

Posterior reversible encephalopathy syndrome: An uncommon sequelae of Eclampsia



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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) refers to a clinical neuro-radiologic entity with characteristic features on neuro-imaging depicting posterior cerebral white matter edema. Clinical symptoms include headache, visual disturbances, confusion, and seizures. We report six cases of acute PRES who had eclampsia and presented with recurrent episodes of convulsions and hypertension. Magnetic resonance imaging scan showed diffuse abnormal signal intensities involving deep white matter of occipital region. Follow-up examination after 2 weeks of conservative management, showed marked improvement clinically and on neuro-imaging following which patients were discharged in stable condition.

Key words: Eclampsia; Obstetrics; Pre-eclampsia

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INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) was first discussed in a case series in 1996 by Hinchey et al.¹ They described it as a clinical syndrome of headache, confusion, visual changes, and characteristic neuro imaging findings suggestive of posterior cerebral white matter edema.¹ Although this is a rare complication and described in a number of medical conditions including hypertensive encephalopathy, sepsis, autoimmune disorders, use of cytotoxic drugs^{2,3}; nowadays, it is being frequently identified in pre-eclampsia and eclampsia.⁴ Pathogenesis of PRES is unclear but compromised cerebral auto-regulation and endothelial dysfunction seem to play a major role

in its occurrence.⁵ Both eclampsia and preeclampsia are associated with endothelial dysfunction and PRES has been suggested to play the key role in eclampsia related primary injury of central nervous system.^{4,6,7} We are presenting here a series of six cases of PRES diagnosed by magnetic resonance imaging (MRI) and we did follow-up imaging as well to exclude residual changes in brain.

Case 1

A 26-year-old primipara was admitted in the hospital with complaint of two episodes of postpartum convulsion at a private nursing home where she had been delivered by cesarean section (CS) under spinal anesthesia, with the neonate alive and well as stated by her family members.

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Following delivery, she had severe headache not subsiding with medications and blurring of vision. On admission her blood pressure (BP) was 140/100 mmHg. She was treated with oral labetalol and magnesium sulfate (Magsulph) was started. Ophthalmological examination revealed hypertensive retinopathy and following completion of Magsulph therapy and stabilization of patient, MRI of brain was done which revealed subtle T2/FLAIR hypertensive signal noted along the bilateral parasagittal and parieto-occipital regions, suggestive of PRES. Biochemical and coagulation parameters were normal except for increased serum uric acid 5.2 mg/dl and LDH 1076 U/l (Table 1). The mother was discharged with tablet Labetalol 100 mg thrice a day and advised to attend neurology OPD for follow-up.

Case 2

A 24 years old primigravida was admitted at 37 weeks period of gestation, with no history of hypertension or any other risk factors for PRES, with the complaint of pain abdomen. After admission her BP was 150/100 mmHg, proteinuria by urinary dipstick +2 and Bedside clotting time (BSCT) 11 min. She was induced with synthetic prostaglandin E2 (PGE2) gel but delivered by CS under spinal anesthesia due to failed induction. Post operatively her BP remained high and 5 h post operatively she developed ominous signs including blurring of vision and epigastric pain and thereafter had one episode of convulsion. Immediately Magsulph was started. In post-ictal state, she was drowsy and had mydriasis and complaint of decreased visual acuity. Her blood parameters revealed elevated liver enzymes with total bilirubin 0.8 mg/dl, AST 140 U/L, ALT 180 U/L, ALP 820 U/L, LDH 1026 IU/L, Uric acid 5.6 mg/dl, Hb 9.2 g/dl, platelet count 98000/cumm, and normal renal function test (Table 1). She was kept on tablet Nifedipine 10 mg and Labetalol 100 mg 12 hourly for the management of hypertension. Following stabilization, her MRI brain was done which revealed T₂ FLAIR hyperintensities in bilateral high fronto-parietal and parieto- occipital cortex and sub cortical white matter and patchy T₂ FLAIR hyperintensities in bilateral para ventricular white matter suggestive of hypertensive encephalopathy/ PRES. Both neonate and mother were discharged in stable condition, with mother on antihypertensives.

Case 3

A 16-year-old primigravida with teenage pregnancy was admitted at 34 week 6 days gestation after being referred from a rural hospital for eclampsia. She was carrying monochorionic diamniotic twin pregnancy and had been normotensive during her antenatal period. On admission she was restless and disoriented with BP of 150/110 mmHg. Her BSCT was 7 min and proteinuria by dipstick was +1. She was delivered by CS under general anesthesia with the indication of eclampsia with cervix

Table 1: Blood parameters of first 24 h in each case after admission

Case No	Hb (g/dl)	WBC Count (/cumm)	DLC: L/M/N/E/B (/mm%)	Platelet Count (/cumm)	Prothrombin Time (seconds) & INR	D-Dimer (µg/mL)	Urea (mg/dL)	Creatinine (mg/dl)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Alk. Phosphatase (U/L)	LDH (U/L)	Uric acid (mg/dL)	Serum Sodium (mEq/L)	Serum Potassium (mEq/L)
1	11.2	13,100	30/1/65/4/0/0	150,000	14.09/1.05	2.04	38	1.10	1	21	33	165	1076	5.2	136	3.8
2	9.2	18,300	40/1/56/2/1/0	98,000	13.5/1	1.90	36	0.85	0.8	140	180	820	1026	5.6	142	4.3
3	11.7	9000	24/2/74/0/0/0	172,000	12.69/0.94	0.94	24	0.93	0.68	20	16	210	962	8.5	138	3.9
4	10.9	14000	28/1/70/0/1/0	142,000	14.97/1.11	2.11	26	1.10	1.31	289	103	245	324	4.1	141	3.8
5	9.8	15,600	29/3/65/3/0/0	196,000	12.3/0.9	1.95	15	0.80	0.88	84	101	150	1500	5.2	138	3.6
6	11.1	13000	22/2/74/2/0/0	162,000	15.0/1.12	1.47	48	1.29	0.58	632	561	168	402	3.8	143	4.1

unfavorable for labor induction. She had already been started Magsulph from referral center, but within 1 h of CS she had another episode of generalized tonic-clonic convulsion with tongue bite for which another 2 gm Magsulph had to be given intravenously. She was initially given intravenous labetalol 80 mg to control her BP, followed by oral antihypertensives to maintain it post-delivery. She was also kept in the obstetric Intensive care unit (ICU) for observation till the completion of Magsulph course. Her hematological parameters were within normal limits, as were renal and liver function reports and electrolytes (Table 1). However, her uric acid and LDH were elevated (8.5 mg/dl and 962 U/L, respectively) persistently with findings of severe preeclampsia. MRI brain was done which confirmed diagnosis of PRES showing T2, FLAIR hyperintensities in both high fronto-parietal cortex in adjoining subcortical white matter including post central gyrus. She was discharged with residual hypertension controlled with tablet Labetalol 200 mg 3 times a day. She was advised to follow-up with MRI post-delivery. The neonate, though preterm, was also discharged in good condition.

Case 4

Another patient of teenage pregnancy of 18 years old at 37 weeks 5 days gestation and was referred from a rural hospital with eclampsia with five episodes of convulsion. On admission, she was in post ictal state, drowsy and disoriented, with dilated pupils and slurring of speech. Her BP was 170/110 mmHg and she was having hematuria. Attempt to induce labor was immediately done with synthetic PGE2 gel but there was induction failure and she had to be delivered by emergency CS under general anesthesia. Magsulph had already been started with 4 gm of loading dose IV followed by maintenance dose. However, following delivery, she continued to remain drowsy and disoriented. Medicine consultation was taken and infusion mannitol was started at 100 ml 8 hourly suspecting cerebral edema and the antiepileptic drug inj. Levetiracetam 1 gm intravenous 8 hourly was added. Laboratory tests revealed decreased platelet count of 70000/mm³ and deranged liver function, with total serum Bilirubin 1.31 mg/dl, AST 289 U/L, ALT 103 U/L, and ALP 245 U/L, but renal function tests and electrolytes were normal (Table 1). Findings were suggestive of eclampsia complicated by HELLP syndrome. Dexamethasone was promptly administered and she improved gradually with improvement in platelet count and liver function. PRES was confirmed on MRI brain which revealed gyral hyperintensities with cerebral edema in adjoining sub cortical white matter in both fronto-parietal and temporo-occipital region. Her neurological deficits gradually resolved and though she had a long hospital stay of almost 3 weeks, both mother and baby were ultimately discharged in stable condition. Mother was advised to attend neurology OPD after discharge.

Case 5

A 17-year-old pregnant mother was admitted at 40 weeks 2 days gestation with no previous history of hypertension. She was also normotensive since admission. She had uncontrolled hypothyroidism for which she was on medication for 3 months. Labour induction was attempted by synthetic PGE2 gel but she was delivered by CS under spinal anaesthesia due to induction failure. Post-operative period was initially uneventful and she remained normotensive in ward. However, she developed wound infection and regular dressing was started. On post-operative day 10, she developed sudden headache and epigastric pain and had one episode of generalized tonic clonic seizure followed by drowsiness. Magsulph was started with 4 gm intravenous as loading dose, followed by maintenance dose as per Pritchard regime. Her urine output was adequate. Medicine consultation was sought and infusion mannitol 100 ml 8 hourly was started, as her drowsy condition was suspicious of cerebral edema. She was kept in ICU for monitoring following stabilization. On completion of Magsulph course, MRI brain was done which revealed cerebral edema involving both posterior cerebellar hemispheres, posterior temporal, and parietal cortex suggestive of PRES. The neurological symptoms subsided gradually and she was discharged after secondary suturing without any antihypertensives. Baby was also discharged in good condition. Blood investigations revealed moderate anemia (Hb 9.8 gm/dl), minimally deranged liver enzymes (AST 84 U/L, ALT 101 U/L, and ALP 150 U/L) and raised LDH 1500 U/L, with uric acid 5.2 mg/dl (Table 1).

Case 6

A 22-year-old primigravida at 36 weeks gestation was referred from a peripheral hospital with history of two eclamptic convulsions at home and two more at the hospital despite administration of loading dose of Magsulph. Maintenance doses could not be given due to reduced urine output and hence she was referred to this tertiary medical college hospital, where she was received about 9 h after the first dose of Magsulph. She was drowsy (E4V5M6) at admission with recorded BP 150/100 mm of Hg and in labor with cervix dilated 4 cm. She was given the first maintenance dose of Magsulph and delivered a low birth weight (1635 g) baby vaginally about 2 h after admission. Her urine output also gradually improved. BP remained high and oral Amlodipine and Labetalol were given to control it. However, the patient remained drowsy and in a confused state and an MRI brain was suggested by Neurologist on referral. This was done 3 days after delivery and showed fairly symmetrical T2/FLAIR hyperintensities involving parasagittal parieto-occipital regions, with rest of cerebral hemispheres showing normal gray white matter differentiation, suggesting (PRES). Her blood/serum reports were mostly within normal limits,

except deranged renal, and liver function tests, with Serum Urea 48 mg/dL, Creatinine 1.29 mg/dL, AST 632 U/L, and ALT 561 U/L but serum Bilirubin normal (Table 1). She was discharged 7 days after delivery with BP controlled with medications and asked to report after 2 weeks for a repeat MRI. Her preterm and growth restricted baby had a prolonged stay in special care baby nursery, but was ultimately discharged in stable condition.

DISCUSSION

Frequent use of MRI resulted in increased diagnosis of PRES in recent years. Hypertension with failure of cerebral auto-regulation might play an important role in majority of patients with PRES. One possible explanation of such regional heterogeneity is that the sympathetic innervations of arterioles that protect brain from sharp rise in BP are in higher concentration in anterior circulation than posteriorly.⁸ Although neuro-imaging shows involvement of parieto-occipital lobes mostly variation may happen, where frontal and temporal lobes are affected too.⁹⁻¹¹ We also found atypical regions of brain like frontal and temporal lobes were affected (case 2,3,4) in addition to posterior cerebrum. In eclampsia or pre-eclampsia the blood brain barrier might be disrupted due to endothelial dysfunction, resulting in involvement of multiple regions of brain.⁴ We found systolic BP did not exceed beyond 140–150 mm of Hg in majority of cases (case 1,2,3) and one patient was normotensive (case 5) despite having PRES. In some series almost half of the patients did not develop severe hypertension and it can be hypothesized that sharp rise or fluctuation in BP is more important than absolute BP in the causation of PRES.^{12,13} Some patients were normotensive and BP was elevated over base line.¹⁴ In these case series almost all patients had deranged or elevated liver enzymes and LDH. Endothelial dysfunction causing hemolysis and poor organ perfusion including liver perfusion might be responsible for such rise in LDH and liver enzymes, respectively, irrespective of presence or absence of HELLP syndrome.⁴ This implies that patients with PRES have more severe endothelial damage than those without PRES and LDH level is an important marker.^{4,15} All of our patients were treated with rapid correction of BP where required, Magsulph and additional anti-seizure drugs like Levetiracetam and supportive management. All of them were discharged successfully with advice to follow up at neuro-medicine outpatient department. Demirel *et al.*,¹⁶ suggested timely intervention with thiopental infusion, antihypertensive and Magsulph can improve the morbidity faster in patients with PRES to avoid permanent damage.¹² We found normalization of brain imaging 2 weeks post-treatment in all of our patients.

CONCLUSION

Prompt and timely intervention can initiate early recovery of brain changes in PRES which is being increasingly diagnosed pre-eclampsia and eclampsia.

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