Ref: Ro Med J. 2022;69(4)
Doi: 10.37897/RMJ.2022.4.3

# Transient neonatal myasthenia gravis: case report

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## ABSTRACT

Transient neonatal myasthenia gravis (TNMG) is a distinct type of myasthenia gravis (MG), a temporary autoimmune condition due to the mother's antibodies crossing over the placenta and affecting the baby. Studies suggest that 10 to 15% of infants born to mothers suffering from MG will develop TNMG. Undoubtedly, if not diagnosed and treated in time, TNMG can be a serious condition, even life-threatening. Almost 80% of newborns will present symptoms in the first 24 hours of life that will last up to 4 weeks and a complete recovery is expected by 2 months of age. Only 10% of the affected infants may still be symptomatic at 4 months.

**Keywords:** myasthenia gravis, acetylcholine receptor, antibodies, hypotonia, neostigmine

## INTRODUCTION

Myasthenia gravis (MG) is a neuromuscular disorder that causes voluntary muscle weakness and can be either inherited or acquired, usually affecting adults. Transient neonatal myasthenia gravis (TNMG) is a distinct type of MG, a temporary condition due to the mother's antibodies crossing over the placenta and affecting the baby, the symptoms disappearing after the first few months after birth. This condition is different from congenital MG, a very rare autosomal recessive disease, that is characterized by permanent neuromuscular symptomatology in the newborn of a healthy mother. TNMG affects a small percentage of infants born to mothers diagnosed with MG, only approximately 10-15% become symptomatic, without a correlation between the severity of the mother's disease and the outcome of the newborn [1].

TNMG is an autoimmune disorder that occurs when anti-acetylcholine receptor (anti-AChR) antibodies from the mother's bloodstream cross the placenta causing nicotinic acetylcholine receptor loss, blocking acetylcholine binding and inducing lysis of the postsynaptic membrane through induction of the complement system [2,3].

The newborns become symptomatic within the first 24 hours of life, most of them expressing poor sucking, weak crying, lack of facial expression, respiratory distress and marked hypotonia. In severe cases swallowing and breathing difficulties may appear and gavage feeding and mechanical ventilation can be necessary. Most of the symptoms last for a period of 2 to 4 months, with clinical improvement being strongly correlated with the disappearance of the maternal antibodies [4,5].

Although the diagnosis could be established only on the mother's medical history of MG and suggestive clinical findings in the neonate, there are also several specific tests that can confirm the TNMG: identifying Anti-acetylcholine Receptor antibodies (highly specific), therapeutic Intramuscular Neostigmine Test and Electromyogram. However, it is not routinely recommended to measure the antibody levels of the neonate born from an MG mother. Problems of differential diagnosis in a floppy infant

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*Article History:*
Received: 5 December 2022
Accepted: 14 December 2022

appear in case of unknown maternal medical history and should consider neonatal sepsis, spinal muscle atrophy, congenital malformation of the central nervous system, congenital myopathies, and genetic disorders.

Management of TNMG includes vital signs monitoring, chronic pharmacotherapy to increase the availability of the acetylcholine neurotransmitter, and immunomodulatory and immunosuppressive drugs, for a variable period – a few days to a few months, decreasing the dose as the symptoms improve [6]. Special consideration should be given to excluding the medication that can exacerbate the symptoms of MG, such as aminoglycosides, fluoroquinolones, beta-blocking agents, chloroquine, and procainamide. Administration of anticholinesterase medication (first-line therapeutic agents), such as Neostigmine or Pyridostigmine, can be necessary in cases with severe illness [7]. Despite not enough scientific evidence, the use of immunoglobulin and corticosteroids is sometimes necessary and may be useful for the rapid removal of antibodies, in most severely affected newborns [8]. Thymectomy is not generally necessary for infants with TNMG [9]. After 2 to 4 months, spontaneous progressive remission without long-term complication was reported in most cases of classical TNMG.

Regarding breastfeeding, studies evidence that maternal IgG levels in milk represent up to 2% of the serum level, so MG mothers should be encouraged to breastfeed their infants since it does not emphasize the immunity transfer [10,12]. MG mothers who require treatment with mycophenolate mofetil, methotrexate or cyclophosphamide are advised against breastfeeding due to the teratogenic potential of the drugs [11]. If the mother had taken corticosteroid medication while pregnant, the newborn warrants close monitoring for adrenal insufficiency during the first month of life [13].

## CASE PRESENTATION

We report a case of a 3030 g newborn male, the first child of a 28-year-old mother with MG after a monitored pregnancy, without pathological events, that was transferred to the neonatal intensive care unit at 12 hours after birth due to generalized hypotonia, feeding difficulties, and choking episodes. The mother was diagnosed with MG at the age of 15, medicated with pyridostigmine and 4 years later, a thymectomy was performed. During pregnancy, she was prescribed pyridostigmine 60 mg daily and methylprednisolone 8 mg/daily starting 27 weeks of gestation.

The baby was born in our clinic after an elective cesarian section at 40 weeks of gestation with Apgar scores of 9 and 9 at one and five minutes. Six hours after birth, while being monitored for vital signs, the baby presented a severe desaturation associated with mild respiratory distress syndrome with intermittent grunting and abundant oropharyngeal secretions that required frequent suctioning. Breastfeeding was not possible due to poor sucking, difficulty swallowing, and choking episodes. Initial laboratory tests: complete blood count, inflammatory markers, liver, and kidney function markers, showed normal results, except for mild hypocalcemia, elevated creatine kinase, and MB-creatine kinase. Subsequently testing identified high levels of anti-AChR antibody concentration: 16.50 nmol/L (normal: <0.25 nmol/L). Cranial ultrasound, chest x-ray and echocardiography revealed no abnormalities.

On admission to NICU, he presented marked hypotonia, swallowing and sucking difficulties, weak cry, and abundant oropharyngeal secretions. Because oral feeding was difficult and the baby did not tolerate orogastric gavage, parenteral nutrition was necessary until a slow progressive increase of milk quantities was possible.

To avoid supplemental antibody transfer through milk, the mother decided not to breastfeed, and the baby was given milk formula appropriate to his age.

The neurological exam confirmed TNMG diagnosis and because the symptoms were persistent and interfered with the baby's feeding and oxygenation on the seventh day of life, neostigmine was initiated at a dose of 0.1mg, six times a day, subcutaneously. Two days later, the baby showed clinical improvement in being able to receive bottle feeding and he was switched on to oral pyridostigmine, 1 mg/kg, six times a day before feeding. On the 11th day of life, full oral nutrition was reached, so the baby was discharged home with a recommendation to progressively reduce pyridostigmine until complete recovery is reached. Follow-up physical and neurological exams after two months were normal, the baby had no feeding problems, and weight gain was appropriate for his age.

## CONCLUSION

Although most newborns from mothers diagnosed with MG may be asymptomatic, careful postnatal monitoring is to be carried out in these cases as the onset of the symptoms is variable and can include life-threatening manifestations; even if TNMG is a self-limited disease, some cases may need a multidisciplinary approach and escalation of treatment from supportive care to complex pharmacological interventions. If the mother does not have a previous antenatal clear diagnostic or if the baby is born premature or neurologically depressed from perinatal complications, evaluation becomes ex-

tremely difficult, and neonatologists should perform supplemental diagnostic tests to be able to identify a TNMG. Therefore, a good maternal anamnesis and integration of pre and postnatal clinical data can prevent costly and stressful investigations of the newborn.

*Conflict of interest:* none declared
*Financial support:* none declared

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