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Myasthenia gravis and pregnancy: Lessons learned from a complex a case report

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Abstract

Myasthenia gravis primarily affects young adults, with a higher incidence in women, particularly between the ages of 20 and 30. When a young woman with myasthenia gravis contemplates pregnancy, healthcare providers must consider the potential implications. The interplay between hormonal factors and changes in the immune system establishes a complex relationship between myasthenia gravis and pregnancy. On one hand, pregnancy can alter the course of the disease, while on the other hand, the disease can impact the progression of the pregnancy and the well-being of the fetus. In this case report, we present the case of a 28-year-old woman suffering from myasthenia gravis who had undergone a thymectomy 5 years ago and was being treated with an acetylcholinesterase inhibitor. After a planned conception, the patient presented a relapse of her disease during the third trimester of pregnancy, with the onset of severe hydramnios. This observation highlights a specific case of decompensation of myasthenia gravis during pregnancy, associated with the presence of severe hydramnios. Subsequently, we delve into the existing literature to examine the reciprocal influence between myasthenia gravis and pregnancy, as well as the effects of anti-myasthenic treatments on pregnancy outcomes.

Keywords

Myasthenia gravis, pregnancy, obstetric outcomes, neonatal myasthenia

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Introduction

Myasthenia gravis (MG) is a chronic disease characterized by autoantibodies that target the acetylcholine receptor (AChR) or muscle kinase, leading to disturbances at the neuromuscular junction. MG patients experience fluctuating muscle weakness, mainly in the muscles of the eyes, limbs, face, and breathing.[1] Although this disease is rare, with a reported prevalence in the general population of 0.3–7.7 per 100,000 people, its prevalence is increasing in women aged between 20 and 30, which may have implications for pregnancy.[2] The course of MG during pregnancy is unpredictable, with a tendency for more frequent exacerbations in the first trimester and after delivery.[3] In this case report, we report a case of decompensation of MG during pregnancy in the context of severe hydramnios. Next, we explore the literature to study the reciprocal influence between MG and pregnancy.

Case report

We present the case of a 28-year-old patient, G2P1, whose first pregnancy went without a problem 5 years ago, with a vaginal delivery of a female infant with no abnormalities. However, the mother developed respiratory distress as a result of efforts to push during delivery. The diagnosis of MG was made on the basis of the presence of anti-AChR antibodies and the disappearance of symptoms following administration of pyridostigmine, an acetylcholinesterase inhibitor, together with an electromyogram showing a 20% reduction in amplitude after nerve stimulation. The patient was treated with pyridostigmine (Mestinon 60 mg) four tablets a day, azathioprine (Imurel 5 mg) three tablets a day, and prednisone (Cortancyl 5 mg) two tablets a day. Two years later, a thymectomy was performed.

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Following the expression of the desire to have a new pregnancy during a preconception consultation and after discussion with the neurologist, it was decided to stop taking pyridostigmine. After a period of 8 months, the patient became pregnant spontaneously. The obstetric team and the neurologist collaborated closely to monitor the patient's pregnancy progress regularly and comprehensively.

The pregnancy was uneventful until the 33rd week when a hydramnios was detected on routine ultrasound with an amniotic fluid index of 36 cm and a large cistern of 16 cm. There were no signs of hydrops, such as pleural effusions, ascites, or subcutaneous edema. No malformations were observed, and the placenta had a normal appearance. It is worth mentioning that throughout the pregnancy, the patient underwent three ultrasounds, all of which yielded normal results and showed no signs of fetal malformation.

The biophysical profile score, also known as the Manning score, indicated a normal value of 10.[4]

The Doppler values obtained were within the normal range. The umbilical Doppler resistance index was measured at 0.4, while the resistance index for the middle cerebral artery was 0.8. Additionally, the peak systolic velocity in the middle cerebral artery was recorded as 42 cm/s, which is considered normal, with a multiple of the median value of 0.9 ruling out fetal anemia.

The patient's blood pressure was normal, with no edema of the lower limbs or proteinuria.

The decision was made to admit the patient to the hospital for an etiological investigation, to perform lung maturation using corticosteroids, and to institute maternal-fetal monitoring. The patient's blood group was O Rh positive, and tests for irregular agglutinin were negative. She was immune to rubella and toxoplasmosis. Fasting glycemia and glucose tolerance tests were unremarkable. Serologies for syphilis, cytomegalovirus, and parvovirus B19 were negative. On the 3rd day of hospitalization, the patient presented with muscular fatigue on exertion, with no sensory or sphincter disorders.

On general examination, the patient was hemodynamically and respiratory stable, and neurological examination revealed a slight motor deficit in the pelvic girdle and proximal musculature of the lower limbs. A diagnosis of myasthenic decompensation was made, and pyridostigmine (Mestinon 60 mg) was reintroduced at a dose of four tablets per day. The patient showed a favorable evolution, with a satisfactory clinical recovery after 1 week.

At 36 weeks of pregnancy, the patient experienced a premature rupture of membranes, followed by spontaneous onset of labor. An amoxicillin-based antibiotic prophylaxis was instituted, and instrumental vaginal delivery (forceps) resulted in the birth of a girl weighing 2980 g, with an Apgar score of 7/10 at 1 min, then 10/10 at 5 min. Clinical examination revealed mild axial hypotonia and signs of respiratory struggle. No malformations or dysmorphia were noted, and the sucking reflex was present. The newborn was transferred to the neonatal unit, where his mild respiratory distress improved on oxygen via nasal cannula.

At 24 h after birth, an evaluation for infectious disease was conducted, which included tests for C-reactive protein and complete blood count. The results of these tests came back negative. A transfontanellar ultrasound revealed no abnormalities. Although antibodies targeting the AChR were detected, the minimal symptoms of neonatal myasthenia did not require treatment with pyridostigmine. Artificial breastfeeding was recommended. The mother showed no signs of postpartum decompensation. On the fifth day, the mother and newborn were discharged from the hospital in good health. The patient was symptom-free after clinical follow-up every 3 months for 1 year.

Discussion

Pregnancy-related hormonal changes have an impact on the evolution of autoimmune diseases, influencing the course and outcome of gestation. Renal and pulmonary diseases, as well as arterial and venous thromboembolic disorders, play a crucial role in the vital prognosis of pregnant women and frequently lead to the loss of the fetus.

Among the autoimmune pathologies, we find MG, which has an unpredictable evolution and impact on pregnancy.

MG is a common disease that mainly affects the neuromuscular junction of skeletal muscles. It is characterized by fluctuating muscle weakness, which tends to be more pronounced in the afternoon. The muscles most often affected are those of the eyes, throat, and extremities. In the United States, the prevalence of MG is 20 cases per 100,000 population. MG is more common in women under the age of 40 and more common in men over the age of 50.[2]

In MG, the pathophysiologic mechanisms vary depending on the type of antibodies involved. In n-AChR MG, IgG1 and IgG3 antibodies bind to the n-ACh receptor in skeletal muscles, activating the complement system and leading to receptor degradation. They can also block ACh binding or enhance receptor endocytosis.[5] In MusK MG and LPR4 MG, IgG4 antibodies bind to the Agrin-LRP4-MuSK protein complex in the neuromuscular junction, leading to a decreased number of n-ACh receptors. This results in muscle weakness, particularly with repeated muscle use due to ACh depletion. These mechanisms contribute to the symptoms observed in MG.[6]

Pregnancy can have a significant impact on MG, with the risk of disease exacerbation reported to be between 30% and 45%.[7] Previous studies have indicated that exacerbations are more likely to occur during the first trimester of pregnancy and the postpartum period.[8] Myasthenic crisis, a serious and potentially fatal complication, has been observed in 6.4% of women during pregnancy and in 8.2% of women in the postpartum period. Common signs of an MG crisis include generalized muscle weakness, particularly in the muscles of the eyes, face, neck, and limbs. Other symptoms may include difficulty speaking, swallowing, breathing, excessive weakness, and impaired coordination.[3]

Preconception management of pregnant women with MG requires a multidisciplinary approach. Routine blood tests,

including measurement of AChR-Abs and MuSK antibodies, are recommended. The first-line treatment consists of acetylcholinesterase inhibitors, which must be adapted to the physiological changes associated with pregnancy. In cases where initial treatment is inadequate, corticosteroids may be considered. Immunosuppressive medications, such as azathioprine, may be contemplated as a potential course of action for individuals with refractory MG. During severe crises, the temporary administration of intravenous immunoglobulin or plasmapheresis can be considered.[9]

Pharmacological treatment is the mainstay of MG management. However, it may need to be modified during pregnancy, depending on the worsening of the disease. Acetylcholine esterase inhibitors such as pyridostigmine, IV Ig, azathioprine, steroids, and prednisolone are often used. Although data and information on acetylcholine esterase inhibitors in pregnancy are limited, none indicates an increased risk of malformation or other adverse pregnancy outcomes.[10] The role of thymectomy is debatable. It can be performed before or during pregnancy and can lead to remission of the disease in a significant number of patients, potentially reducing the need for immunosuppressants. However, the timing of thymectomy must be carefully considered to optimize benefits and minimize risks to mother and fetus.[11]

Ultrasound scans performed in the first trimester of pregnancy enable precise dating and assessment of the micromorphology of the fetus.[9]

An early fetal ultrasound carried out between 16 and 18 weeks is designed to detect the first signs of congenital arthrogryposis multiplex (CAM), which is the result of maternal antibodies targeting fetal receptors. This leads to joint contractures and reduced fetal movement.[12]

Given the ease with which anti-AChR antibodies cross the placenta during pregnancy, it is possible that the symptoms of MG appear in the fetus during the prenatal period. Severe cases of prenatal MG have manifested as polyhydramnios. This phenomenon seems to result from the absence of swallowing in the fetus, which can be confirmed by repeated ultrasound scans.[13]

Women with MG are not at increased risk of malformations, with the exception of CAM. A routine ultrasound scan in the second trimester can detect most major fetal anomalies. In the event of reduced fetal movements or a rapid increase in the size of the abdomen, ultrasound evaluation is recommended. Regular ultrasound scans every 2–4 weeks are recommended to monitor the growth, well-being, and movements of the fetus, as well as the amniotic fluid.[9]

The impact of MG on the risk of preterm labor and delivery has been controversial in the literature.[8,14]

Previous studies have produced contradictory results regarding the impact of MG on fetal growth. Some series have reported high rates of small for gestational-age fetuses,[15,16] while others have not observed this association.[7,17]

It is important to stratify the risk of pregnancy according to maternal and/or fetal complications rather than basing it solely on the MG. Vaginal delivery is preferred unless there are obstetric indications requiring a cesarean section. Local anesthesia, in particular epidural block, is preferred. Instrumental vaginal births are more common in mothers with gestational diabetes to avoid maternal fatigue.[18]

Mothers affected by MG have a risk of 10%–20% for their child to be born with transient neonatal MG. This risk is higher in women who experience exacerbations of myasthenic symptoms and in those who are reluctant to undergo treatment or have not undergone thymectomy.[19]

The course of MG during pregnancy is unpredictable. After childbirth, it may deteriorate. A postnatal consultation is essential to adapt treatments. Breastfeeding is not recommended for newborns with transient neonatal myasthenia gravis (TNMG). Anticholinesterase inhibitors are safe during breastfeeding. Mothers taking azathioprine or mycophenolate should avoid breastfeeding.[9]

Conclusion

MG in pregnancy can lead to serious life-threatening complications. Patients with MG require multidisciplinary management to ensure optimal therapy. The course of MG is sometimes unpredictable, but many pregnant women remain stable. MG does not significantly increase other complications of pregnancy. Approximately half of women with MG are able to give birth vaginally. The risk of CAM is less than 1%, and the risk of neonatal transmission of MG is 10%–20%.

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Author contributions

A.B. wrote the article, designed the project, analyzed the data, and contributed to the discussion of the article; A.B., Y.B., H.M., and J.K. treated the patient, gathered the patient's information, and supervised the project and research. All authors have read and approved the article. All the authors have accepted responsibility for the entire content of this submitted article and approved the submission.

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References

1. Li L, Xiong W-C and Mei L. Neuromuscular junction formation, aging, and disorders. *Ann Rev Physiol* 2018; 80: 159–188.
2. Jayam Trouth A, Dabi A, Solieman N, et al. Myasthenia gravis: a review. *Autoimmune Dis* 2012; 2012: 874680.
3. Banner H, Niles KM, Ryu M, et al. Myasthenia gravis in pregnancy: systematic review and case series. *Obstetr Med* 2022; 15(2): 108–117.
4. Manning FA, Morrison I, Lange IR, et al. Fetal assessment based on fetal biophysical profile scoring: experience in 12,620 referred high-risk pregnancies: I. Perinatal mortality by frequency and etiology. *Am J Obstetr Gynecol* 1985; 151(3): 343–350.
5. Verschuuren JJ, Huijbers MG, Plomp JJ, et al. Pathophysiology of myasthenia gravis with antibodies to the acetylcholine receptor, muscle-specific kinase and low-density lipoprotein receptor-related protein 4. *Autoimmununе Rev* 2013; 12(9): 918–923.
6. Conti-Fine BM, Milani M and Kaminski HJ. Myasthenia gravis: past, present, and future. *J Clin Investig* 2006; 116(11): 2843–2854.
7. Djelmis J, Sostarko M, Mayer D, et al. Myasthenia gravis in pregnancy: report on 69 cases. *Eur J Obstetr Gynecol Reprod Biol* 2002; 104(1): 21–25.
8. Tanacan A, Fadiloglu E, Ozten G, et al. Myasthenia gravis and pregnancy: retrospective evaluation of 27 pregnancies in a tertiary center and comparison with previous studies. *Irish J Med Sci (1971-)* 2019; 188: 1261–1267.
9. Cimpoca-Raptis BA, Ciobanu AM, Gica N, et al. Fetal surveillance in pregnancies with myasthenia gravis. *Medicina* 2021; 57(11): 1277.
10. Farmakidis C, Pasnoor M, Dimachkie MM, et al. Treatment of myasthenia gravis. *Neurol Clin* 2018; 36(2): 311–337.
11. Kumar L, Kachhadia MP, Kaur J, et al. Choices and challenges with treatment of myasthenia gravis in pregnancy: a systematic review. *Cureus*. 2023; 15(7): e42772.
12. Polizzi A, Huson S and Vincent A. Teratogen update: maternal myasthenia gravis as a cause of congenital arthrogryposis. *Teratology* 2000; 62(5): 332–341.
13. Verspyck E, Mandelbrot L, Dommergues M, et al. Myasthenia gravis with polyhydramnios in the fetus of an asymptomatic mother. *Prenatal Diagnosis* 1993; 13(6): 539–542.
14. Ducci RD, Lorenzoni PJ, Kay CS, et al. Clinical follow-up of pregnancy in myasthenia gravis patients. *Neuromusc Disord* 2017; 27(4): 352–357.
15. Qi Q-W, Wang D, Liu J-T, et al. Management of pregnancy with myasthenia gravis: 7 cases report. *Zhonghua fu chan ke za zhi* 2012; 47(4): 241–244.
16. Wen JC, Liu TC, Chen YH, et al. No increased risk of adverse pregnancy outcomes for women with myasthenia gravis: a nationwide population-based study. *Eur J Neurol* 2009; 16(8): 889–894.
17. Braga AC, Pinto C, Santos E, et al. Myasthenia gravis in pregnancy: experience of a portuguese center. *Muscle Nerve* 2016; 54(4): 715–720.
18. Almeida C, Coutinho E, Moreira D, et al. Myasthenia gravis and pregnancy: anaesthetic management–a series of cases. *Eur J Anaesthesiol| EJA* 2010; 27(11): 985–990.
19. Panaitescu AM and Nicolaides K. Maternal autoimmune disorders and fetal defects. *J Matern-Fetal Neonatal Med* 2018; 31(13): 1798–1806.