International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Jha N et al. Int J Reprod Contracept Obstet Gynecol. 2022 Apr;11(4):1296-1299
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20220922

Case Report

Co-existence of hypertensive urgency and hemolysis elevated liver enzymes and low platelets syndrome in a parturient with myasthenia gravis: a therapeutic challenge

Nivedita Jha*, Divya Bhukya, Shruthi Shreenivas Subhedhar, Sasirekha Rengaraj, Haritha Sagili, Veena P.

Department of Obstetrics and Gynaecology, JIPMER, Puducherry, India

Received: 01 February 2022
Accepted: 05 March 2022

***Correspondence:**
Dr. Nivedita Jha,
E-mail: dr.niveditajha@gmail.com

ABSTRACT

Hemolysis elevated liver enzymes and low platelets (HELLP syndrome) is an obstetric emergency developed in the settings of hypertensive disorder of pregnancy and it is associated with a heightened risk of adverse fetomaternal outcomes. Obstetric and anaesthetic management is indeed challenging in HELLP syndrome. The presence of myasthenia gravis further complicates the managements issues in these women. Here, in this report, we describe a 35 years G2P1L1 known case of myasthenia gravis, who presented in emergency with uncontrolled hypertension, imminent eclampsia and HELLP syndrome at 29+1 weeks of gestation. Antihypertensive medication included hydralazine, alpha methyldopa, infusions of labetolol and nitroglycerine. She underwent successful vaginal delivery using fentanyl as labour analgesia. Prompt decision making using multidisciplinary team appeared vital in controlling the hypertension adequately and quickly without aggravating myasthenic crisis.

Keywords: HELLP syndrome, Myasthenia gravis, Pregnancy, Preeclampsia, Multidisciplinary approach

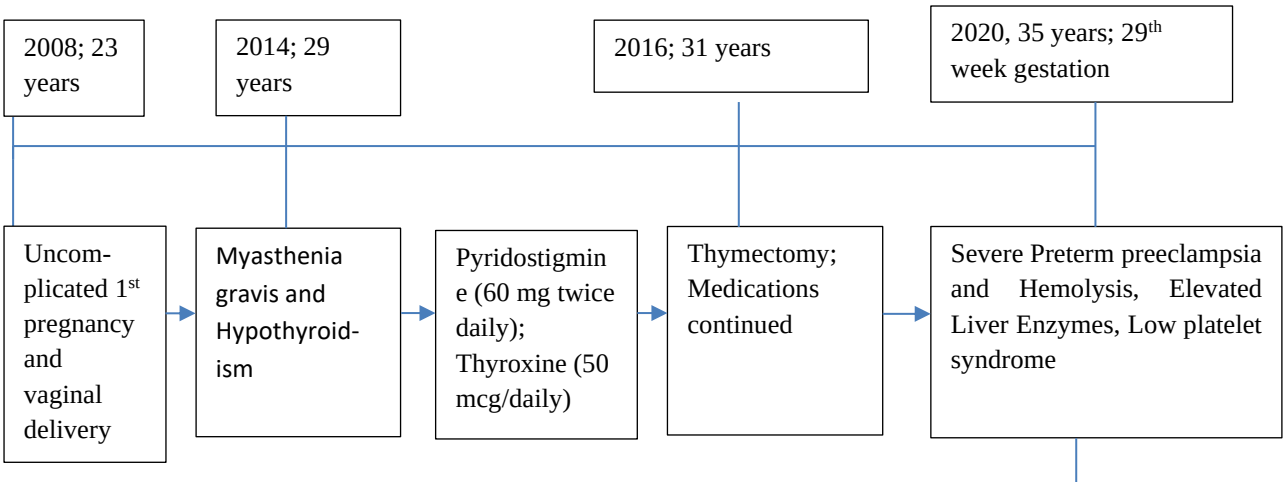
INTRODUCTION

Hypertensive disorder complicates 5-10% of all pregnancies globally and is associated with considerable maternal and fetal morbidity and mortality.[1] HELLP syndrome develops in 10-20% of severe preeclampsia and is characterised by hemolysis, elevated liver enzymes and low platelet count.[2] Myasthenia gravis is a neuromuscular disorder and commonly involves ocular, bulbar, limb and respiratory muscles. Recent reports from Asia quoted an incidence of 5-7 per 20,000.[3,4] However, the presence of these two entities in a parturient has been rarely reported. Herein this report we have described a 35 years G2P1L1 a known case myasthenia gravis presenting in emergency with uncontrolled hypertension and had laboratory features of HELLP syndrome. Myasthenia may remit, relapse or remain unchanged during the course of pregnancy. However, several stressors namely labour pains, medication, hypertension, surgical stress may precipitate myasthenic crisis towards the end of pregnancy.[5] Moreover, HELLP syndrome may require urgent termination of pregnancy to improve fetomaternal outcomes.[6] Therefore, in this complex scenario, clinical and therapeutic decision making becomes challenging. In this report, we have briefly described the case which had a successful maternal outcome.

CASE REPORT

A 35 years gravida 2, para 1, live 1 at 29+1 weeks of pregnancy was referred from a rural hospital to our emergency obstetric department with complaints of headache for 1 day. She had an uncomplicated pregnancy and vaginal delivery 12 years back. She was diagnosed with myasthenia gravis 6 years ago and she underwent thymectomy 2 years later. She was taking oral

pyridostigmine (60 mg twice daily) since diagnosis of myasthenia gravis. She also had hypothyroidism and was receiving thyroxine (50 mcg once daily). However, she did not have any specific sign and symptom of hypothyroidism and her thyroid profile was normal at the time of presentation in our hospital (Figure 1). On examination, she was alert, conscious and oriented. Physical examination revealed bilateral pedal edema, blood pressure of 190/120 mm Hg. Neurological examination revealed bilateral ptosis and reduced muscle power in both upper and lower limbs (4/5) and hyperreflexia.



Laboratory parameters	1st Day	2nd Day	3rd Day
Hb (gm/dl)	13.5	13.6	14.5
TLC (cells/µl)	16730	21810	15740
Platelet count(cells/µl)	1.70	78000	1.08
Urea (mg/dl)	23	44	23
Creatinine (mg/dl)	0.53	0.6	0.58
Total bilirubin (mg/dl)	0.22	0.42	0.22
Direct bilirubin (mg/dl)	0.02	0.07	0.03
Total protein (g/dl)	5.3	4.7	5.1
Albumin (g/dl)	2.3	2	2.3
Aspartate aminotransferase/alanine aminotransferase (units/l)	69/55	131/134	29/73
Na+/K+/Cl (meq/l)	128/4.38/98	130/4.4/102	137/3.93
TSH (mIU/l)	3.12		

Figure 1: Time line of presentation.

This was a spontaneous conception and she was compliant with all her medications. She had hypertension first detected at 27 weeks (150/100 mm Hg), along with proteinuria (3+ on spot urinalysis) and was on oral labetalol 100 mg 12th hourly and subsequently dose increased to 200 mg 8th hourly. Escalating boluses of intravenous labetalol (20-40 mg) were administered on her arrival to the emergency department. Laboratory investigations included hemoglobin-14.5 g/dl and platelet count of 70×10^3 cells/ µL with increased liver enzymes [aspartate aminotransferase (AST) of 131 IU/L and alanine aminotransferase (ALT) of 134 IU/L]. There were schitocytes in peripheral smear. She also had nephrotic range proteinuria (6 gm/24 hours). Rest of the systemic examination and relevant laboratory investigations were unremarkable. Fetal surveillance showed single live intrauterine fetus in cephalic presentation with estimated fetal weight of 887 grams and stage 2 fetal growth restriction (FGR). Intravenous labetalol (30 mg/hr) could not lower the mean blood pressure below 100 mmHg. Her mean blood pressure remained above 130 mmHg and she required hydralazine (20 mg 12th hourly) and oral methyldopa (500 mg 12th hourly) in addition to intravenous labetalol. An invasive arterial line was secured. Nitroglycerin (NTG) infusion was initiated to target the MAP between 80- and 100-mm Hg. Oral Leviteracetam (500 mg 12th hourly) was used for seizure prophylaxis. Betamethasone was administered for fetal lung maturity. Multidisciplinary team (comprising obstetrician, anesthesiologist, neonatologist, cardiologist and neurologist) decided to terminate the pregnancy after steroid cover. Laboratory parameters repeated on the day of induction revealed haemoglobin 11 g/dl, platelet count of 60×10^3 cells/ µL, AST of 210 IU/L and ALT of 190 IU. Labour was induced with extra amniotic saline infusion (EASI). Intrapartum MAP remained above 110 mm Hg despite NTG infusion rate of 2 mcg/kg/hour. Patient received intravenous bolus doses of fentanyl (25-50 mcg)

for labour analgesia. After EASI induction and oxytocin augmentation patient had uneventful vaginal delivery of a live female baby of weighing 880 grams with APGAR of 7 and 8 at 1 and 5 minutes, respectively. The baby was shifted to neonatal intensive care unit for further care. In early postpartum period MAP dropped to 100 mm Hg and all intravenous antihypertensive medications were tapered. Subsequently she was put on oral enalapril 12.5 mg once daily. Patient was discharged on postnatal day 7 with prescription of oral enalapril 2.5 mg OD, Eltroxin 50 mcg OD, Pyridostigmine 60 mg BD. Baby succumbed to neonatal sepsis on fifth day of life. The patient was doing well at six weeks postpartum and she no longer required antihypertensive medications. Furthermore, the patient provided written informed consent for publication of anonymized data during her 1st follow up visit to our hospital.

DISCUSSION

HELLP syndrome in a parturient with myasthenia gravis and hypothyroidism has been rarely reported. Therefore, a relevant clinical history, examination and detailed work up become pertinent to ensure proper management in such a scenario. Moreover, a detailed consideration of drug pharmacokinetics and pharmacodynamics is essential to ensure amelioration of signs and symptoms in a timely manner. HELLP syndrome in the presence of refractory systemic hypertension may culminate into rapid deterioration of several vital organs. Only a few selective drugs are available to treat severe preeclampsia with hypertensive crisis. Myasthenia gravis further narrows down our choice of antihypertensive and antiseizure medications.[7] Magnesium sulfate, calcium channel blockers and beta blockers are known to aggravate myasthenia. In this case we used hydralazine, alpha methyldopa, sodium nitroglycerine and intravenous labetalol to combat hypertensive crisis. Despite these antihypertensive measures we struggled to control the blood pressure adequately and therefore the multidisciplinary team decided to terminate the pregnancy. Myasthenia poses unique challenges during vaginal as well as caesarean delivery.[8] Physical stress, emotional stress, labour pain and inadequate expulsive efforts may pose hurdles in successful vaginal delivery.[9] Additionally, epidural catheter as a choice of labour analgesia in this patient with HELLP syndrome could not have been an appropriate option. Choice of anaesthesia for caesarean delivery still seems an unsettled issue. Regional anaesthesia is usually contraindicated in thrombocytopenia and coagulopathy and it may delay the motor recovery.[10] Similarly, use of muscle relaxant and endotracheal intubation during general anaesthesia may lead to failed extubation and prolonged mechanical ventilation.[11] We used fentanyl boluses in our patient and fortunately she had an uncomplicated spontaneous vaginal delivery.

The clinical course of myasthenia gravis in pregnancy is variable, with an improvement of symptoms in 29% of pregnancies, worsening in 41%, and no change in 30%.[12] The first trimester and immediate postpartum period are the times of highest risk of exacerbation. Longer the duration of myasthenia before pregnancy, lesser are the chances of worsening during pregnancy with highest risk of mortality within the first year after disease onset.[13] The diagnosis and management of exacerbation of myasthenia in pregnancy is similar to non-pregnant women. However, several drugs which are used to treat other medical complications of pregnancy may aggravate myasthenia (Table 1). Prompt recognition of crisis and management is mandatory and both intravenous immunoglobulin and plasma exchange can safely be offered during pregnancy.

Table 1: Medications associated with exacerbations of myasthenia gravis.

Magnesium salts	Magnesium sulfate
Ophthalmic solutions	Timolol and tropicamide
Anti-arrhythmic drugs	Procainamide and quinidine
Inhalation and local anesthetic agents	Isoflurane, halothane, bupivacaine, lidocaine, and procaine
Calcium channel blockers	Amlodipine, nifedipine, and verapamil
β-blockers	Atenolol, propranolol, nadolol
Aminoglycosides	Gentamycin, clindamycin, streptomycin
Macrolides	Azithromycin and erythromycin
Fluoroquinolones	Ciprofloxacin and levofloxacin
Steroids	High doses of steroids
Antiepileptics	Phenytoin
Others	Thyroxine

Vaginal birth appears a safer option as the uterus is comprised of smooth muscles only and myasthenia affects striated muscles.[14] However, second stage of labour may require forceps or vacuum assistance due to inadequate expulsive efforts. Caesarean delivery may be considered for obstetric indication.

The American congress of obstetrics and gynecology suggests magnesium sulphate for seizure prophylaxis in preeclampsia.[15] However, magnesium impairs already slowed nerve-muscle contractions through a competitive mechanism involving calcium at the neuromuscular junction. Several other antiepileptic drugs namely phenytoin, levetiracetam, and diazepam may also be prescribed for seizure prophylaxis but they are not as effective as magnesium sulfate. We used levetiracetam as seizure prophylaxis as phenytoin is known to aggravate myasthenia. Levetiracetam is a relatively safe (Pregnancy risk category C) antiepileptic medication. Our patient did well and had no neurological signs and symptoms at six weeks follow up. Unfortunately, the baby succumbed to

prematurity and sepsis. Early delivery appeared inevitable because of refractory hypertension.

CONCLUSION

HELLP syndrome in a setting of myasthenia gravis is a clinical and therapeutic challenge and needs to be diagnosed early to provide multidisciplinary care. A proper medication chart, anaesthetic and delivery plan must be reinforced to avoid exacerbation of both of these complications in order to optimize fetomaternal outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Tesfa E, Nibret E, Gizaw ST, Zenebe Y, Mekonnen Z, Assefa S et al. Prevalence and determinants of hypertensive disorders of pregnancy in Ethiopia: A systematic review and meta-analysis. PLoS One. 2020;15(9):e0239048.
2. Alese MO, Moodley J, Naicker T. Preeclampsia and HELLP syndrome, the role of the liver. J Matern Fetal Neonatal Med. 2021;34(1):117-23.
3. Wen JC, Liu TC, Chen YH, Chen SF, Lin HC, Tsai WC. No increased risk of adverse pregnancy outcomes for women with myasthenia gravis: a nationwide population-based study. Eur J Neurol. 2009;16:889-94.
4. Qi QW, Wang D, Liu JT, Bian XM. Management of pregnancy with myasthenia gravis: 7 cases report. Zhonghua Fu Chan Ke ZaZhi. 2012;47:241-4.
5. Roche P, Bouhour F. Myasthenia gravis and pregnancy. Rev Neurol (Paris). 2021;177(3):215-9.
6. Lisonkova S, Razaz N, Sabr Y, Muraca GM, Boutin A, Mayer C et al. Maternal risk factors and adverse birth outcomes associated with HELLP syndrome: a population-based study. BJOG. 2020;127(10):1189-98.
7. Lake AJ, Al Khabbaz A, Keeney R. Severe Preeclampsia in the Setting of Myasthenia Gravis. Case Rep Obstetr Gynecol. 2017;2017:1-5.
8. Nicholls-Dempsey L, Czuzoj-Shulman N, Abenhaim HA. Maternal and neonatal outcomes among pregnant women with myasthenia gravis. J Perinat Med. 2020;48(8):793-8.
9. Hamel J, Ciafaloni E. An Update: Myasthenia Gravis and Pregnancy. Neurol Clin. 2018;36(2):355-65.
10. del-Rio-Vellosillo M, Garcia-Medina JJ. Anesthetic considerations in HELLP syndrome. Acta Anaesthesiol Scand. 2016;60(2):144-57.
11. Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. Acta Anaesthesiol Scand. 2012;56(1):17-22.
12. Varner M. Myasthenia gravis and pregnancy. Clin Obstet Gynecol. 2013;56(2):372-81.
13. Chaudhry SA, Vignarajah B, Koren G. Myasthenia gravis during pregnancy. Can Fam Physician. 2012;58:1346-9.
14. Djelmis J, Sostarko M, Mayer D, Ivanisevic M. Myasthenia gravis in pregnancy: report on 69 cases. Eur J Obstet Gynecol Reprod Biol. 2002;104(1):21-5.
15. Cohen BA, London RS, Goldstein PJ. Myasthenia gravis and preeclampsia. Obstet Gynecol 1976;48:35S-7.

Cite this article as: Jha N, Bhukya D, Subhedhar SS, Rengaraj S, Sagili H, Veena P. Co-existence of hypertensive urgency and hemolysis elevated liver enzymes and low platelets syndrome in a parturient with myasthenia gravis: a therapeutic challenge. Int J Reprod Contracept Obstet Gynecol 2022;11:1296-9.