Journal of Advances in Medicine and Medical Research

23(1): 1-7, 2017; Article no.JAMMR.34997
Previously known as British Journal of Medicine and Medical Research
ISSN: 2231-0614, NLM ID: 101570965

Atypical Post Partum Eclampsia and Posterior Reversible Encephalopathy Syndrome

Nidhi Sharma[1*], Sasireka Manivel[1], Shanthi Ethiraj[1], Kalimuthu Kohila[1] and Cauvery Aarthi[1]

[1]Department of Obstetrics and Gynaecology, Saveetha Medical College, India.

Authors' contributions

This work was carried out in collaboration between all authors. Authors SM and SE admitted the patient, performed the caesarean section, wrote the protocol and wrote the first draft of the manuscript. Authors KK, NS and CA managed the patient at the time of convulsions. Author NS managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI:10.9734/JAMMR/2017/34997
Editor(s):
(1) Andrea Tinelli, Lab of Experimental Endoscopic Surgery, Imaging, Minimally Invasive Therapy & Technology, Department of Gynecology and Obstetric, Vito Fazzi Hospital, Lecce, Italy.
Reviewers:
(1) Junji Takaya, Kansai Medical University, Japan.
(2) Marzena Laskowska, Medical University in Lublin, Poland.
(3) Imaralu John Osaigbovoh, Babcock University, Nigeria.
Complete Peer review History: http://www.sciencedomain.org/review-history/20213

Case Report

Received 22nd June 2017
Accepted 21st July 2017
Published 26th July 2017

ABSTRACT

Pregnancy induced Hypertension also called as "Gestosis" plural "Gestoses" has a heterogeneous etiology. A case of atypical eclampsia with seizures in the postpartum, that required intravenous Magnesium sulphate is described. The two proposed theories of etiopathogeniesis of cerebral edema, "Vasogenic Theory" and "Cytotoxic theory" are discussed. The concept of "delta hypertension" is emphasized. Impaired fluid mobilization, decreased sodium excretion and imbalance between angiopoietic factors in the post partum period is discussed as the likely cause of post partum eclampsia.

Keywords: Preeclampsia; vascular; encephalopathy; reversible.

**Corresponding author: E-mail: drbonuramkumar@yahoo.co.in;*

1. INTRODUCTION

There are four categories of hypertension in pregnancy: chronic hypertension, gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension. A maternal Blood pressure measurement of 140/90 mm Hg or greater on two occasions before 20 weeks of gestation indicates chronic hypertension. Gestational hypertension is a provisional diagnosis for women with new-onset, nonproteinuric hypertension after 20 weeks of gestation; many of these women are eventually diagnosed with preeclampsia or chronic hypertension. Preeclampsia is the development of new-onset hypertension with proteinuria after 20 weeks of gestation. Atypical eclampsia is defined as development at < 20 weeks of gestation and > 48 hours after delivery and that have some of the signs and symptoms of preeclampsia without the usual hypertension or proteinuria [1].

Vasogenic edema is defined as extracellular accumulation of fluid resulting from the disruption of the Blood Brain Barrier and extravasation of serum proteins. Cytotoxic edema on the other hand is characterized by cell swelling caused by intracellular accumulation of fluid. Many soluble factors and functional molecules have been confirmed to induce BBB disruption [2]. When a patient convulses in the postpartum period multiple differential diagnoses are contemplated. MRI brain is helpful in differentiating Cortical Vein Thrombosis (CVT) from Posterior Reversible Encephalopathy Syndrome (PRES).

2. CASE REPORT

2.1 Case Presentation

A 27 year old, Second Gravida, with a previous full term delivery by caesarean section, 38 weeks and 5 days of gestation with oligohydramnios (Amniotic Fluid Index 5) was admitted for planned Caesarean section. She had no scar tenderness. Her blood pressure was 110/70 mm Hg. There was no proteinuria. She perceived good fetal movements. Caesarean section was done after due consent by Lower Segment Caesarean Section. She delivered a male baby of 2.5 kg and placental examination was normal. Her postoperative hemoglobin was 8.6 g/dl.

On postoperative day 4, the patient was conscious, oriented, and afebrile, with normal pulse rate and a blood pressure of 100/70 mm Hg measured in the right arm in the supine position. Cardiovascular and respiratory system examination were unremarkable. Abdominal examination showed a well-contracted uterus and caesarean wound was healing well. She was breast-feeding the baby and lochia rubra was normal. Packed red transfusion was done in view of moderate anaemia. Eight hours after the blood transfusion the patient complained of headache and had two episodes of vomiting. Her blood pressure was 120/80 mm Hg and pulse rate was 60/min. She was given tablet paracetamol 600 mg and Tab ondansetron 4 mg. One hour later, she had generalized tonic clonic convulsions in the ward. Her pulse rate was 134/min and blood pressure was 160/100 mm Hg. Urine albumin was negative and deep tendon reflexes were normal.

2.2 Investigations

Investigations (complete blood count, liver and renal function tests, coagulation profile) were sent and were found to be within normal limits. Blood sugar and serum electrolytes {Serum Ca++ 8.2, Na+ 138, K+3.7, Cl^- 96, HCO_3^- 21, Anion Gap = Na+ -(Cl^- + HCO_3^-)= 138-(96+21)=21} were within normal limits at the time of first convulsion. Urine albumin was nil. MRI (Magnetic Resonance Imaging) with MRV (Magnetic Resonance Venography) scans of the brain showed subtle small foci of FLAIR (FLuid Attenuated Inversion Recovery) increased intensity, involving bilateral parietooccipital parenchyma and left cerebellum. There was no intraparenchymal hemorrhage and no diffusion restriction (Fig. 1). Ophthalmology reference taken for fundus examination was suggestive of no papilledema.

2.3 Treatment

Intravenous MgSo4 dilution in normal saline was started as slow intravenous with infusion pump. Injection lorazepam 2 mg intramuscular was given. Tab nifedepine 10 mg oral was given. For around 5 hours post convulsion, the highest BP recorded was 130/100 mm Hg. She was further managed in the intensive care unit (ICU). Injection magnesium sulphate was continued. Oral Nifedipine were continued. She had no sensory or motor deficits and no cerebellar signs. Neurologist advised to start injection Mannitol 100 mg intravenous three times a day, Injection Dexamethasone 4 mg twice a day and injection phenytoin 100 mg three times a day. Blood pressure stabilized and normalized gradually to 130/90 mm Hg. Injection MgSO4 was stopped 24 hours after the convulsion.

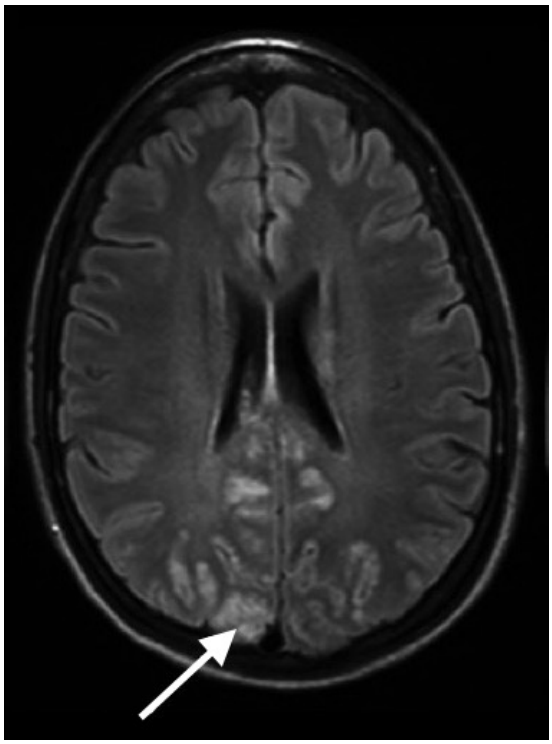

Fig. 1. Magnetic resonance image showing small foci of FLAIR increased intensity, involving bilateral parieto-occipital parenchyma and left cerebellum

2.4 Follow Up

She did not convulse again and she had no residual neurological deficits on discharge. Phenytoin is not required in a case of PRES and nonrecurring post partum convulsions and hence was tapered off after MRI MRV showed no lesions suggestive of other causes of convulsions. Dexamethasone and mannitol were indicated in our patient as they have a role in subcortical cerebral edema and PRES. Single dose benzodiazepine was given only for post ictal confusion. She was discharged on tablet phenytoin, and nifedipine and tablet prednisolone, which were gradually tapered.

3. DISCUSSION

The incidence of PRES in post partum eclampsia is obscure with only a few case reports [3]. The drug of choice for control of seizures in post partum eclampsia is magnesium sulphate. Compared to other anticonvulsant agents, magnesium sulphate is neuroprotective and also reduces the risk ratio of recurrence of seizures [4]. After endothelial dysfunction, first there is minimal leak leading to cerebral edema and hypertensive crises and, later there is massive leak leading to intracranial haemorrhage. Dexamethasone improves the microcirculation in Blood Brain Barrier (BBB). As an anti-inflammatory, it reduces the cytokines and chemokines that cause BBB breakdown. Moreover dexamethasone increases the levels of Angiopoitein I, which stabilise the BBB structure and decreases the level of VEGF in astrocyte and pericyte through glucocorticoid activation. In addition, Dexamethasone has been shown to decrease the trans monolayer para cellular permeability by increasing the tight junction regulating proteins such as Zonula Occludens-1 and Occludin in cultured brain endothelial cells in animal models. Mannitol is thought to decrease brain volume by decreasing overall water content, to reduce blood volume by vasoconstriction, to reduce CSF volume by decreasing water content. Mannitol may also improve cerebral perfusion by decreasing viscosity or altering red blood cell rheology. Lastly, mannitol may exert a protective effect against biochemical injury [5]. Phenytoin acts on the motor cortex where the spread of seizure activity is inhibited by inhibiting the Sustained high frequency Repetitive Firing (SRF) of action potentials. Benzodiazepines modify SRF and postsynaptic GABA (Gamma amino butyric acid) mediated transmission [6].

Our patient had a sudden rise in blood pressure from 110/70 to 160/100 mm Hg. The criterion of only an increase in blood pressure is no longer used in the definition of preeclampsia [7]. However, a concept of “delta hypertension” is being emphasized in modern obstetrics. This refers to a sudden increase in blood pressure in otherwise normotensive women during late pregnancy, labor and postpartum period [8]. Delta hypertension has been proven to have higher incidence of readmission in postpartum period with severe preeclampsia/ eclampsia. Eclamptic patients with high mean arterial pressure had been shown to have adverse neurological outcomes.

Our patient had a neurological complication, namely “Posterior Reversible encephalopathy Syndrome”. A term coined by Hinchey et al., is described as the presence of neurological and radiological signs, with associated confusion, headaches, arousal problems, occasionally coma, visual disturbances and generalized seizures [9].

In our patient, the highest blood pressure recording was of 160/100 mm Hg. Though hypertensive emergencies and eclampsia are characteristic causes of PRES, it can occur in seemingly normotensive patients also. While PRES commonly occurs at term, extremely rare cases presenting during the first trimester as a complication of hydatidiform mole [10] and also in late postpartum period [11] have been described.

The patient had the classical neuro-radiological findings of PRES that is reversible vasogenic subcortical edema without infarction in MRI MRV. MRI brain is superior to CT brain in identifying the typical abnormalities of PRES.

The “Vasogenic theory” or the “Hyperperfusion theory” hypothesizes that when severe hypertension exceeds the physiological limits of auto regulation, breakthrough brain edema occurs, precipitating the condition. There is lack of sympathetic innervation of vessels emanating from basilar and vertebral arteries (posterior brain). The elevated capillary filtration pressure damages the capillary vessels in the posterior brain; this increases the permeability of the blood brain barrier leading to cerebral edema [12,13,14]. The posterior circulation is preferentially affected. Owing to this, visual disturbances may be a common phenomenon.

This theory states that chronic hypertensives have hypertrophic arterial walls and the permeability of blood brain barrier is less. The pregnant preeclampsia patients have sudden rise in blood pressure and they do not have hypertrophic arterial walls. Thus even a sudden rise in blood pressure with hyper dynamic circulation can cause them to respond with increased permeability of blood brain barrier thus the “Vasogenic theory” is likely in our patient. The radiological imaging in our patient showed more posterior involvement than anterior involvement, the anterior involvement, is more classical of PRES due to malignant etiologies rather than obstetric etiology [15].

However, “the cytotoxic theory” that was earlier postulated can explain PRES in a nonhypertensive patient. It is believed that any stress in the form of transplant, sepsis, autoimmune diseases, immunosuppressant therapy can led to cerebral auto regulatory vasoconstriction and in turn led to ischemia, finally resulting in brain edema. This is supported by the fact that Posterior reversible encephalopathy is also seen in patients without hypertension. The most common conditions are post transplant, during immunosuppressant treatment, sepsis, auto immune diseases and during cancer chemotherapy [16,17,18].

There exists a beneficial effect of magnesium sulphate in PRES also. Naidu et al. studied cerebral artery flow velocity waveforms using ultrasonography by trans-temporal approach. They determined that the waveforms suggested a significant reduction in cerebral vasospasm among those treated with magnesium sulphate than when compared to other anticonvulsant medications.

During Pregnancy there is a change in vascular function. Table 1 compares the differenences in the concentrations of vascular mediaters in preeclampsia as compared to normal pregnancy (Table 1). The likely etiology of post partum preeclampsia is hyper dynamic circulation. There may be inadequate mobilization of liquid from the interstitial and intravascular to extravascular space (6-8 liters of the total body water, return of 950 mEq of total body sodium accumulated during pregnancy). Several factors lead to increased urinary sodium excretion between three and five days after birth (increase of atrial natriuretic peptide in the first week after delivery, natriuresis and inhibition of aldosterone, angiotensin II, vasopressin). These changes can be documented by monitoring Central venous pressure, pulmonary capillary wedge pressure and colloid osmotic pressure in the peurperium [19].

In the edematous brain, the excessive accumulation of extracellular fluid results in elevation of intracranial pressure, leading to impaired nerve function. Vasogenic edema is defined as extracellular accumulation of fluid resulting from the disruption of the Blood Brain Barrier and extravasation of serum proteins. Cytotoxic edema on the other hand is characterized by cell swelling caused by intracellular accumulation of fluid. Many soluble factors and functional molecules have been confirmed to induce BBB disruption. In our patient, MRI brain T2 signal intensity was used to differentiate between vasogenic and cytotoxic edema. The increased ADC (Apparent Diffusion Coefficient) T2 values in our patient reflectthe development of vasogenic edema. Reduced ADC value in MRI correlate with cytotoxic edema. In Preeclampsia the likely cause is

Table 1. The reported concentrations of vascular mediators in preeclampsia patients as compared to normal pregnancy

Substance	Vasoactive effect	Measured metabolite (M)	Concentration
Prostaglandin I2	Vasodilation	Peripheral blood / Urine M, Placental production M	Decreased
Thromboxane	Vasoconstriction	Peripheral blood / Urine M, Placental production M	Increased
Renin, Aldosterone, Angiotensin II	Vasoconstriction	Peripheral blood	Decreased
Endothelium derived hyperpolarising factor	Vasodilation		?
Endothelin	Vasoconstriction	Peripheral blood/ Uterine vein	Increased
Nitric oxide	Vasodilation	Peripheral blood/ Urine M	Increased/Decreased/ No change
Catecholamines	Vasoconstriction	Peripheral blood/ Urine M	Increased/Decreased
Atrial natriuretic peptide	Vasodilation	Peripheral blood	Increased
Vascular endothelial growth factor	Vasoconstriction	Peripheral blood	Increased/Decreased

increased endothelial damage and capillary leak leading to posterior brain vasogenic edema. Endothelial dysfunction usually improves after delivery. While our patient had cerebral edema four days post partum. The convulsions manifested after blood transfusion, but the possibility of cytotoxic cerebral edema was ruled out by MRI which clearly demonstrated vasogenic posterior cerebral subcortical edema. The unique point is that an increased cardiac load due to blood transfusion might have precipitated a cascade of events leading to endothelial dysfunction and leaky blood brain barrier.

Another point of interest is that recently it is being hypothesized that placenta is a casualty rather than the cause of preeclampsia [20]. Increased VEGF secreted from maternal decidual natural killer cells after implantation as a response to superadded uteroplacental circulation leads to leaky capillaries, low oncotic pressure and high blood viscosity induced vasoconstriction, and hence placental ischaemia. The ischemic placenta secretes sFLT (soluble fms like tyrosine kinase) and sEng (soluble endoglin), which tries to mop the excessive VEGF and TGF respectively by binding it [21]. sFLT (soluble fms like tyrosine kinase) and sENG (soluble ENDOGLIN) are decoy molecules that trap the available growth factors. The molecule sFLT is a free floating variant of FLT-1.FLT 1 is a receptor –a docking point of Vascular Endothelial Growth Factor (VEGF) and Placental Growth Factor (PLGF) in the vessel wall. Endoglin receptor on the vessel wall is a docking point of Transforming growth factor β. The free circulating levels of sENG act as a decoy diverting TGF β away from vessels. In our post partum patient, there was no sflt and sEng to bind the VEGF and TGF released in response to increased blood volume. This might have lead to VEGF and TGF induced leaky capillaries, vasoconstriction, vasogenic cerebral edema and convulsions.

The control of the blood pressure or of the offending disease process results in the complete resolution with no sequel and this can be identified by repeat neuroimaging after 2 weeks. Recurrence of PRES is not common, but increasingly in recent years, studies demonstrate recurrence of this syndrome in populations with different diseases. The likely cause of low birth weight and oligohydramnios is moderate maternal iron deficiency anemia, which was confirmed by peripheral smear and low serum ferritin levels [22].

4. CONCLUSION

This case highlights the importance of blood pressure monitoring in the postpartum state. The above case is atypical postpartum eclampsia with PRES, likely explained by hyper dynamic circulation, delta hypertension and vasogenic theory. PRES is reversible, has classical clinico-radiological features in MRI and has good prognosis with treatment.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this paper and accompanying images'.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ACKNOWLEDGEMENT

All authors hereby thank the Department of Emergency Medicine, Department of Neurology, Department of Transfusion Medicine and Department of neonatology for the care given to the patient and newborn.

All authors hereby thank the Department of Radiology for conducting the Magnetic Resonance Imaging with Magnetic resonance venography in the patient. We thank the staff of Department of Biochemistry and Department of Pathology. We also thank the staff of labour room, blood bank, operating room and intensive care unit.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. Am J Obstet Gynecol. 2009; 200:481.e1-481.
2. Banks WA. Characteristics of compounds that cross the blood-brain barrier. BMC Neurology. 2009;9(Suppl 1):S3. DOI: 10.1186/1471-2377-9-S1-S3
3. Ülkü Mete Ural, Gülsah Balik, Şenol Şentürk, Işık Üstüner, Uğur Çobanoğlu, Figen Kır Şahin. Posterior reversible encephalopathy syndrome in a postpartum preeclamptic woman without seizure. Case Reports in Obstetrics and Gynecology; 2014. Article ID 657903, 3 pages. DOI: 10.1155/2014/657903
4. Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database Syst Rev. 2010;10:CD000128.
5. Diringer MN, Scalfani MT, Zazulia AR, Videen TO, Dhar R, Powers WJ. Effect of mannitol on cerebral blood volume in patients with head injury. Neurosurgery. 2012;70(5):1215–1219. Available:http://doi.org/10.1227/NEU.0b013e3182417bc2
6. Erwin Sigel, Michael E. Steinmann. Structure, function and modulation of $GABA_A$ receptors. Journal of Biological Chemistry; 2012. DOI: 10.1074/jbc.R112.386664
7. Dekker G. Hypertension. In James D, Steer PJ, Weiner CP, Gonik B, Crowther CA, Robson SC, editors. High-risk pregnancy. Management options. 4th ed. Missouri: Elsevier Saunders. 2011;800.
8. Cunningham FG. Obstetrical hemorrhage. In Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BS, editors. Williams' obstetrics. 24th ed. New York: McGraw Hill. 2014;729.
9. Ait S, Gilbert T, Cotton F, Bonnefoy M. Cortical blindness and posterior reversible encephalopathy syndrome in an older patient. BMJ Case Rep. May 26; 2012. Available:http://www.ncbi.nlm.nih.gov/pubmed/22669215
10. Ottanelli S, Simeone S, Serena C, Rambaldi MP, Villanucci A, Tavella K, et al. Hydatidiform mole as a cause of eclampsia in the first trimester: A case report. Pregnancy Hypertension An Int J Women's Cardiovasc Heal. 2012;2(3): 304.

11. Rijal JP, Giri S, Dawadi S, Dahal K V. Posterior reversible encephalopathy syndrome (PRES) in a patient with late postpartum eclampsia. BMJ Case Rep [Internet]; 2014.
Available:http://www.ncbi.nlm.nih.gov/pubmed/24577180
12. Cipolla MI. Cerebrovasular function in pregnancy eclampsia. Hypertension. 2007; 50:14-24
13. Pedraza R, Mrik PE, Varon J. Posterior reversible encephalopathy syndrome: A review. Crit. Care Shock. 2009;12:135-143.
14. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: Controversies surrounding the pathophysiology of vasogenic edema. AJNR Am J Neuroradiology. 2008;29: 1043-1049
15. Liman TG, Bohner G, Heuschmann PU, Scheel M, Endres M, Siebert E. Clinical and radiological differences in posterior reversible encephalopathy syndrome between patients with preeclampsia eclampsia and other predisposing diseases. Eur. J. Neurol. 2012;19:935-943.
16. Fugate JE, Classen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: Associated clinical and radiological findings. Mayo Clin. Proc. 2010;85:427-432.
17. Lamy C, Oppenheim C, Mas JL. Posterior reversible encephalopathy syndrome. Handb Clin Neurol. 2014;121:1687-701.
18. Cozzolino M, Bianchi C, Mariani G, Marchi L, Fambrini M, Mecacci F. Therapy and differential diagnosis of posterior reversible encephalopathy syndrome (PRES) during pregnancy and postpartum. Arch Gynecol Obstet. 2015;292(6):1217–23.
19. Magee Laura, von Dadelszen Peter. Prevention and treatment of postpartum hypertension. Cochrane Database of Systematic Reviews. In: The Cochrane Library, Issue 11, Art. No. CD004351.
DOI: 10.1002/14651858.CD004351.pub1
20. James M Roberts, Carl A. Hubel. The two-stage model of preeclampsia: Variations on the theme. Placenta. 2009; 30(Supple A):S32–S37.
DOI: 10.1016/j.placenta.2008.11.009
21. Davaasambuu Enkhmaa, Danielle Wall, Puja K. Mehta, Jennifer J. Stuart, Janet Wilson Rich-Edwards, Noel Bairey Merz C, Chrisandra Shufelt. Preeclampsia and vascular function: A window to future cardiovascular disease risk. Journal of Women's Health. 2016;25:3.
DOI: 10.1089/jwh.2015.5414
22. Md. Mizanaur Rahman. Maternal anaemia and risk of adverse birth and health outcomes in low and middle income countries: Systematic review and meta-analysis. Am J Clin Nutr. 2016;103(2):495-504.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/20213