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Case Series

Myasthenia gravis in pregnancy: Successful outcome with multidisciplinary management

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ABSTRACT

Myasthenia gravis (MG) is a rare autoimmune disorder characterized by nicotinic acetylcholine receptor autoantibodies, affecting the neuromuscular transmission leading to progressive weakness. MG during pregnancy is a high-risk condition that may affect both the mother and the fetus leading to adverse perinatal outcomes. We are presenting clinical course of two pregnant women, one of them was already diagnosed case of MG and second was diagnosed during postpartum period while waiting for discharge of baby. Literature review of the previously published cases and their management is also presented.

1. Introduction

Myasthenia gravis (MG) is an antibody mediated disorder of the neuromuscular junction resulting in variable weakness of different muscles. Prevalence of MG ranges between 1 in 10,000 to 1 in 50,000 and almost 2/3 victims are females.[1] Women are commonly affected in their reproductive years in second and third decades of life and therefore, MG can impact pregnancy and perinatal outcome[2] We are presenting two cases of MG; one case was already a known case of MG and second one diagnosed during postpartum period. Literature review and role of interdisciplinary diagnostic and therapeutic management strategies adopted during pregnancy is also presented.

2. Case Report

2.1. Case 1

A 28 years old female G3P 0+1+1+0 with Rh negative, hypothyroidism and bronchial asthma presented in OPD at around 2 months amenorrhea. She developed high BP records around 10 weeks of gestation and was started on tablet labetalol 100 mg twice a day. At 29+3 weeks period of gestation (POG), patient presented with preterm premature rupture of membrane (PPROM) and underwent emergency pre-term lower segment cesarean section (PTLSCS) in view of anhydroamnios with breech presentation at 30 weeks POG. Intra-operative period was uneventful, and the baby was shifted to neonatal intensive care unit (NICU) in view of prematurity.

On postpartum day 7, patient complained of lower limb proximal muscle weakness. On leading questions, she accepted the history of proximal muscle weakness involving bilateral lower limbs for the last two years, but never get evaluated for this. In the post-partum period, symptoms progressed and she was even not able to walk and perform her daily routine activities due to the severe weakness in the lower limb muscles.

During investigations for proximal muscle weakness, creatinine phosphokinase (CPK) and LDH levels were within normal limits. The levels of anti-cholinergic receptor antibody (Ach-R-Ab) were found to be elevated with levels 16 mmol/L (normal value of <0.4 nmol/L). Electrophysiological studies (nerve conduction and

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electromyogram) revealed findings suggestive of post-synaptic nerve-muscle junction disorder. Repetitive nerve stimulation test (RNST) was suggestive of postsynaptic disorder. There was no involvement of facial, ocular, or bulbar muscles. With the diagnosis of MG, patient was started on oral pyridostigmine 60 mg thrice daily and dose increased to 90 mg four times a day due to partial response along with prednisolone tablet 10 mg once daily and tablet azathioprine 25 mg OD for 1 week followed by 50 mg once daily. Breast feeding was continued. The baby was evaluated for neonatal MG and there was no evidence of neonatal MG in the baby initially as well as over the period of time.

Patient was continuing with oral pyridostigmine tablet 90 mg 4 times a day and planned for thymectomy.

2.2. Case 2

26 years old, primigravida, known case of MG for the last one year, presented at 29 weeks with preeclampsia with severe features and stage 1 fetal growth restriction. Patient was Ach-R-Ab positive having predominant ocular and bulbar features and was on prednisolone 17.5 mg and 20 mg on alternate days and pyridostigmine 60 mg TDS for the same. The patient was initially started on tablet prazosin 2.5 mg BD and later tablet clonidine 0.1 mg OD was also added due to uncontrolled blood pressure records.

Patient underwent an emergency caesarean at 31 weeks POG in view of severe preeclampsia with partial HELLP syndrome. Patient was closely monitored by a multidisciplinary team of anesthetists, obstetricians, and neurologists. In the postoperative period, the patient had high BP records in the range of 220/120 mmHg and required nitroglycerine infusion (up to 3ml/hour) for 24 hours for blood pressure control, which was gradually tapered. She was shifted to oral prazosin 5 mg BD and arkamine 0.1 mg TDS. However, due to uncontrolled BP, she was started on a combination of isosorbide dinitrate (20 mg) and hydralazine (37.5 mg). Blood pressures was controlled, and subsequently, these drugs were tapered, and the patient switched to tablet telmisartan 40 mg OD. On POD-29, the patient had exacerbation of her symptoms, complained of increasing neck stiffness. On neurology evaluation, the patient had a single breath count of 26 with slight ptosis of the left eye, with diplopia on lateral gaze occurring in 55-60 sec. The dose of prednisolone was increased to 30 mg daily. The baby was closely monitored by the neonatology team, however, did not develop any signs of neonatal myasthenia at birth or after that. Currently, patient is not on any antihypertensives, and she is continuing with prednisolone and pyridostigmine.

3. Discussion

The present two cases describe the different presentations of MG during antenatal and postpartum period and their multidisciplinary management involving anesthesiologists, neonatologist, neurologists, and cardiologist.

3.1. Diagnosis

In all the suspected cases of MG, diagnosis needs to be confirmed either by immunological or electrodiagnostic testing. Seropositive MG are the patients who are positive for AChR-Ab and is a more common type of this disorder seen in 80% of patients. Both of our cases tested positive for AChR-Ab. Picone et al reviewed 13 cases and Djelmis et al reviewed 69 cases, all are positive for AChR-AB.[6,7]

3.2. The effect of pregnancy hormones on the disease

During pregnancy, distinct hormones with varied concentrations may affect the immune network for MG pathogenesis in bidirectional modulation effect. As compare to healthy controls, MG patients with anti-AChR/MuSK antibodies had low levels of galactosylated IgG2 (Immunoglobulin G2).[8] In contrast, galactosylation and sialylation of IgG1 and G2 rises during pregnancy and reach maximum levels in the third trimester and fall during postpartum period.[9] Regulatory B cells (Bregs) repress pro-inflammatory responses via interleukin 10 (IL-10), as Bregs are largely increses by the stimulation of estrogens via the PD-1/PD-L1 pathway from early pregnancy.[10] However, the pathogenic autoreactive B cells were reported to be boosted by Estrogens in the animal (mice) model of experimental autoimmune MG (EOMG).[11] One of the most abundant hormones during pregnancy, progesterone may inhibit the formation of interleukin-17 (IL-17) producing Th17 cells and increase the frequency of regulatory T cells (Tregs).[12] Other likely mechanisms included an inhibitory effect of alpha-fetoprotein (AFP) on the binding of autoantibody to the AChR in MG patients.

3.3. Clinical course of disease

Course of MG during pregnancy and its impact on pregnancy outcome are unpredictable. The disease course may show improvement in 29%, worsening of symptoms in 41% and may remain unchanged in 30% of patients.[1] Although possible at any state during pregnancy, it is more likely during the first trimester and the first month postpartum.[13,14]

Djelmis et al,[7] reviewed 69 cases of pregnant females suffering from MG and found clinical deterioration in 15%, a further 16% during puerperium, Tanacan et al, reviewed 27 pregnancies with MG[15] and found exacerbation in 25.9% of cases and Picone et al[6] reviewed 14 cases, exacerbation seen in 35% of cases.

Table 1: The case reports of MG in pregnancy reported from India

Author	Age (Years)	Known case of MG	Mode of delivery	Complication	Treatment	Neonatal MG
Sanwal et al (2012)[3]	28	+	LSCS (Obstetrical indication)	Developed muscular weakness along with ptosis, dysarthria, and dyspnea on third postoperative day	Pyridostigmine (120 mg three times a day) Dose increased	Present but resolved spontaneously
Sikka et al (2015)[4]	25	+	LSCS (Obstetric indication)	Severe pre-eclampsia	Injection neostigmine along with oral pyridostigmine and steroids.	No
Jaleel et al (2019)[5]	22	+	LSCS (Obstetric indication)	-	Oral pyridostigmine and steroids	No

In our both the cases patient had exacerbation of symptoms in postpartum period. Similarly, in the case reported by Berlit et al in 2012, patient (known case of MG) developed respiratory insufficiency on post-operative day 2 of elective lower segment cesarean section. She had developed myasthenic crisis followed by secondary generalized seizures with cardiac-circulatory arrest. Patient managed with interdisciplinary therapeutic approach and discharged in a stable condition.[2] Similarly a case reported by Robles et al in 2009, patient underwent LSCS and in immediate post-partum period she developed respiratory difficulty and hypoxemia but managed successfully with interdisciplinary approach.

3.4. Complications

MG in pregnancy has been associated with increased risk of miscarriage, preterm birth and premature rupture of membranes, LSCS and neonatal MG. In present cases, both the patients had preterm delivery less than 34 weeks and in our first case, patient presented with the PPROM at 29 weeks POG. Similarly in the case reported by Berlit et al, patient presented with PPROM.[2,16] In a retrospective study done by Tanacan et al[15] in 2019, they had evaluated 27 pregnancies with MG and showed that 14.8% of patients had PPROM, 11.8% had preterm birth and 14.8% had miscarriage. This study showed that the pregnancies with deterioration of disease were more likely to be associated with high chances of miscarriage, preterm birth, PPROM, CS and neonatal MG.

3.5. Treatment of MG

Management of MG includes multiple therapeutic strategies and approaches. It usually requires multidisciplinary approach comprising of obstetricians, neonatologist/pediatrician, neurologist with important contribution from the patient and her relatives.

The mainstay of MG treatment includes acetylcholinesterase enzyme inhibitors drugs for symptomatic relief as well as steroids and other immunosuppressant drugs. Medical treatment should not be changed in pregnancy. Anticholinesterase inhibitors have been safely used in pregnant patients with MG, and in 50% of patients, single-drug therapy is sufficient.[17] In our first case, patient initially started on tablet pyridostigmine (anticholinesterase inhibitor) but symptoms don't improved therefore, steroids and azthiopurine were added along with anticholinesterase inhibitor. In second case, patient was already on pyridostigmine and prednisolone, but the dose of prednisolone increased in post-partum period due to worsening of symptoms. Myasthenic crisis or severe acute exacerbations may require plasmapheresis or intravenous immunoglobulins along with ventilatory support.

3.6. Mode of delivery

Vaginal delivery is usually preferred as the uterus doesn't consist of striated muscles and is not affected by autoantibodies.[16] Cesarean section should be performed only for the obstetrical indication. In our cases, both the patients had emergency preterm caesarean section for obstetrics indication. Djelmis et al[7] in 2002 reviewed 69 cases of MG during pregnancy and 17% had cesarean section. Tanacan et al,[15] Cheng et al[16] and Picone et al[6] showed LSCS in 78%, 76% and 35% of cases respectively.

Very few case reports were reported from India. (Table 1)[3–5]

4. Conclusion

Myasthenia gravis especially when associated with pregnancy is a high-risk condition, and its pregnancy course is unpredictable. Both the mother and baby should be carefully monitored for the neuromuscular symptoms. As this disease is commonly seen in the reproductive age group, clinicians need to be aware of this condition and its multidisciplinary management which is the key to successful outcome.

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6. Conflict of Interest

None.

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