Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria

Submitted on: 09/26/2024
Approved on: 02/04/2025

CASE REPORT

Transient Neonatal Myasthenia Gravis: A Pediatric Case Report

Transient Neonatal Myasthenia Gravis: a pediatric case report

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Keywords:
Myasthenia Gravis, Myasthenia Gravis, Neonatal, Infant, Newborn, Diseases.

Abstract

Objective: Report the evolution of a newborn with Transient Neonatal Myasthenia Gravis in its first days of life, from a mother with Myasthenia Gravis. **Case report:** Female newborn, Apgar score of 7/9, birth weight of 2,490g, Capurro assessment at 36 weeks and 2 days, mother with myasthenia gravis. Presented at birth with weak crying and mild hypotonia. Was referred to the neonatal intensive care unit due to respiratory distress, with low intercostal retractions and difficulty maintaining oxygen saturation above 90%. Respiratory symptoms resolved within 8 hours at continuous positive airway pressure (CPAP). At the 12-hour physical examination, hypotonicity, decreased perioral mimicry, and absence of sucking reflex were noted, and Pyridostigmine was initiated as a therapeutic trial. After two days of medication use, symptoms improved. On the fifth day of life, the newborn exhibited good breastfeeding suction and appropriate weight gain, leading to subsequent hospital discharge with Pyridostigmine and outpatient follow-up. **Comments:** Transient neonatal myasthenia gravis (MG) is a rare condition that affects about 12 to 20% of newborns whose mothers have myasthenia gravis. This condition occurs due to the placental transfer of immunoglobulin G antibodies during gestation. Transient neonatal myasthenia gravis is a clinical diagnosis, presenting within the first 12 to 72 hours of life and usually does not require treatment. In this case, the patient was diagnosed clinically within the first 24 hours of life and showed a good response to pyridostigmine. Approved by the Ethics and Research Committee under CAAE 81212524.8.0000.0120.

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Resid Pediatr. 2025;15(4). DOI: 10.25060/residpediatr-2025.v15n4-1342

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INTRODUCTION

Transient neonatal myasthenia gravis (TNMG) is a rare condition, affecting approximately 12 to 20% of newborns whose mothers have myasthenia gravis. Myasthenia gravis (MG) is a chronic, autoimmune disease, characterized by intermittent muscle weakness and fatigue, occurring 2 to 3 times more often in women than in men during the second and third decades of life[1]. TNMG occurs due to placental transfer of immunoglobulin G antibodies during gestation. These antibodies bind to nicotinic acetylcholine post-synaptic receptors (AChR) at the neuromuscular junction of skeletal muscles or to alternative targets such as muscle-specific tyrosine kinase (MuSK), resulting in skeletal muscle weakness[2]. As the IgG antibodies are degraded in the baby, the symptoms gradually disappear, restoring full function[3].

Newborns affected by TNMG may present, usually within 72 hours after birth, with inadequate sucking, generalized hypotonia, hyperreflexia, respiratory distress, apnea, swallowing difficulty, and weak cry[4]. Clinical diagnosis is made through anamnesis and examination of both the mother and the newborn. Generally, postnatal monitoring of infants is recommended in case of possible complications[5]. As this is a rare condition, this article aims to report and share the evolution of a case of TNMG. Approved by the Ethics and Research Committee under CAAE 81212524.8.0000.0120.

CASE REPORT

Female newborn, birth weight of 2,490g, Capurro score of 36 weeks and 2 days, mother diagnosed with myasthenia gravis, positive AChR antibodies, diagnosed 5 years ago, previous history of thyroid cancer, on high doses of vitamin D and Levothyroxine. At birth, presented with weak cry and mild hypotonia, with improvement in limb mobility at the fifth minute of life, maintaining a weak cry. Apgar scores of 7 at the first minute and 9 at the fifth minute of life. Presence of hematoma on the face, left auricular pavilion, right hand, and left forearm. Started with mild intercostal retractions and difficulty maintaining adequate saturation at the fifteenth minute of life, requiring a tent with an oxygen inspiratory fraction (FiO2) of 40% for 20 minutes. Referred to the neonatal intensive care unit due to persistent respiratory distress (low intercostal retractions and need for oxygen to maintain saturation above 90%, without groaning or nasal flaring), provided ventilatory support through continuous positive airway pressure (CPAP) with FiO2 of 21% and positive end-expiratory pressure (PEEP) of 6 cmH2O. Maintained on fasting, intravenous fluid support, with orogastric tube and capillary blood glucose measurement every six hours. Respiratory status resolved within eight hours, enteral feeding with breast milk started every three hours with progressive daily increase and decrease in intravenous fluid according to acceptance. At the 12 hour physical examination, limbs were slightly hypotonic, with decreased facial expression, mainly peri-oral. Evaluation revealed absence of suction. On the second day, due to persistence of symptoms, a therapeutic trial with pyridostigmine 1.44 mg/kg/day, every 4 hours for TNMG was initiated. After two days of medication use, there was significant improvement in suction and hypotonia. However, still with some periods of worsening hypotonia and suction difficulty after two hours of medication, pyridostigmine was increased to 1 mg/kg/dose every four hours at the beginning of the fourth day. On the fourth and fifth days of life, had adequate suction and weight gain, discharged from the hospital with medication, referred for outpatient follow-up with a pediatrician and pediatric neurologist. AChR antibody levels were requested but not performed. The patient showed complete improvement in the first month of life, with medication gradually discontinued throughout the neonatal period, and continues to be followed up in outpatient care.

COMMENTS

Myasthenia gravis is an autoimmune disorder involving the neuromuscular junction, usually caused by anti-AChR autoantibodies, or alternatively by anti-MuSK antibodies, thus disrupting nerve impulse transmission to skeletal muscle[6]. In TNMG, the pathophysiology results from the passage of IgG antibodies through the placenta[6]. It is inferred that the mechanism by which antibodies act in pathogenesis is related to the acceleration of degradation of acetylcholine nicotinic receptors, blockade of acetylcholine access to the receptor, and lysis of the postsynaptic membrane through complement system activation[7]. Consequently, newborns may present symptoms such as sucking difficulty, weak cry, generalized hypotonia, ptosis, and respiratory failure. The onset of these symptoms may not be immediate, appearing within the first 12 to 72 hours of life and may persist for up to four months without medication[6,7]. Spontaneous recovery usually occurs within four weeks. However, babies whose mothers have taken anticholinesterase agents tend to present symptoms later than babies whose mothers were not treated [7]. Therefore, due to the possibility of later symptoms, close monitoring of asymptomatic patients for at least three days is important to avoid complications[5,6].

The patient in this case initially presented with a weak cry at birth, mild limb hypotonia, progressing to mild respiratory failure, characterized by intercostal retractions and difficulty maintaining adequate saturation. Oxygen tent was used in the delivery room for 20 minutes until the infant was referred to the neonatal unit where non-invasive ventilation in

CPAP mode was initiated, emphasizing the importance of early ventilatory assistance, and if possible, starting CPAP already in the delivery room. Initially, no facial mimic alteration was observed, which became more evident after 12 hours of life.

TNMG is a clinical diagnosis. A strongly suggestive history of a mother with known autoimmune MG and physical examination with typical disease presentation may be sufficient for diagnosis[5-8]. However, in rare cases, the clinical presentation is not classical and the mother is asymptomatic for MG, requiring diagnostic confirmation. This can be done through serum dosage of anti-AChR and anti-MuSK antibodies or according to a therapeutic test with neostigmine 0.15 mg/kg via subcutaneous or intramuscular injection, which will lead to significant improvement within 15 minutes if positive[5-9].

Although MG-AChR is the most common type among pregnant women, highly specific for TNMG, MG-MuSK may be associated with a higher prevalence, early onset, and more severe manifestations of TNMG. The patient in this case had characteristics consistent with transient neonatal myasthenia, based on maternal history and without anti-AChR antibody measurement. TNMG cannot be clinically confused with Congenital Myasthenia, a non-autoimmune genetic disease with distinct and later clinical presentation. Most subtypes of congenital myasthenic syndrome usually do not respond to usual anticholinesterase agents, characterized by a variable combination of muscle hypotonia and focal signs[6].

First-line treatment consists of acetylcholinesterase inhibitors, such as pyridostigmine, with an initial dose in children of 1.0 mg/kg[10], with a maximum dose of 600 mg/day, which provides sufficient symptom control in patients with mild manifestations or isolated ocular symptoms. Dose adjustments may be necessary due to increased renal clearance and maternal blood volume, delayed gastric emptying, and frequent vomiting[7]. In cases of insufficient response to pyridostigmine, administration intervals may be reduced; doses should only be increased if symptoms persist[7]. In moderate and severe cases, intravenous immunoglobulins and exsanguinotransfusion treatment may be administered[10]. These are usually performed in TNMG derived from anti-MuSK, as it tends to be more resistant to first-line treatment[5].

Therefore, due to the suction difficulty in the reported case, pyridostigmine was started at a lower initial dose of 1.4 mg/kg/day every four hours with significant therapeutic response, with improvement in suction but with a duration of effect of approximately two hours. After increasing the dose to 1 mg/kg every four hours, good breastfeeding suction and adequate global tone were achieved. Supportive treatment should be performed according to the clinical condition of each patient, as hospitalization in an intensive care unit, ventilatory support, nasogastric tube use, among other measures, may be necessary, as well as anticholinesterase administration. These care measures are recommended according to symptomatology, which gradually decreases until maternal antibodies are eliminated and the newborn recovers[10].

The patient fully recovered in the first month, with medication gradually withdrawn and continued outpatient follow-up, as anticipated for this benign condition. Generally, TNMG does not require treatment[10]. In some babies, a more severe and potentially fatal form of congenital myasthenia may occur. This occurs more frequently in children of mothers who produce antibodies against fetal AChR rather than adult AChR[7]. In these severe cases, oral or intramuscular neostigmine use may be necessary, as well as tube feeding. Administration of neostigmine 30 minutes before feeding can help with dysphagia[6].

The transfer of antibodies through breast milk is discussed. However, breastfeeding is encouraged by guidelines since IgG levels in milk are only 2%, and most antibodies are transferred via the placenta[3-7]. Therefore, breastfeeding is recommended, except in cases where the mother's treatment is based on methotrexate, mycophenolate mofetil, or cyclophosphamide due to the risks of these medications to the baby[3-7].The clinical presentation of MG during pregnancy varies among patients, and even among pregnancies of the same woman. Women with the diagnosis who wish to become pregnant should not be discouraged; however, for a good outcome, their children should be monitored in the neonatal period, optimizing treatment and avoiding complications[3].

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