

Prehodna neonatalna miastenija gravis: študija primera

Transient Neonatal Myasthenia Gravis: Case Report

Avtor / Author

Ustanova / Institute

Sara Sitar¹, Milena Treiber¹

¹Univerzitetni klinični center Maribor, Klinika za ginekologijo in perinatologijo, Oddelek za perinatologijo (porodnišnica), Neonatologija, Maribor, Slovenija;

¹University Medical Centre Maribor, Division of Gynecology and Perinatology, Department of Perinatology, Neonatology;

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Correspondence

Sara Sitar, Gosposvetska cesta 41 a,
2000 Maribor
milena.treiber@ukc-mb.si

Izvleček

Namen: Prehodna neonatalna miastenija gravis (NMG) je posledica transplacentarnega prenosa protiteles mater, obolelih z avtoimunske MG. Otroci obolelih mater razvijejo klinično sliko v 10–20 %.

Poročilo o primeru: Prikaz novorojenke s prehodno NMG, rojeno materi z znano MG. Tipično se bolezen kaže kot generalizirana hipotonija, šibek jok, dihalna stiska, zmanjšana sesalna moč, šibkost ekstraokularnih mišic. Simptomi so navadno samoomejujoči, prehodno je potrebna podporna terapija. Diagnostični preizkus je dober klinični odziv otroka na administracijo inhibitorja acetilholinesteraze. Po očiščenju protiteles iz krvi otroka dolgoročna terapija ni potrebna in bolezen izzveni. Zdravljenje je podporno, zajema hranjenje z manjšimi in pogostejšimi obroki s pomočjo sonde, neinvazivno ali invazivno podporo dihalne funkcije, od zdravlil pa se uporabljajo

Abstract

Purpose: Transient neonatal myasthenia gravis (NMG) results from the transplacental transfer of antibodies of mothers with an autoimmune form of myasthenia gravis. The clinical presentation develops in 10%–20% of their children. This study aimed to present a case of a newborn with transient myasthenia gravis (MG) born to a mother diagnosed with MG.

Case presentation: The disease manifested itself as generalized hypotonia, weak cry, respiratory distress, poor sucking, and facial diplegia. The symptoms were usually self-limiting, and transient supportive treatment was required. A diagnostic test was a good clinical response of the child to the administration of an acetylcholinesterase inhibitor. After the clearance of antibodies from the child's blood, long-term therapy was not necessary and the disease resolved. Treatment was supportive and included

inhibitorji acetilholinesteraze (neostigmin, piridostigmin).

Zaključek: Opisani primer obravnave dekllice z dokazano prehodno NMG je v vsakdanji klinični praksi izjemno redek, zato je pomembno poznavanje le-tega.

the administration of smaller and more frequent meals via a tube, noninvasive or invasive support of respiratory function, and use of acetylcholinesterase inhibitors (neostigmine and pyridostigmine).

Conclusion: Pediatric patients diagnosed with transient NMG are extremely rare in everyday clinical practice, and hence it is important to be familiar with it.

INTRODUCTION

Myasthenia gravis (MG) is a rare disease characterized by impaired signal transmission at the neuromuscular junction, with consequent muscle fatigue and alternating muscle weakness (1). The incidence varies between 2.8 and 14.8 cases per million inhabitants (2). Furthermore, 10%–20% of children of mothers with an active MG during pregnancy are affected (3). The probability of developing the disease correlates with the antibody titer in the mother (4), whereas the degree of clinical involvement/disability of the child does not (5).

Transient neonatal myasthenia gravis (NMG) results from the transplacental transmission of immunoglobulin (Ig)G1 or IgG3 antibodies to acetylcholine receptors in mothers with autoimmune MG (1) and less commonly of antibodies to muscle-specific kinase (6). Maternal thymectomy reduces the likelihood of neonatal morbidity (7). Typically, the disease manifests itself as generalized hypotonia, weak cry, poor sucking, and facial diplegia (8), with the characteristic presence of tendon reflexes. Respiratory muscles may be involved, leading to respiratory distress. Symptoms are usually self-limiting, and transient supportive therapy is required (1). They can develop in 78% of the cases within the first day of life; the onset 3 days after birth is not described (8).

A diagnostic test is the child's response to the administration of the acetylcholinesterase inhibitor (neostigmine methylsulfate) at a dose of 0.15 mg/kg intramuscularly or subcutaneously, which leads to clinical improvement within 15 min that lasts 1–3 h. Occasionally, the addition of atropine is required to control muscarinic side effects. Compared with neostigmine, pyridostigmine has a longer duration of action (3–4 h) and fewer muscarinic effects but it requires

more time (45 min) for the onset of action (8).

Transient NMG is distinguished from congenital myasthenia syndrome by the detection of autoantibodies and spontaneous clinical improvement. The long-term therapy is not necessary, and the disease resolves after the clearance of antibodies from the child's blood. (1). Treatment is supportive. It includes tube feeding and noninvasive or invasive support of respiratory function, if necessary. Among the medications, neostigmine methylsulfate is used at a dose of 0.05–0.1 mg/kg IM or SC, 30 min before each feeding. After clinical improvement, the medication can be administered orally at a higher dose (0.5–1.0 mg/kg per os, 45 min before feeding). The side effects of the drug include diarrhea, weakness, and fasciculations. The average duration of pharmacotherapy is 4 weeks; feeding and breathing problems are, on average, present for about 2 weeks (3). Breastfeeding is recommended (9).

CASE PRESENTATION

A female infant weighing 2,880 g was born to a 37-year-old mother who had been receiving treatment for MG since her youth and underwent a thymectomy. During pregnancy, she received pyridostigmine and methylprednisolone on a daily basis and toremide once weekly. Her 4-year-old firstborn child had no recognized symptoms of NMG during the neonatal period. A second child (girl) was delivered with the cesarean section at 39 weeks of gestation. The Apgar score was 6/7/8 after 1, 5, and 10 min, respectively. After the birth, the girl required ventilation through a mask with the addition

of oxygen for a few minutes. She continued to breathe spontaneously, but insufficiently. We observed sucking and swallowing problems, weak crying, and lower muscle tone and weakness besides respiratory distress a few hours after birth.

At the age of 10 h, a diagnostic and therapeutic experiment with neostigmine was performed, followed by an evident improvement in the girl's condition clinically evident in 20–30 min after the administration. The girl no longer required oxygen supplementation, and her respiratory function was satisfactory. The neostigmine dose was then titrated to achieve the appropriate clinical effect with respect to the pronounced adverse effects of muscarinic receptor antagonists (fluid discharge, increased tracheal secretion, and transient bradycardia without systemic hemodynamic consequences). The neostigmine therapy was replaced with pyridostigmine in the following days. The girl's neurological status demonstrated diminished spontaneous motor skills, facial diplegia, weak crying, and decreased axial and limb muscle tone with proprioceptive reflexes. The girl was discharged at the age of 18 days. Four blood samples were taken to determine the level of AChR antibodies: the concentration was 7.97 nmol/L in the first sample (day 1), 210.5 nmol/L in the second sample (14 days), 79.5 nmol/L in the third sample (34 days), and 0.4 nmol/L in the fourth sample (64 days). Difficulties in interpreting the results arose from an unexpected increase in the level of antibodies, as the level was lower in the first sample than in the second sample taken after 14 days, while we recorded an evident decrease in the level of antibodies in the subsequent samples. According to the opinion provided by the laboratory staff, the first sample was an analytical error due to an excess of disruptive substances, which is why the interpretation of the first sample was not correct. We observed evident neurological improvement in the facial muscles as well as in the general muscle tone

and strength of crying and sucking at the last clinical examination of the girl. She received pyridostigmine until 6 weeks of postnatal age. The intervals between doses were prolonged accordingly to girl's needs (achieving sufficient feedings) in the last 2 weeks.

DISCUSSION

NMG is just one of the diseases in which the passive transfer of autoantibodies from the mother to the fetus results in fetal and neonatal disease. Diagnostic evaluation of a hypotonic newborn can be a challenge, and an excellent medical history helps with the diagnosis, as it was in the presented case. NMG is ultimately a clinical diagnosis. The newborn girl born to the mother with known MG developed typical NMG symptoms immediately after birth. The diagnostic-therapeutic test with neostigmine was clearly positive, confirming the clinical suspicion. The performed tests showed the presence of antibodies in the child's blood. Early treatment and good clinical suspicion avoid serious situations that can put the child's life at risk when the disease is severely symptomatic.

CONCLUSIONS

Transient NMG is a rare disease diagnosed based on the maternal medical history data, neonatal clinical status, and a therapeutic experiment with an acetylcholinesterase inhibitor. The disease is of temporary nature with no long-term consequences. We presented the management of a girl with a typical clinical picture of transient NMG and confirmed the presence of anti-AChR antibodies. The girl was treated appropriately and further monitored by a pediatric neurologist.

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