Posterior Reversible Encephalopathy Syndrome (PRES) and Low Serum Magnesium in Cesarean Delivery: Causative Factor or Coincidence in the Absence of Previous Co-morbidities?

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Abstract

Abstract: Posterior reversible encephalopathy syndrome (PRES) is an acute or subacute transient neurological condition usually presents in pregnancies complicated with hypertensive disorders like preeclampsia or eclampsia and characterized by spectrum of nonspecific symptoms, including seizures, headaches, altered consciousness and focal neurological deficits. Preeclampsia and eclampsia are probably the most common causes of PRES however, many causes of PRES have been reported in the literature including hypertensive encephalopathy, renal failure, immunosuppressant therapy, thrombotic thrombocytopenic purpura, systemic lupus erythematosus (SLE), and acute intermittent porphyria. We present here an unusual case involving a 29-year-old parturient at 37 weeks of gestation who experienced sudden headache, irritability, tachypnoea followed by seizures, during caesarean delivery and the early postpartum stage. Additionally, her laboratory reports were normal except hypomagnesemia which was corrected postoperatively. She had no prior history of hypertension, preeclampsia or other common PRES-associated conditions. Brain magnetic resonance imaging (MRI) revealed subtle flair hyperintensity in the posterior occipital region and left cerebellar hemispheres with adjacent sulcal effacement, indicative of PRES.

Keywords: Posterior reversible encephalopathy syndrome, magnesium, pregnancy, vasogenic oedema

Introduction

Posterior reversible encephalopathy syndrome (PRES), also recognized as reversible posterior leukoencephalopathy syndrome (RPLS), presents a distinctive form of cerebrovascular disease characterized by clinical and imaging features. Despite its recognition, the precise pathophysiological mechanisms underlying PRES remain incompletely understood and subject to debate. Utilizing MRI as the gold standard for diagnosis, PRES typically exhibits vasogenic oedema in subcortical white matter, often accompanied by cytotoxic oedema in certain cases. Commonly associated with conditions like pre-eclampsia, eclampsia, hypertension, post-transplant immunosuppression, cancer chemotherapy, and autoimmune disorders.[1,2] PRES primarily manifests lesions in parietal and occipital lobes (up to 50% of cases), superior frontal sulcus (up to 27%), and both anterior and posterior watershed zones (up to 29%), with less frequent occurrences in deep white matter, basal ganglia, thalami, brainstem, and pons (up to 13%).[3] Clinical presentation of PRES includes impaired consciousness, headaches, seizure episodes, focal neurological signs, and nausea/vomiting. Notably, upon removal of the underlying cause, PRES is typically reversible. Recent reports have associated hypomagnesemia with the acute phase of PRES, independent of its etiology[4]. Magnesium, a crucial trace element in the body, plays an important

role in stabilizing blood pressure by regulating vascular function and exhibits neuroprotective effects by reducing inflammation and blood-brain barrier permeability. Magnesium sulphate, a conventional treatment for conditions like pre-eclampsia and eclampsia, highlights its relevance in neuroprotection. Here, we present a unique case of clinically and radiologically diagnosed PRES, notable for its occurrence without a prior history of hypertension, preeclampsia, eclampsia, or other common triggers of PRES.

Case Report

A 29-year-old female, gravida 2, para 1, with one previous lower segment caesarean section (LSCS), presented for an emergency LSCS due to non-reassuring foetal status. She had no known comorbidities. Her preoperative lab investigations and baseline vitals were within normal limits. (HR- 92 beats/min, BP- 110/78 mmHg, RR- 18/min, SPO2- 100% at room air) After obtaining informed consent, under strict aseptic precaution, subarachnoid block (SAB) was given with 25G Quincke's needle using 0.5% heavy bupivacaine (2.0 ml) at L3-L4 level and surgery was started after adequate level of anaesthesia (T6) achieved. After 10 mins of commencement of surgery patient developed hypotension (90/50 mmHg) which was managed with IV fluid and single bolus dose of 6 mg IV Mephentermine. Subsequently after 10 min, the patient had one more episode of hypotension (86/50 mmHg) with bradycardia (50 beats/min) which was managed with a bolus dose of Atropine 0.6mg IV and Mephentermine 6 mg IV. The episode of bradycardia and hypotension was terminated however owing to the effect of IV Atropine, the patient developed tachycardia (130 beats/min) and raised blood pressure (160/100 mmHg). Also, she started complaining of a severe headache and her blood pressure and heart rate remained elevated. Approximately 40 minutes post spinal anaesthesia blockade (SAB) and subsequent delivery, she developed generalized tonic-clonic seizures (GTCS), which was terminated by bolus dose of IV Midazolam 1mg immediately. Again after 15 minutes of the previous seizure (55 minutes after SAB), the patient again developed GTCS which was further managed with IV Midazolam 1mg and seizure prophylaxis given with loading dose of IV Phenytoin 1 gm in 100 ml NS over 30 min. Notably, her blood pressure and heart rate remains elevated for approximately 30 minutes after the dose of atropine (50 minutes post SAB). She had post-ictal confusion and irritability although she was maintaining her respiration without the need of airway management or mechanical ventilation after seizure termination. She delivered a healthy, crying female infant with Apgar scores of 6 and 7 at 3 and 5 minutes, respectively. After 75 minutes, she was shifted to postoperative area on completion of surgery. Effect of spinal anaesthesia lasted for approximately 96 min (sensory block regression to T10). Throughout her postoperative period, she experienced two additional episodes of GTCS accompanied by post-ictal confusion, headache, nausea, and tachypnoea within 12 hours of delivery, which were treated with IV lorazepam 4 mg. Despite her irritability, tachypnoea and complaint of headache, her vital signs were within normal limits in the post-operative ward.

Arterial blood gas (ABG) analysis after 2nd episode of seizure revealed respiratory acidosis (pH–7.30, pO2–433 mmHg, pCO2–54.1 mmHg, HCO3–26.9 mmol/L, Na+–138 mmol/L, K^{+}-4.0 mmol/L, Ca^{2+}-1.02 mmol/L). Postoperatively all laboratory investigation were within normal limits except low serum magnesium (1.45 mg/dl), which was replaced by loading dose of 4g IV Magnesium sulphate over 30 minutes followed by maintenance of 2g/hour for 24 hours postpartum. After 24 hours of careful observation, no further episode of seizure and correction of hypomagnesimia (1.84 mg/dl), she was shifted to the obstetrical ward for recovery. Interestingly, her previous pregnancy had been uneventful, and she maintained regular antenatal visits during her current gestation and there was no significant family history, addiction, or known substance allergies.

Further diagnostic evaluation was initiated, including electroencephalography (EEG) and brain magnetic resonance imaging (MRI). The result of EEG done after 24hr was normal, while MRI findings indicated hyper-intensity in the posterior occipital region with adjacent sulcal effacement, consistent with a diagnosis of PRES. [Figure 1]. After 5 days, patient was discharged home after surgical recovery. Her telephonic follow-up was continued for 4 months. She was advised for follow-up MRI after 3 weeks, however she did not consented for the same.

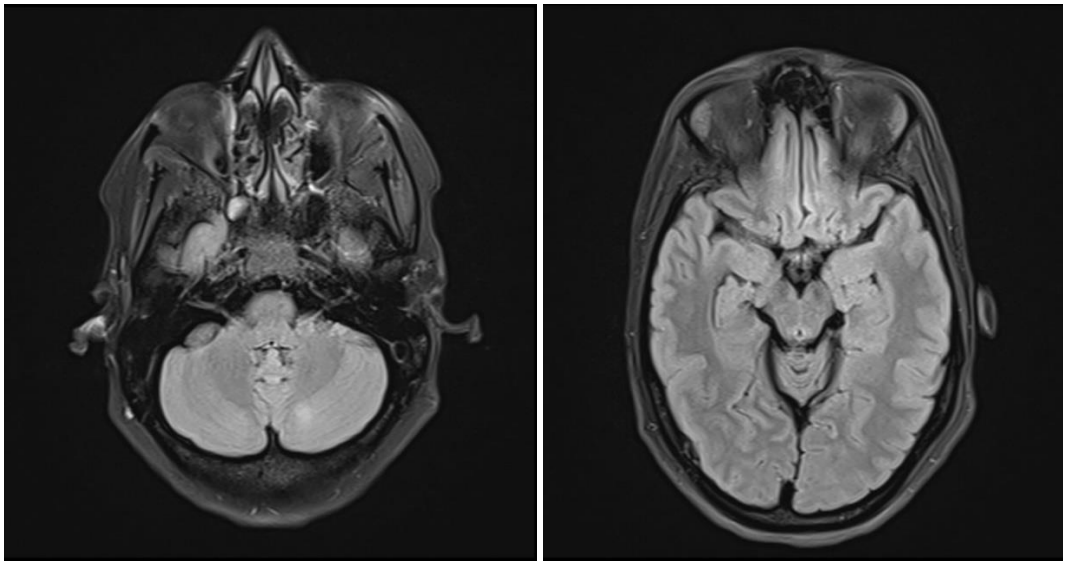

Figure 1: MRI showing hyper-intensity in the posterior occipital region with adjacent sulcal effacement.

Discussion

Posterior reversible encephalopathy syndrome (PRES) should be considered in pregnant women presenting with sudden-onset headaches, seizures, vomiting, and altered mental status.[3] In our case, patient had normal antenatal history, but experienced an intra-operative increase in blood pressure following the administration of bolus doses of Mephentermine and Atropine to address hypotension triggered by the subarachnoid block and subsequently developed headache followed by seizure. Differential diagnosis was made for undiagnosed preeclampsia or eclampsia, HELLP syndrome, PRES, cerebrovascular event and Local anaesthetic systemic toxicity (LAST). Neuroimaging manifestations of eclampsia and preeclampsia often overlap, and present as posterior reversible encephalopathy syndrome (PRES),[5] however, no sign and symptoms of preeclampsia were present in our patient. HELLP syndrome was ruled out because of normal blood investigations and lack of history of raised blood pressure during the antenatal visits. Local anaesthetic systemic toxicity (LAST) could also not be explained, particularly with small doses of local anaesthetic, episodes of seizure after 40 minutes of SAB, and the absence of prodromal symptoms, such as tinnitus and perioral numbness. Fundus examination and cranial nerve assessments did not reveal any abnormalities suggestive of cerebrovascular events.

Although the precise pathophysiology of PRES remains incompletely elucidated, there is a convergence of pathogenic mechanisms among its different aetiologies. The most popular theory is that rapidly developing hypertension exceeds the upper limit of cerebral blood flow autoregulation which causes hyperperfusion, disruption of the blood–brain barrier leading to vasogenic edema.[6] Vasogenic edema is extracellular edema which predominantly impacts the white matter due to fluid leakage from capillaries. Presence of bilateral and extensive edema may suggest posterior reversible encephalopathy syndrome (PRES). In vasogenic edema, MRI reveals hyperintense T2 and Fluid-attenuated inversion recovery (FLAIR) signals without restricted diffusion. In contrast, cytotoxic cerebral edema involves intact blood-brain barrier, affecting gray matter, white matter, or both, with MRI indicating diffusion restriction.[7] Also, magnesium, a vital microelement extensively involved in various physiological processes, especially in cardiovascular regulation, plays a crucial role in blood pressure regulation. Blood pressure fluctuations and hypomagnesemia might be the contributing factor for PRES in our case.[4,6] However there has been a case report of magnesium toxicity leading to PRES in a preeclampsia patient.[8] So any dysregulation in magnesium serum level might be the contributing factor for PRES, however more robust evidence is wanted to confirm the etiology of PRES and its relation to serum magnesium level.

Prognosis in PRES cases are generally favourable, primarily contingent upon timely and adequate management of the underlying condition. Recovery occurs in approximately 70% to 90% of PRES patients within 2 to 8 days.[9] However, adverse outcomes, such as cerebral haemorrhage, ischemia, irreversible neurological deficits, and mortality, have been reported in a subset of patients, ranging from 8% to 17%.

Conclusion

This case highlights two significant learning points. Firstly, it underscores that PRES can manifest in pregnancy even in the absence of pre-eclampsia, eclampsia, or other conventional risk factors. This expands the spectrum of potential causes for PRES, emphasizing the need for heightened vigilance in pregnant patients presenting with relevant symptoms. Secondly, considering the association between hypomagnesemia and PRES, implementing routine serum magnesium assessments in all pregnant individuals could aid in preventing PRES associated with magnesium deficiency. Timely interventions aimed at addressing potential deficiencies may contribute significantly to mitigating complications linked to PRES.

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