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Case Report

Obstetrics and Gynaecology Section

Very Early Onset Severe Preeclampsia and Eclampsia Syndrome with Posterior Reversible Encephalopathy Syndrome- A Catastrophe

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ABSTRACT

Early onset severe preeclampsia and eclampsia is a direct cause in the deadly triad of maternal mortality along with haemorrhage and sepsis with high perinatal mortality. Antiphospholipid Syndrome (APS) with Recurrent Pregnancy Loss (RPL) may also result in early onset severe preeclampsia, eclampsia and its catastrophic complications. Present report is a rarest case of a 33-year-old, unbooked G6A5 at 21+4 weeks gestation with eclampsia, HELLP (Haemolysis, Elevated liver Enzymes, Low Platelet count) syndrome, Posterior Reversible Encephalopathy Syndrome (PRES), Intrauterine foetal demise (IUFD) with RPL due to APS with Hepatitis B positive status. Patient was managed by a multidisciplinary team of Obstetricians, Intensivists, Cardiologists and Neurologists. Eclampsia was managed with magnesium sulphate (Pritchard's regime), intravenous labetalol and delivery of stillborn male foetus weighing 645 gm achieved within 24 hours of eclamptic seizure. Lupus anticoagulant and beta-2 glycoprotein IgM (Immnoglobulin M) antibodies were positive in high titres confirming APS. Postdelivery patient had persistent headache with blurring of vision. A diagnosis of PRES was confirmed on Magnetic Resonance Imaging (MRI) brain. Patient was put on Levetiracetam and low molecular weight heparin and was discharged in satisfactory condition on seventh postpartum day with an advice to follow-up at two weeks, six weeks and 12 weeks. Early onset preeclampsia is encountered in Obstetrics but very early onset severe preeclampsia (<24 weeks of gestation) and eclampsia with HELLP syndrome, PRES in a patient of RPL due to APS is rarest. Early diagnosis of APS and early onset preeclampsia with timely referral to tertiary care and multidisciplinary management can save women from severe dreaded complications with a good obstetric outcome in future.

Keywords: Antiphospholipid syndrome, Hypertensive disorders of pregnancy, Intrauterine foetal demise, Recurrent pregnancy loss

CASE REPORT

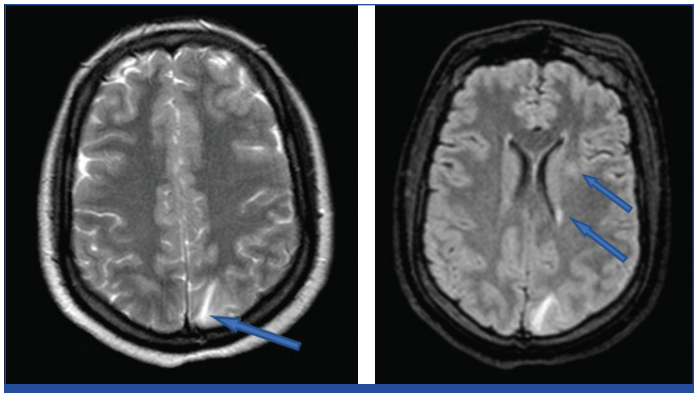
A 33-year-old, unbooked, G6A5 referred to emergency obstetric unit of a tertiary care hospital in rural Haryana with multiple episodes of seizures and high Blood Pressure (BP) after receiving loading dose of magnesium sulphate and intravenous Labetalol at level II care. She had previous five consecutive miscarriages at 8-10 weeks gestation. There was no history of any known chronic medical illness, drug intake, substance abuse or history of any significant disease in family.

On examination, patient was irritable, confused responding to verbal commands. Patient had tongue bite, massive facial, abdominal and pedal oedema. Pulse rate was 110/min and BP- 190/120 mm of Hg. She had a further episode of seizure on admission. Airway, breathing and circulation were established. Additional intravenous loading dose of magnesium sulphate (2 gm of 20% magnesium sulphate) followed by maintenance dose as per Pritchard's regime was given [1]. Intravenous Labetalol 20 mg-40 mg-40 mg was repeated after every 10 minutes to tide over acute hypertensive crisis. On catheterisation, 100 mL of cola-coloured urine was drained. On local examination, uterus was relaxed, non tense and non tender. Symphysio-fundal height was 22 cm, foetal heart sound was not audible by foetal Doppler. Cervix was uneffaced, long and tubular.

Investigations: Blood group- B positive, Hb- 16 gm/dL, Total Leucocyte Count (TLC)- 15,200 per mm^3, Platelet count- 98,000/µL (low), Lactate Dehydrogenase (LDH)- 1397 U/L (highly raised), Aspartate Transaminase (AST)-159 IU/L (raised), Alanine Transaminase (ALT)-138 IU/L (raised). Blood urea- 23 mg/dL and serum creatinine- 0.59 mg/dL, serum uric acid level- 11.9 mg/dL (raised). Urine albumin (dipstick)-2+ and 24-hour urinary protein-920 mg. HbsAg was positive. ECG and fundus examination- normal. Antiphospholipid syndrome screen was positive: Lupus anticoagulant test- positive, beta 2 glycoprotein 1 antibody levels- IgA-50 GPL/mL (Immunoglobulin phospholipid Units/mL), IgM- 20 GPL/mL. Ultrasound (USG) confirmed IUFD of 21 weeks gestation with no evidence of any retroplacental clot. Cervical length was 3.5 cm. Maternal renal artery doppler was normal with normal liver architecture. No suprarenal mass was found.

A diagnosis of a 33-year-old, unbooked G6A5 at 21+4 weeks gestation with severe very early onset preeclampsia, eclampsia, HELLP syndrome, IUFD with RPL with APS was confirmed. Induction of labour was done with vaginal misoprostol (Prostaglandin E1). Patient delivered stillborn male foetus weighing 645 gm with no gross morphological abnormality within 24 hours of seizures. Areas of haemorrhage, infarction and calcification were reported on histopathological examination of placenta. Postdelivery, patient was conscious with blurred vision and confusion. Headache was persistent and intractable to treatment. Neurology consultation and MRI brain confirmed diagnosis of PRES [Table/Fig-1,2]. Low molecular weight heparin (Inj. Enoxaparin 40 mg s/c OD) was started along with anti-epileptic (Inj. Levetiracetam 1 mg i.v. stat followed by tablet levetiracetam 500 mg BD) and Ecospirin 150 mg OD. Antihypertensive were (Tablet labetalol 200 mg TDS and Tab Amlodipine 5 mg BD) continued.

Patient recovered well with complete resolution of clinical and laboratory parameters by day six postpartum and was discharged in satisfactory condition. Follow-up was done in postpartum and neurology clinic at two, six, and 12 weeks. Repeat APL screen at 12 weeks was positive confirming the diagnosis of APS. USG (TVS 3D) ruled out any uterine malformation.



[Table/Fig-1]: White matter t2 flair hyperintensities are seen in bilateral occipital lobe (l>r). **[Table/Fig-2]:** Posterior limb of left internal capsule and posterior part of left lentiform nucleus. (Images from left to right)

DISCUSSION

Hypertensive disorders, form a deadly triad of maternal mortality as a direct cause along with haemorrhage and sepsis [2]. Preeclampsia and eclampsia affect 2-8% of pregnancies globally [3]. Early onset preeclampsia develops before 34 weeks of gestation and is usually associated with catastrophic maternal and foetal complications such as eclampsia, HELLP syndrome, prematurity, and foetal growth restriction and stillbirth. Many authors consider early-onset as a part of severity of preeclampsia [4,5].

Although very early onset preeclampsia has not been defined with definite cut-offs for gestational age, most of the studies in literature identify different cut-offs ranging from 22 weeks to 26 weeks [6,7]. Only occasional cases of very early onset severe preeclampsia, eclampsia have been reported in literature [Table/Fig-3] [5-11]. In a 10 year study, at a tertiary university referral centre at Rotterdam, only 26 women could fit the criteria of preeclampsia onset before 24 weeks of gestation in a decade which was termed as very early onset preeclampsia [6]. This also points towards the rarity of occurrence of very early onset preeclampsia, severe preeclampsia and eclampsia before 24 weeks.

Eclampsia and HELLP syndrome are markers of high maternal mortality, an indication for immediate termination of pregnancy. HELLP syndrome is found in 5-20% of women with preeclampsia [10]. Data on HELLP with very early onset preeclampsia is scarce which is attributable to the rarity of this condition before 24 weeks [11-13]. Foetal outcome is adversely affected. In a multicentre study, the foetal outcomes in severe early onset preeclampsia including babies from 22-26 weeks of gestation were poor with 84% of babies suffering from complications [7].

The case reports available in literature at earlier gestations have ascribed the occurrence of very early preeclampsia to causes such as pre-existing hypertension with superimposed preeclampsia, APS, thrombophilia, excessive liquorice intake other than more known causes such as molar pregnancy and multiple pregnancy [8,9,13].

The APS is a systemic autoimmune disorder characterised by venous or arterial thrombosis and/or pregnancy loss in presence of persistent antiphospholipid antibodies [12]. In index case, APS may not only be a cause for RPL, but also a strong risk factor for very early onset severe preeclampsia, eclampsia, PRES and IUFD.

The PRES, an acute neurological disorder occurs due to inability of posterior cerebral circulation to autoregulate in response to acute changes in blood pressure which leads to disruption of blood brain barrier causing vasogenic oedema in brain [13]. It is rare but a known complication of severe preeclampsia, eclampsia. Other underlying causes are acute renal failure, autoimmune disorders such as Systemic Lupus Erythematosus (SLE) and Guillain-Barre Syndrome, neoplasias, bone marrow transplant, solid organ transplant (immunosuppressive drugs), sickle cell anaemia and blood transfusion [14]. PRES should be kept in differential diagnosis while evaluating a patient whose neurological symptoms do not improve even after treatment of severe preeclampsia and eclampsia as in present case. If diagnosed and treated promptly, prognosis of PRES is better than many other encephalopathies.

S. No.	Study	No. of cases	Maternal age (years)	Gestational age	Maternal complications during course of disease and obstetric outcome	Evaluation/Associated conditions reported
1.	Gaugler-Senden IP et al., (2006) [5]- Audit	26	31 (median)	<24 wk	HELLP syndrome- 61.5% Eclampsia- 19.2% Pulmonary oedema- 15.4% Maternal death-3.8% Perinatal mortality- 82%	Chronic Hypertension (55%)
2.	Connor K et al., (2013)- Case report [9]	1	38	21 wk	HELLP syndrome TOP* (Previable)	Negative screen for APS
3.	Berry E and Iqbal SN (2014)- Case report [10]	1	41	17 wk+6 days	HELLP syndrome, AKI†, Pleural effusion, Placental abruption, IUFD‡ TOP (Previable)	Negative screen for APS and complement factors and TTP§
4.	Hauksdottir D et al., (2015)- Case report [7]	1	18	18 wk	HELLP syndrome TOP (Previable)	Excessive liquorice consumption
5.	Rotshehker-Olshinka K et al., (2016)- Case report [8]	1	40	17 wk	Uncontrolled BP TOP (Previable)	Grand Multipara
6.	Van Oostward MF et al., (2017) Case series [6]	<26 wks- 133 Subset: <24 wks- 61	-	<26 wk	HELLP syndrome- 32% Eclampsia- 3% Pulmonary oedema- 8.5% Renal failure- 0.8% Liver capsule rupture-0.8% Placental Abruption-3.8% Foetal survival-19% <24 wks survival rate-6.6%	Chronic Hypertension, SLE‖, Thrombophilia, Renal disease, Pulmonary disease, Diabetes, Coronary diseases, Autoimmune diseases, Haemoglobinopathies, Thyroid disorders.
7.	Kascak P et al., (2017)- Case report [11]	1 case- Two consecutive pregnancies	36 40	21 wk+3 days 21 wk+2 days	HELLP syndrome TOP (Previable -280 gm) HELLP syndrome TOP (non viable -455 gm)	Heterozygous for Factor V Leiden mutation
8.	Present case report	1 case	33	21 wk+4 days	HELLP Syndrome PRES** ‡IUFD TOP (645 gm stillborn)	APS screen positive

[Table/Fig-3]: Review of literature on very early onset preeclampsia and eclampsia [5-11].
*TOP: Termination of pregnancy; †Acute kidney Injury; ‡Intrauterine foetal demise; §Thrombotic thrombocytopenic purpura; ‖Systemic lupus erythematosus; **Posterior reversible encephalopathy syndrome; APS: Antiphospholipid syndrome; BP: Blood pressure

CONCLUSION(S)

Women with history of RPL, severe early onset preeclampsia, eclampsia, IUGR and IUFD should be screened for antiphospholipid antibodies and any other underlying causes such as chronic renal disease, chronic hypertension and other autoimmune diseases. High index of suspicion for underlying medical disorders, prompt intervention with multidisciplinary management at tertiary care is lifesaving for mother and may contribute towards better foeto-maternal outcome.

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