

Case Reports

Seronegative Neonatal Myasthenia Gravis in One of the Twins

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Neonatal myasthenia gravis has been described as a transient condition affecting only a small percent of neonates. We report a twin gestation in a seronegative mother with myasthenia gravis, in which only one twin was affected.

Key words: Neonate, Myasthenia gravis, Twins.

Neonatal myasthenia gravis (NMG) is a transient postsynaptic neuromuscular transmission defect that occurs in up to 10-15% of infants born to mothers with myasthenia gravis (MG). Majority of patients with MG have demonstrable antibodies to acetylcholine receptors (AChR) by radioimmunoassay. Seronegative MG (SNMG) is defined as generalized MG in which the diagnosis is made on clinical, electrophysiological and pharmacological grounds but in which AChR

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antibodies are missing. The term is misleading as clinical and experimental evidence indicates that the disease is caused by serum (humoral) factors(1). The diagnosis confirmation depends on neurophysiological findings or on a response to anticholinesterase therapy (ACT). Since neither test has the sensitivity nor specificity profile of AChR antibodies, diagnostic uncertainties can arise(1).

In NMG (seronegative as well as seropositive), the symptoms are usually noted in the first 72 hours of life that include feeding difficulty, generalized hypotonia, weakness, poor respiratory effort and may last for about 3 weeks (range 1 to 6 weeks)(2). The severity of the infant symptomatology is not related to the duration, severity of maternal disease or the maternal antibody titers(2). NMG is a self-limited disorder but it can be potentially life threatening and therefore early postnatal diagnosis and treatment is necessary. We recently treated twins born to a SNMG mother in whom, only one twin was affected with NMG.

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A 2198 g female infant, second of the twins, was born by elective cesarean section at 36 weeks of gestation to a 28-year-old G4P2012 mother with SNMG with normal fetal heart tracing and cord blood gases. She was recently diagnosed with grade 3 SNMG (Osserman's grading) during second trimester of pregnancy and was well controlled on neostigmine and prednisone at the time of delivery.

The second infant delivered 34 minutes after the first baby, required resuscitation with positive pressure ventilation and was assigned an Apgar score of 5, 6 and 9 at 1, 5 and 10

minutes respectively. The placenta was dichorionic-diamniotic without any abnormality. The physical examination revealed a 36 weeks preterm infant with respiratory distress, which required nasal continuous positive airway pressure support (NCPAP) with 40% oxygen. Chest X-ray was consistent with a diagnosis of transient tachypnea of the newborn. The infant was hemodynamically stable. Neurological examination revealed a fully conscious infant with slightly decreased tone and diminished neonatal reflexes without ptosis. Complete blood counts and glucose was normal. After 48 hours, the infant developed frequent apneic and bradycardia episodes along with marked hypotonia and diminished neonatal reflexes. The tendon reflexes were normal and no fasciculations were discernible. The infant exhibited intercostal and sub costal retractions and had drooling of saliva, which required intermittent suctioning. Cerebrospinal fluid was normal for cytology and chemistry. Herpes simplex virus DNA was not detected by polymerase chain reaction and viral/bacterial cultures were negative. Urine and blood cultures did not grow any organisms. Head ultrasound revealed no abnormality. Her AchR antibody titer was negative by RIA. Creatine kinase levels were within normal limits (55 U/mL; normal range 20-200 U/mL).

After 48 hours of NCPAP, the infant required ventilation due to poor respiratory effort and ACT with neostigmine was initiated with good response. Parenteral neostigmine was changed to oral pyridostigmine on the fifth day. Her spontaneous movements, respiratory effort and tone improved gradually and the baby was successfully extubated on the 12th day of life. Nasogastric tube feedings were initiated on the 7th day and by 26th day she was taking all her feeds by bottle. Pyridostigmine was tapered gradually over a week and was off medication by the 29th day. The first twin, a

male infant did not reveal any symptoms of NMG and also had negative AchR antibodies by RIA. Follow up examination by a Pediatric Neurologist revealed a normal neurological and developmental examination.

Discussion

The transmission of the disorder from mother to child clearly indicates that there is a circulating serum factor, probably IgG in SNMG(3). Reports of findings of predominant involvement of diaphragmatic and pharyngeal paralysis in neonates born to a seronegative mother, suggest a putative antibody to diaphragmatic antigen determinants not shared by calf muscle acetylcholine receptor(3,4) Recently, IgG antibodies against muscle-specific kinase (MuSK) have been demonstrated in up to 2/3rd of cases with SNMG(5). Moreover, plasma from patients with SNMG also seems to contain a factor, possibly IgM that indirectly inhibits AchR function by phosphorylation of AchR(6) Collectively, these results suggest the presence of an antibody binding to a membrane receptor other than AchR. In the case described above, only one of the twins was affected points to a complex mechanism. The similarity between maternal and fetal human leukocyte antigens (HLA) in affected neonates may suggest genetic predisposition to develop NMG(7).

A strong correlation has been observed in seropositive myasthenic mothers with a high fetal/adult AChR Ab ratio to the occurrence of NMG in their first child suggesting that auto antibodies directed against the fetal form of AChR could play a predominant role in the pathogenesis of NMG(8).

The treatment of NMG irrespective of serology status is directed to support vital functions based on the severity of the disease—small frequent feeds, pharyngeal suctioning, respiratory support, avoidance of amino-

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glycosides and ACT (neostigmine 0.01-0.04 mg/kg/dose IM, IV or SC q3H 15 minutes prior to feeds, followed by pyridostigmine 7 mg/kg/day in 5-6 divided doses PO, when stable). Exchange transfusion and IVIG therapy has been tried to achieve rapid improvement. The efficacy of exchange transfusion is unclear, due to conflicting reports in the literature(2,9). IVIG therapy though successful in adult MG patients, did not prove to be definitively beneficial in neonates(10).

Majority of children with NMG had a normal course during a follow up study of muscle function, however 2 out of 11 cases of NMG developed stationary myopathy in Ahlsten's study, probably unrelated to the MG of their mothers(7)

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