hyperintense. In cytotoxic edema, DWI shows highly increased signal intensity and the ADC is hypointense.[26,27,29]

Treatment

Patients manifesting symptoms of imminent eclampsia (eg, severe headache, blurred vision, or epigastric

pain) should be started on magnesium sulfate immediately to avoid the harmful sequelae of seizures.[1] A magnesium sulfate loading dose of 6 g over 15 to 20 minutes followed by 2 g per hour continuous intravenous infusion has been recommended.[1] Treatment should be continued for at least 24 hours after the last convulsion.

Severe hypertension should be controlled to keep blood pressure within a safe range while maintaining cerebral perfusion pressure, which can be difficult with fluctuating blood pressure. When blood pressure becomes severely elevated (SBP > 160 mm Hg or DBP > 110 mm Hg), intravenous labetalol or hydralazine can be used. Patients can be placed on longer-acting antihypertensives once their severe hypertension has been controlled. Sibai[1] recommends treating to a SBP between 140 and 160 mm Hg and a DBP between 90 and 110 mm Hg.

CONCLUSION

Patients are routinely counseled about the signs and symptoms of preeclampsia during pregnancy. Likewise, before hospital discharge, patients should be told to watch for signs of an LPE prodrome in the postpartum period. Counseling should discuss the warning signs of severe persistent headache, nausea/vomiting, visual changes, and generalized or focal neurologic deficits. Seizures usually prompt ED admission. Such complaints up to 1 month after delivery should be worked up for the LPE prodrome with the goal of preventing seizures in imminent eclampsia (severe headache, blurred vision, or epigastric pain) and promptly managing eclampsia should it occur. If seizures and blood pressure are not appropriately controlled, permanent neurologic deficits and even death can occur.[3,5,7,12,13] **HP**

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