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CASE REPORT

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An unusual presentation of severe preeclampsia presenting with maternal collapse in the post-cesarean section secondary to drug toxicity associated with pituitary hemorrhage: a case report

Krishna Mylavarapu Kumar[1*], Shyam Madabushi[1], Amit Lall[1] and Pranjali D. Dwivedi[2]

Abstract

Background Severe preeclampsia presenting with maternal collapse post-cesarean section secondary to drug toxicity associated with pituitary hemorrhage is rare.

Case presentation A 24-year-old primigravida 27 weeks of gestation presented with severe preeclampsia, and underwent emergency cesarean section; postoperatively, she had a sudden maternal collapse and cardiac arrest while on labetalol and magnesium infusion. Following the return of spontaneous circulation (ROSC), the patient was found to have severe bradycardia with prolonged QTc interval and recurrent hypoglycemic episodes. Investigations had revealed low serum cortisol with the brain showing pituitary hemorrhage with features of atypical Sheehan's syndrome without lactation failure.

Conclusions Drug toxicity is an important cause of maternal collapse and cardiac arrest. Pituitary hemorrhage needs to be suspected in maternal patients with recurrent hypoglycemic episodes with or without postpartum hemorrhage (PPH). Continuous monitoring, use of maternal early warning scoring systems (MEWS), and prudence in the perioperative period/labor room will help in reducing the complications.

Keywords Pituitary hemorrhage, Maternal collapse, Sheehan's syndrome

Background

Maternal collapse can occur during any stage of pregnancy and up to 6 weeks after delivery. It usually involves the cardiorespiratory/central nervous system resulting in reduced or absent consciousness and may even result in death. Acute pituitary hemorrhage associated with maternal collapse secondary to drug toxicity is rare.

Case presentation

Prior informed consent was taken from the patient with approval from the hospital ethics committee to publish this case report. A 24-year-old primigravida at 27 weeks and 4 days of gestational age, with a body mass index (BMI) of 22.5 kg/m^2, was referred to our tertiary care center with severe preeclampsia.

The patient's blood pressure was poorly controlled on oral labetalol. Investigations revealed massive proteinuria (urine albumin 4+) with features of HELLP syndrome

*Correspondence:
Krishna Mylavarapu Kumar
krishnakm312@gmail.com
[1] Department of Anaesthesiology & Critical Care, Army Hospital Research and Referral Delhi Cantt, New Delhi 110010, India
[2] Department of Obstetrics and Gynaecology, Army Hospital Research and Referral Delhi Cantt, New Delhi 110010, India

(hemolysis, elevated liver enzymes, and low platelet count). Serum lactate dehydrogenase (LDH)-574 IU/l, serum (aspartate transaminase/alanine transaminase) AST/ALT-171/184 IU/l, and platelets were 70,000/mm^3, respectively.

An emergency lower segment cesarean section (LSCS) was done under general anesthesia (GA) at 28-week POG for hypertensive crisis and a non-reassuring fetal nonstress test (NST) with an impending abruption of the placenta. Her blood pressure remained high (180/130 mmHg–190/138 mmHg with a heart rate of 90–100/min) during the perioperative period, and there was a blood loss of 450 ml during the surgery. A female child weighing 657 g was delivered. Intravenous labetalol infusion at 30 mg/h was started during the intraoperative period for optimizing the blood pressure, and the mother was successfully extubated uneventfully in the postoperative period and was transferred to maternal HDU (high-dependency unit). Magnesium sulfate infusion was started as per the Zuspan regimen (4-g i.v. in 100-ml NS over 20 min) along with labetalol infusion with continuous electrocardiogram (ECG) and urine output monitoring. Twenty minutes post-magnesium sulfate infusion, the patient became unresponsive, with an absent carotid pulse and asystole.

The code blue team was activated, and the patient was resuscitated with cardiopulmonary resuscitation (CPR) as per the advanced cardiac life support (ACLS) protocol with chest compressions and i.v. adrenaline boluses repeated every 3 min, and the trachea was intubated. Eclampsia/intracerebral hemorrhage/drug toxicity (β-blocker and hypermagnesemia) was suspected as the likely etiology of cardiac arrest. Intravenous calcium gluconate 3 g was given for suspected magnesium toxicity. A return of spontaneous circulation (ROSC) was achieved after 15 min of resuscitation.

A point-of-care ultrasound (POCUS) was done for evaluation of sudden collapse. 2D echocardiography showed normal left ventricular function with no RA/RV (right atrium/right ventricular dilation) or pericardial collection. A lung scan ruled out pneumothorax. There was no evidence of deep vein thrombosis in the lower limbs, and abdominal scanning showed a minimal fluid collection in the pouch of Douglas. There was no obvious bleeding from the operated site or per vagina. Pupils were dilated and unresponsive initially but were responding after 12-h post-resuscitation. Targeted temperature management (TTM) at 36 °C was done by external cooling measures. The patient was placed on mechanical ventilation with sedation and muscle relaxation for 24 h. Post-ROSC, the patient had stable hemodynamics with ECG showing persistent bradycardia (*HR*: 30–35/min) with prolonged QTc interval (526 ms) (see Fig. 1) which responded transiently to i.v. atropine.

Drug toxicity with magnesium and labetalol overdose was suspected, and both infusions were stopped. Serum magnesium level after 1-h post-ROSC was 7.1 mg/dl. Acute hemodialysis (HD) was done to reduce the magnesium levels (3.4 mg/dL post 3 h of dialysis) following which the heart rate (70/min) and the QTc (480 ms) were stabilized. A temporary pacemaker though kept standby was not contemplated as the heart rate had remained normal post-dialysis. She had recurrent hypoglycemic episodes which were managed with an intravenous infusion of 50% dextrose.

Clinical investigations included a complete endocrine workup that was done after ICU admission are shown in Table 1.

The serum cortisol, LH, and FSH were low, with elevated insulin levels. A primary adrenal failure (secondary to hemorrhage) with the involvement of the HPA (hypothalamic–pituitary–adrenal) axis was suspected. The patient was started on i.v. hydrocortisone which corrected her hypoglycemic episodes. Non-contrast computed tomography (CT) imaging of the brain and abdomen was done which showed pituitary hemorrhage with a normal CT abdomen (Fig. 2). Magnetic resonance imaging (MRI) T1-weighted images (Fig. 2) of the brain confirmed the findings.

A diagnosis of pituitary hemorrhage with atypical features of Sheehan's syndrome was made as there was no lactation failure. The neonate delivered had developed sepsis with acute respiratory distress syndrome (ARDS) and necrotizing enterocolitis (NEC) which was managed with surfactant, antibiotics, continuous-positive pressure ventilation (CPAP), and intra-abdominal drain.

The patient was successfully extubated after 36 h on mechanical ventilation without any residual neurological deficits and was followed up for 3-month duration during the above period the neonate was in the neonatal intensive care unit (NICU). Steroids were tapered and stopped after 3 months. Currently, both the mother and child were discharged with regular follow-ups.

Discussion

An electronic search was done between January 1990 and June 2022 for the atypical presentation of Sheehan's syndromefollowing post-maternal cardiovascular collapse with nil available literature. The most probable cause of cardiac arrest in our patient could be the simultaneous use of intravenous labetalol and magnesium, both of which are known to cause severe bradycardia and prolongation of the QTc interval (Bennett et al. 2014; Choi et al. 2008). Though labetalol is poorly dialyzable, following hemodialysis, there was a significant reduction in serum

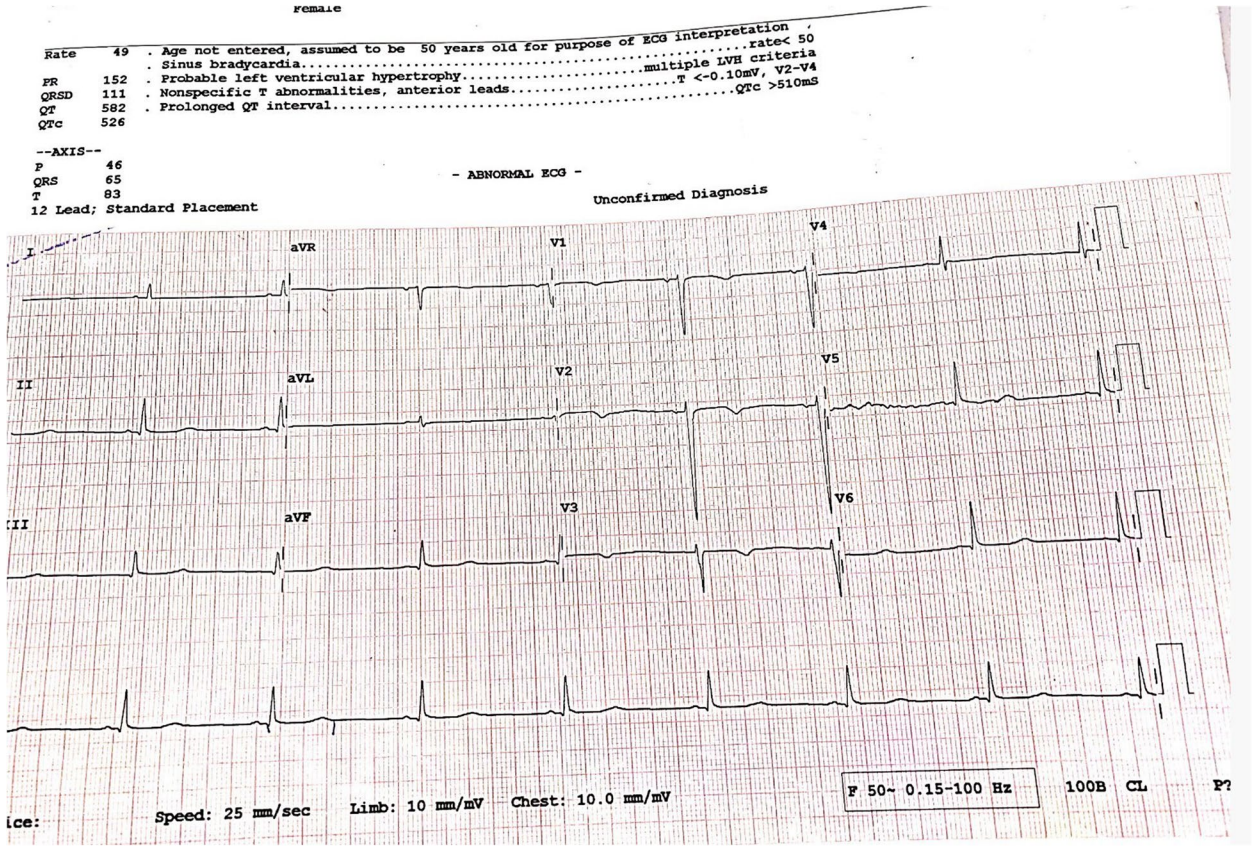

Fig. 1 ECG showing prolonged QTc interval

Table 1 ICU admission investigations with serum hormone levels

Parameter	Lab value	Normal range
Hb	10.6 g/dl	11.5–13.5 g/dl
Platelets	63 × 10^3/µl	150–400 µl
BUN/creatinine	20 mg/dl/0.77 mg/dl	7–20/0.2–1.3 mg/dl
AST/ALT/ALP	127 U/l/83 U/l/127 U/l	15–37/4–50/46–126
LDH	574 U/l	100–290
Sodium	139 mmol/l	135–145 mmol/dl
Potassium	3.6 mmol/l	3.5–5.5 mmol/dl
Random blood sugar	**54 mg/dl**	**80–120 mg/dl**
Triiodothyronine (T3)	2.93 pg/ml	2.0–4.4 pg/ml
Thyroxine T4	1.18 ng/dl	0.8–1.8 ng/dl
TSH	4.22 mIU/ml	0.5–5.0 mIU/ml
S. cortisol	**11.50 µg/dl**	**20–28 µg/dl**
S. insulin	**25.5 mIU/ml**	**3.21–16.32 mIU/ml**
Insulin-like growth factor 1	47.46 ng/ml	18.1–49.1 ng/ml
Leutinizing hormone (LH)	0.20 mIU/l	2.0–9.0 mIU/l
Follicle-stimulating hormone (FSH)	0.25 mIU/l	1.8–11.2 mIU/l
Prolactin	**335 ng/ml**	**80–400 ng/ml**

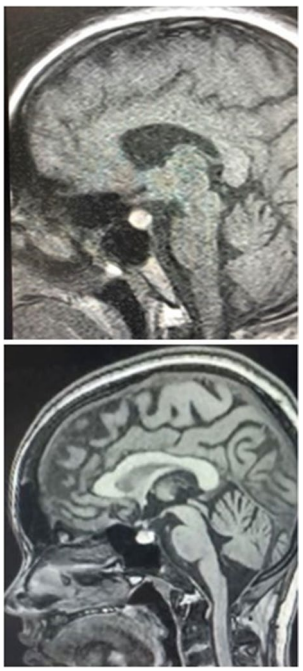

Fig. 2 NCCT and MRI T1 sagittal images of the brain

magnesium levels with clinical improvement in the heart rate and QTc interval (Tella et al. 2022).

Recurrent hypoglycemic episodes raised the suspicion of cortisol insufficiency secondary to adrenal/pituitary hemorrhage. A hormonal workup (see Table 1) along with the NCCT brain, abdomen, and MRI brain imaging was done to rule out intracerebral/pituitary/adrenal gland hemorrhage (Diri et al. 2014). Our patient did not have the classical features of Sheehan's syndrome which is usually seen after massive postpartum hemorrhage (PPH) with shock. The syndrome may be asymptomatic with long periods of latency until the person is exposed to stressful conditions in life, e.g., surgery or infection, and usually manifests clinically as acute adrenal insufficiency (Ramiandrasoa et al. 2013).

The symptoms of Sheehan's syndrome following pituitary hemorrhage secondary to PPH may present with acute life-threatening symptoms such as severe hypotension which may be associated with lactational failure, amenorrhea, hematological, and neuropsychiatric disturbances, where the diagnosis is straightforward or it may present as partial deficiencies specific to the particular anterior pituitary hormonal deficiency, such as an insufficiency of prolactin and gonadotropin hormone may present as lactation failure and amenorrhea respectively. Adreno-corticotrophin insufficiency may present with nausea, headache, fatigue, weakness, or hypoglycemia, while growth hormone deficiency may manifest as severe fatigue and weight loss. Patients may also develop features of hypothyroidism with low T3 or T4 levels and normal or low TSH levels (Diri et al. 2014; Karaca et al. 2010).

Furthermore, there could be a delay in diagnosing Sheehan's syndrome and clinical signs with some studies showing a mean delay of 3 ± 2.5 months for lactational failure, 8.3 ± 8 years for amenorrhea, 8.5 ± 8.1 years for hypothyroidism, and 10.6 ± 9.4 years for acute adrenal insufficiency, respectively (Ramiandrasoa et al. 2013). Laboratory tests usually reveal hyponatremia secondary to hypothyroidism, panhypopituitarism, glucocorticoid insufficiency, and decreased free water clearance (Özkan and Colak 2005).

Radiological imaging such as an MRI of the pituitary gland remains a very sensitive diagnostic tool with late scans typically showing an *empty sella*which is considered the classical finding in Sheehan's syndrome (Kaplun et al. 2008).

In our patient, the diagnosis was confounded by severe preeclampsia with HELLP syndrome followed by sudden maternal collapse with cardiac arrest in the postoperative period which was attributed to the drugs used for controlling blood pressure(β-blockers) and for prophylaxis of eclampsia (magnesium sulfate). There was no postpartum hemorrhage or hypotension other than during the period of cardiac arrest and resuscitation. Recurrent episodes of hypoglycemia in the post-ROSC period had raised the suspicion of adrenal/pituitary gland insult. The classical symptomatology such as lactation failure, and hypotension which may be typically seen in Sheehan's syndrome, was absent in our patient which made the clinical diagnosis challenging.

The use of continuous ECG monitoring in the postoperative period as the use of maternal early warning scoring (MEWS) in the HDU/labor room for the signs of maternal collapse helped in identifying cardiac arrest (Chu et al. 2020).

Conclusions

Clinicians caring for pregnant mothers should be aware of the possibility of drug toxicity as the cause of the maternal collapse and atypical presentation of Sheehan's syndrome which may be present with/without postpartum hemorrhage.

Abbreviations

ROSC	Return of spontaneous circulation
QTc interval	QT segment of the ECG
PPH	Postpartum hemorrhage
MEWS	Maternal early warning scoring systems
POG	Period of gestation
BMI	Body mass index
HELLP	Hemolysis, elevated liver enzymes, and low platelet count syndrome
LDH	Lactate dehydrogenase

AST/ALT	Aspartate transaminase/alanine transaminase
CPR	Cardiopulmonary resuscitation
ACLS	Advanced cardiac life support
GA	General anesthesia
LSCS	Lower segment cesarean section
NST	Nonstress test
POCUS	Point-of-care ultrasound
TTM	Targeted temperature management
HPA	Hypothalamic-pituitary-adrenal axis
ARDS	Acute respiratory distress syndrome
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NCCT	Non-contrast computerized tomography
MRI	Magnetic resonance imaging

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(a) Dept. of Anaesthesiology, Army Hospital Research and Referral, New Delhi, India, 110010, and (b) Dept. of Obstetrics and Gynaecology, Army Hospital Research and Referral, New Delhi, India, 110010.

Authors' contributions
Primary author KMK was involved in managing the case, obtaining permissions, data entry, collecting, reference managing, and writing the article. The second author SM was involved in collecting and editing the data, the third author AL was involved in presenting and collecting the data, and the fourth author PDD was involved in collecting the data. All authors have read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
The Army Hospital Research and Referral, New Delhi, 110010, Institutional Ethical Committee approval was taken. Written informed consent was taken from the patient.

Consent for publication
Written informed consent was taken from the "study participant" to publish.

Competing interests
The authors declare that they have no competing interests.

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