MANAGEMENT OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN AN UNBOOKED TERM PREGNANT CASE WITH ECLAMPSIA.

Anaesthesiology

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) usually presents with headache, confusion, visual disturbances or blindness and seizures. MRI is gold standard with parieto-occipital white matter changes due to vasogenic oedema in most of the cases. We report a 20-year-old unbooked primigravida with eclampsia prior to delivery which got complicated by PRES after delivery on day 1 postpartum. General anesthesia was given for caesarean section and post operatively patient was managed in ICU with strict blood pressure and seizure control. Clinical improvement with complete resolution without any complications was observed on the day 10 postpartum.

Introduction: Posterior reversible leukoencephalopathy syndrome (PRES), also known as reversible posterior cerebral oedema syndrome, hyperperfusion encephalopathy, or brain capillary leak syndrome presents with typical clinical and radiological features.

Common causes are hypertensive encephalopathy, preeclampsia, eclampsia, cortical venous sinus thrombosis acute or chronic renal diseases, haemolytic uremic syndrome, use of cytotoxic and immunosuppressant drugs, blood transfusion, and electrolyte disturbances, isolated^[1].

Clinical features of PRES include headache, encephalopathy, seizures, cortical visual changes and on brain imaging parieto-occipital white matter oedema is most commonly visualized^[2].

In this case report, we present a 20 yr. old, unbooked term eclamptic pregnant woman complicated by PRES after delivery.

KEYWORDS

Posterior reversible leukoencephalopathy syndrome (PRES), preeclampsia, eclampsia.

Case Report

A 20-year-old unbooked primigravida at the 38th week of gestation presented to emergency with one episode of generalized tonic clonic seizures for around 30 seconds in previous one hour along with disorientation, and irrelevant talking post seizure episode. She had h/o headaches for past one-week, visual hallucinations for one day. On examination, the findings were- blood pressure- 180/120mmHg, heart rate- 110/min, respiratory rate -24/min, oxygen saturation (SpO₂) of 96% with face mask O₂, flow of 6l/min, temperature- 37°C, Glasgow coma scale (GCS)- E4V4M5, pupils equal size with normal reaction to light, bilateral plantar reflexes were flexor, foetal heart rate: 146, uterine height: 38 cm, cervix-closed, uterine contractions- negative, chest-clear on auscultation, abdominal examination- normal, her legs- bilateral 2+ pitting oedema without size differences, on fundoscopic examination, both optic discs were normal and there was no focal neurological deficit. There was no past history of hypertension, palpitations, limbs swelling, vision abnormalities, seizures, or any other cardiovascular and neurological disease. She was started on injection labetalol 20 mg bolus f/b 1mg /min and iv magnesium 4g bolus f/b 1g/hr iv infusion in emergency targeting magnesium between 1.8-3 mmol/l. Her BP after labetalol bolus and infusion was 140 mmHg systolic and diastolic blood pressure of 90 mmHg. There was no further episodes of seizures and magnesium iv infusion was continued. On investigation, Hb: 13.1%, Platelet count: 222000 per microliter, Urine Protein: 4+. Liver function test, kidney function test, electrolytes and clotting parameters were normal. ECG -normal, serum magnesium was 2.5 mmol/l. She was posted for emergency lscs with in four hours of presentation in view of eclampsia preoperatively. She was on magnesium infusion @ 1g/hr and labetalol infusion @1mg/min. She was also administered metoclopramide 10mg, ranitidine 50mg preoperatively. Pre-operative BP was 150/98mmHg, HR 80/min, RR 22/min, SpO₂ 98 with face mask O₂, flow of 6l/min, GCS E4V4M5. FHR 140/min and no foetal distress. She had irrelevant talking with disorientation. One wide bore 16 g canula was in situ in left forearm. In the operation room, her trachea was intubated with rapid sequence induction using thiopentone and succinylcholine. Anaesthesia was maintained with oxygen, air and sevoflurane targeting MAC of 1 to avoid any rise in BP. Intravenous fentanyl 100 mcg was also given prior to incision. Another wide bore 16 g was secured in right forearm. Intraoperative hypertension was managed with IV labetalol with invasive blood pressure monitoring. Magnesium infusion was continued at same rate. A male infant weighing 3300 g, with APGAR score of 9 and 10 respectively in the first and fifth minutes was delivered. Analgesia was augmented with 100 µg of IV fentanyl as there was plan of mechanical ventilation post

operatively. A total of 1000 ml of Ringer's lactate was infused during the entire procedure which lasted for 1 hour. Urine output was approximately 100 ml in 1 hour. Postoperatively, she was shifted to an intensive care unit (ICU) for planned mechanical ventilation and invasive monitoring. Her treatment in ICU included MgSO₄, i.v. infusion at same rate for next 24 hours, tablet labetalol 100mg bd after stopping the infusion, amlodipine 10 mg od, inj paracetamol 1gm iv tds, inj. mannitol 20 gm iv bd for two days, inj. lasix 20 mg bd. U/O was 60ml/hr. On 1st post op day her GCS deteriorated from E4V4M5 to E2VTM4 after six hours of ICU admission. Neurology opinion was taken and MRI was advised for GCS deterioration. Differential diagnosis was: PRES, subarachnoid haemorrhage, haemorrhagic or ischemic CVA of occipital lobe, cortical venous sinus thrombosis, tumour. MRI brain images obtained revealed hyperintense and FLAIR signal lesions extending beyond the occipital lobes and involved both cerebellar hemispheres (Figures 1, 2). Clinical and radiological findings were assumed to be consistent with PRES. Antihypertensives drug were continued targeting BP less than 140/90 and magnesium infusion was continued till 24 hours targeting mg of 1.8-3 mmol/l. LMWH dvt prophylaxis was added after ruling out risk of surgical site bleeding with gynaecologist. On 2nd day, GCS remained same E2VTM4 and magnesium infusion was stopped and tablet phenytoin 100 mg tds was started. On day 3 mannitol was stopped. BP was maintained in range of 140-120 systolic 90-80 diastolic. No further episode of seizures was noted. ABG & Serum electrolytes - WNL. Complete blood count revealed a haemoglobin level of 9.1mg/dL and a platelet count of 162,000/mm³. Renal and hepatic function tests as well as ECG & ECHO were within normal limits. On day 5 her GCS improved to E3VTM5 which further improved to E4VTM6 on day 7 with complete hemodynamic stability and intact cough and gag reflex. She was extubated uneventfully and kept on face mask with 6l/min O₂ flow for two hours and nasal prongs @ 2l/min for 8 hrs targeting SpO₂ more than 95%. Thereafter she was maintaining SpO₂ more than 95% on room air. Oral feeding started on day 8 and inj. Lasix and tablet phenytoin was stopped and she was discharged from ICU on day 10. On day 14 postpartum she was discharged from ward uneventfully.

Figure 1: FLAIR axial images: hyperintense signal involving the white matter typically in occipital regions.

Figure 2: MRI, T2-weighted coronal image: hyperintense signal on bilateral occipital and cerebellar regions.

DISCUSSION

Posterior reversible encephalopathy syndrome is a clinical and radiological entity mostly associated with severe preeclampsia and eclampsia, characterized by headache, altered mental status, seizures, and visual hallucinations and visual loss.

In a retrospective observational study by PN nobis et al. collecting data from 1976 to 2014, around 1.5% of pregnant females in India have eclampsia^[3], with not much change in the incidence of eclampsia over these years. They also noted that 71% of eclamptic women developed posterior reversible encephalopathy syndrome^[3].

Significant predictors of PRES as determined on multivariate analysis by AK Verma et al. were unbooked pregnancy, the primigravida status, and the presence of visual impairment.^[4] The common symptoms were seizures (45%), visual disturbances (34%, with complete blindness in 17% of these), and alteration of consciousness (19%).^[4]

Our case also was unbooked primigravida who had deterioration of her consciousness in post-operative ICU, 12 hours after of eclamptic episode. As the patient was intubated visual symptoms could not be elicited.

For pathogenesis of PRES two theories are debatable, "The vasogenic theory and Cytotoxic theory"^[5]. The vasogenic theory is considered to be the most likely and accepted cause of PRES. Elevated capillary filtration pressure due to elevated bp with loss of cerebral autoregulation and endothelial dysfunction due to pre-eclampsia, eventually leading to increased blood-brain barrier permeability and the consequence is cerebral oedema. In support of vasogenic theory, a retrospective study by Ryan T Fitzgerald et al, serum LDH which is a marker of endothelial dysfunction had statistically significant elevation at the onset of PRES in cancer patients^[6]. In cytotoxic theory, it is thought that patients with chronic hypertension have hypertrophic artery walls, including in the CNS, causing reduced permeability of the blood-brain barrier, even small increases in blood pressure can cause them to respond with increased permeability of the blood-brain barrier.

MRI, which is the golden standard for diagnosing PRES, is best detected on T2- weighted and fluid-attenuated inversion recovery (FLAIR) images which usually shows symmetrical hyperdense white matter oedema in the posterior parietotemporooccipital areas, but also in the anterior regions (14%), basal ganglia (11%), brain stem (3%), and cerebellum (5%)^[7].

The reason for the primary involvement of posterior brain regions may be due to the regional heterogeneity of the sympathetic innervation of the intracranial arterioles, with better sympathetic innervations in anterior circulation leading to better autoregulation as compared to the posterior circulation^[8].

Further, more severe is the clinical picture, the more prominent are radiological findings.^[9]

For EEG pattern in PRES, a retrospective study by Kastrup et al. analysed 49 patients affected by PRES and characterized epileptic focus activity at frontal or occipital lobe.^[10]

PRES is reversible with strict blood pressure control, airway and ventilation management in case of low GCS, seizure control and prophylaxis with magnesium infusion, correction of hypoglycaemia and electrolyte imbalance, thiamine in patients with evidence of vitamin B1 deficiency and delivery of placenta^[11]. International society of hypertension recent guidelines recommend lowering the bp less than 140/90 using iv infusions and to maintain below that level^[12]. Intravenous antihypertensive drugs are necessary and appropriate choices include labetalol, nicardipine, or fenoldopam^[12].

Our patient had eclampsia on presentation, so general anaesthesia was given. Most important is to prevent hypertensive response to intubation as it directly increases maternal mortality in PRES^[13]. Lack of proper blood pressure control can increase catecholamine levels and cause intracranial hypertension increasing cerebral oedema^[14]. Therefore, fentanyl was administered during induction despite knowing its ability to cross the blood placental barrier. Moreover, in preeclamptic patients with PRES, a higher MAC of sevoflurane than recommended for pregnant patients was used to achieve a deeper level of anesthesia maintaining a stable blood pressure with surgical manipulation. Induction and maintenance doses of general anaesthesia drugs should not be reduced in the belief that the baby will be harmed^{[15][16]}. Magnesium is the drug of choice in controlling seizures in eclampsia and PRES and was continued till 24 hrs postpartum^[17]. The management of seizures in PRES is with treatment with antiepileptic drugs till the acute phase of PRES is resolved^[18]. So, our patient was continued on phenytoin tablet till day 8 post-partum.

In most cases of PRES, neurological symptoms and cerebral lesions disappear completely within days to weeks with treatment. Subjective cognitive problems, development of chronic epilepsy, and progress to irreversible partial blindness can be long-time consequences after years from acute episode.^[19]

CONCLUSION

Posterior reversible leukoencephalopathy syndrome may be a diagnostic and therapeutic challenge when it develops in eclampsia and preeclampsia. Preeclampsia and eclampsia may be the most common causes of PRES. This syndrome is generally characterized by seizures but visual loss occurring in a preeclamptic woman must remind PRES. Differential diagnosis of neurological signs and symptoms in severe preeclampsia and eclampsia would be PRES, subarachnoid haemorrhage, haemorrhagic or ischemic CVA of occipital lobe, cortical venous sinus thrombosis and tumour MRI brain is the investigation of choice in differentiating these aetiologies. Most cases of PRES, early treatment usually results in complete reversal of the deficits over few days to several weeks. For general anaesthesia higher MAC and adequate analgesia with short acting opioids should be used to achieve stable blood pressure. Control of blood pressure, avoidance of further episode of seizures and urgent delivery of baby is vital to avoid irreversible damage to central nervous system.

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