

Case Report

Myasthenia Crisis in Pregnancy

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Introduction

Myasthenia Gravis (MG) is an autoimmune disorder of the neuromuscular junction characterized by fluctuating weakness of skeletal muscles. It is caused by autoantibodies against post synaptic acetylcholine receptor (AChR) [1].

In pregnancy, myasthenia gravis has both maternal and fetal implications, and can manifest in various degrees of weakness and fatigability of skeletal muscles. Respiratory failure is a life threatening complication of this rare disorder [2].

We present a rare case of myasthenia crisis with respiratory failure in pregnancy as well as a review of the available literature. We highlight the importance of a multispecialty approach in the management of myasthenia gravis in pregnancy. We also wish to highlight management issues in the postpartum and neonatal period.

The patient presented in this case provided informed written consent.

Case Report

A 29-year-old patient with Myasthenia Gravis presented with a myasthenia crisis resulting in respiratory depression at 32

weeks gestational age [3]. Her symptoms specifically included bulbar, limb, ocular and respiratory weakness. She required immediate intubation, mechanical ventilation and plasmapheresis.

Her MG diagnosis was made four years prior to this pregnancy. She had a history of one previous myasthenia crisis outside of pregnancy. This required admission to the intensive care unit. The patient had a history of poor compliance with medications, developmental delay, anorexia and a significant psychiatric history. Her myasthenia gravis was being managed with azathioprine, prednisone, IVIG and mestinon prior to pregnancy.

During pregnancy she was to continue with mestinon 60 mg three times daily, prednisone 20 mg daily and IVIG 1g/kg every two to four weeks, which was being managed by her neurologist. Unfortunately the patient was poorly adherent to this regimen. She developed progressive weakness during the week prior to presentation, which manifested predominately as dysphagia secondary to bulbar weakness.

Upon admission to our facility, she was in severe myasthenia crisis with respiratory failure at 32 weeks gestation [3]. She was immediately admitted to the intensive care unit for intubation and management. Her blood gases prior to intubation

were: pH 7.26/ pCO₂ 36/ pO₂ 32/ HCO₃ 16/base excess -10.0, with a calculated oxygen saturation of 51% and measured at 63%. A fetal ultrasound including cord dopplers and biophysical profile were normal on the day of presentation. During her admission she received plasmapheresis (PLEX), responding well after five doses and was eventually transitioned to prednisone and mestinon. Her blood work abnormalities consisted of a fibrinogen level of 0.8 and hemoglobin of 70, which were investigated and found to be secondary to the PLEX treatment. The patient was weaned from the ventilator after several days with close monitoring by both the intensive care and neurology team. Respiratory status was monitored by SVC (Slow Vital Capacity), MIPs (Maximum Inspiratory Pressure) and MEPs (Maximum Expiratory Pressure). Her MIPs and MEPs were below an absolute value of 15 during the first few days of admission with a significantly decreased SVC. Her SVC increased to 2.0 and her MIPS and MEPS were satisfactorily stable for extubation after several days. Monitoring continued by the neurology team. While in the intensive care unit she was closely followed by obstetrics with serial non-stress tests and obstetrical ultrasounds, which were found to be normal. She did have signs and symptoms of threatened preterm labour, which required close fetal and maternal monitoring.

She was transferred from the intensive care unit once she was extubated and remained in hospital under Neurology until she was full term. A decision was made to proceed with vaginal route of delivery, as she was compliant to medications allowing for a safe, controlled procedure for delivery. The only indication for a cesarean section in her context would have been due to fetal concerns. The patient was induced at 37 weeks to accomplish delivery while she was medically optimized. Throughout the course of her induction and labour she was stable. She obtained an epidural anesthetic. She had a prolonged passive second stage of labour. She had a successful vacuum-assisted vaginal delivery of a live female weighing 3102 grams with APGARS of 9 and 9 at one and five minutes respectively and did not show any signs of muscular weakness.

The patient had an uncomplicated postpartum period and was discharged home in stable condition with follow-up with her Obstetrician and Neurologist. Postpartum management of her myasthenia gravis consisted of IVIG to be reinitiated on a monthly basis, continuation of mestinon and prednisone with recommencement of Azathioprine. Thymectomy is planned following the puerperium.

Discussion

The management of MG in pregnancy requires a multispecialty team including a neurologist, maternal fetal medicine obstetrician, neonatologist and an obstetric anesthetist. Involvement of these should be ensured prenatally and during labor and delivery. The course of MG during gestation is highly variable and unpredictable and can change in subsequent pregnancies

[2]. Approximately one third of patients remain the same, one third improve and the remaining one third worsen [4,5]. Clinical dilemmas that may be faced by the neurologic and obstetrical teams can include: 1) appropriate method of delivery that would be safest for the patient given myasthenic crisis and 2) discussing treatment most appropriate for her myasthenia to stabilize/optimize in setting of impending labour.

Treatment of MG in Pregnancy

A neurologist and an obstetrician should see patients with MG relatively frequently throughout the pregnancy. Therapy must be chosen considering severity of disease and potential side effects on fetus [2]. Treatment of MG during pregnancy requires that women be educated to not over exert themselves to avoid unnecessary fatigue. Emotional stress and lack of sleep should be kept to minimum [6]. Oral anticholinesterases are the drug of choice for symptomatic treatment of MG [7]. (Class B)

Immunosuppressant drugs such as corticosteroids should be avoided in women with purely ocular symptoms or very mild generalized weakness [1,8]. Corticosteroid therapy presents little if any teratogen risk to fetus, and only slight increase in incidence of cleft palate has been reported [8]. IVIG has been proven to be effective and safe for deteriorating MG in pregnancy however it has been postulated that there may be an increased risk of venous thromboembolism due to higher risk of hyperviscosity and volume overload during pregnancy [1,2]. Mycophenolate mofetil, methotrexate and cyclophosphamide are contraindicated in pregnancy [2]. Azathioprine is not recommended in pregnancy as exposed fetuses are at increased risk of myelosuppression [9]. Due to the theoretical risk of thromboembolism with IVIG, PLEX was used in the above patient to treat her myasthenic crisis.

Hypoventilation is a risk during pregnancy because MG weakens respiratory muscles, which, in addition to the elevation of diaphragm caused by enlarging uterus, may cause reduced oxygenation [9]. Respiratory crises requiring mechanical ventilation constitute the most severe complications [2,9]. Therefore management of a myasthenia crisis requires careful monitoring in an intensive care setting [10]. Together with steroids, plasmapheresis should be used in pregnant women in myasthenia crisis. The literature suggests that this is safe during pregnancy [11]. Patients undergoing plasmapheresis should always be carefully monitored because complications may occur, such as hypovolemic reactions or allergies [1,11]. In addition, large hormone shifts may cause preterm delivery [11]. Risk of preterm birth may occur in the setting of congenital myasthenia, primarily as a consequence of associated polyhydramnios [1]. Screening for asymptomatic bacteriuria should be performed and appropriate treatment for urinary tract infections is required especially for patients on steroids [1,10].

Coexisting pre-eclampsia

It is rare that MG patients develop pre-eclampsia during pregnancy however the coexistence of these disorders may produce high degree of morbidity and mortality for both mother and fetus [12]. Of note the use of magnesium sulfate is contraindicated in patients with MG. Magnesium interferes with the neuromuscular transmission by inhibiting the release of acetylcholine. In addition, it may competitively block calcium entry at the motor nerve terminal thus potentiating the negative effects of MG on pregnancy.

Mode of Delivery

Generally, mode of delivery can be safely completed vaginally. MG does not affect uterine smooth muscle therefore the first stage of labor is not compromised. The second stage involves striated muscles, which are at risk for fatigue. The patient may become exhausted during labor and will require assistance with forceps or a vacuum [13]. Surgical delivery poses several risks for MG patients and should be reserved for patients with severe myasthenia exacerbation, myasthenia crisis and obstetrical indications. In the described case, since both surgical and vaginal delivery were associated with potential risks given her recent crisis, not one was clearly safer than the other, ultimately, the obstetrics team chose assisted vaginal delivery. Generally epidural anesthesia should be preferred and narcotic analgesia and muscle relaxants avoided [1,10].

Neonatal Care

Every newborn of MG mothers should be carefully monitored for signs of muscle weakness and impaired respiratory and bulbar function. It is not possible to predict the occurrence and severity of neonatal MG [10]. Placental transfer of IgG antibodies against fetal AChR can cause arthrogryposis multiplex congenital (AMC), a syndrome of multiple congenital joint contractures in utero from lack of fetal movement and abnormal joint formation [13]. Approximately 10-20% of infants born to MG women show signs of neonatal MG (NMG) [14]. Evidence suggests that there may be some correlation between maternal antibody levels and severity of NMG however this is not absolute [14]. Some literature suggests that alfa-fetoprotein (AFP) may be protective for newborns as it inhibits ACHR ab binding [15]. Neuromuscular symptoms in newborns manifest clinically within first 12 – 48 hours postpartum [1]. Fetal complications such as pulmonary hypoplasia, arthrogryposis congenital and nonspecific hyperbilirubinemia have been reported [1,10]. Therefore MG patients should be informed that though clinical state throughout pregnancy may have been stable, fetal complications might occur.

Post-partum monitoring

MG exacerbations may occur within the postpartum period. It

is important patients are seen by a physician within the first three weeks after delivery. Closer observation is recommended for infants of mothers with myasthenia gravis secondary to muscle-specific tyrosine kinase (MuSK) antibodies (which may be associated with early and more severe neonatal manifestations)[13].

Thymectomy has been recommended in certain populations for treatment of MG and is primary disease controlling modality. It has been shown that incidence of exacerbations are higher in nonthymectomized than thymectomized patients, while there is no difference in neonatal MG between the two groups [14]. Complete remission has been described in approximately 45% of thymectomized patients and clinical improvement is not noted until years after surgery. Therefore, women may undergo thymectomy after delivery as there is not enough evidence to suggest improved prognosis of MG during pregnancy [9,14]. Breastfeeding is not contraindicated in women taking cholinesterase inhibitors or prednisone, although it is suggested to avoid feeding for four hours after taking these medications [1,15].

Conclusion

Myasthenia Gravis can have an unpredictable course in pregnancy. Its peak lifetime incidence is in women of reproductive age. Respiratory insufficiency is a potentially life threatening complication of poorly controlled Myasthenia Gravis. An interdisciplinary approach including Obstetricians, Anaesthetists, Neurologists, Intensivists and Neonatologists is essential to optimize the outcome for both the woman and neonate.

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