

NEUROMUSCULAR DISORDERS

FETAL ACETYLCHOLINE RECEPTOR INACTIVATION SYNDROME AND MATERNAL MYASTHENIA GRAVIS

Three brothers with facial diplegia and a myasthenic mother are reported from McGill University, Canada; University of Oxford, UK; and Columbia University, New York. Mother developed myasthenia at 33 years of age, presenting with ptosis, facial weakness, generalized fatigue, and elevated AChR Ab (>1000; normal <0.4). Her symptoms improved following thymectomy, pyridostigmine, prednisone, and plasmapheresis. Subsequently, three successive pregnancies were complicated by polyhydramnios, and at birth the infants were hypotonic, had a poor suck, and swallowing difficulty. In the first pregnancy, mother received no plasmapheresis. The infant remained in the NICU with transient neonatal myasthenia gravis (TNMG) for 5 weeks and improved with IV immunoglobulin. At 5 years he has microcephaly, facial diplegia, excessive drooling, and hypernasal speech. Brain MRI, serum CK, and repetitive nerve stimulation are normal. In the second pregnancy, mother received plasmapheresis biweekly after the first trimester, but the infant developed TNMG and neurologic abnormalities, similar to the first infant. In the third pregnancy, mother received plasmapheresis biweekly throughout the pregnancy, and the infant was the least severely affected. He was hypotonic and sucked poorly at birth but he swallowed. He remained in the NICU with TNMG for 3 weeks, and improved with nasogastric tube feedings. At 2 years, he has mild facial diplegia, full mouth and eye closure, and mild speech difficulties. All 3 siblings have facial diplegia, incomplete mouth closure (see photo provided in article), high arched palate, excessive drooling, normal milestones of motor development, normal muscle strength, pes cavus deformities, areflexia, no arthrogryposis, surgically corrected cryptorchidism and inguinal hernias, and middle ear effusions with conductive hearing loss. Mother's serum obtained when asymptomatic after the third pregnancy was positive for AChR antibodies. The titer was 1,890 nM against fetal AChR and 157 nM against adult AChR (normal values <0.5 nM). More aggressive plasmapheresis during pregnancy correlates with decreasing phenotypic severity of this syndrome. (Oskoui M, Jacobson L, Chung WK et al. Fetal acetylcholine receptor inactivation syndrome and maternal myasthenia gravis. **Neurology** Dec 2008;71:2010-2012). (Reprints: Dr Darryl C De Vivo, 710 168th St, 2nd Floor, New York, NY 10032. E-Mail: dcd1@columbia.edu).

COMMENT. The authors comment that fetal AChR persists until 33 weeks gestation, when the fetal (g) subunit is replaced by the adult (e) subunit. Despite intrauterine exposure to AChR antibodies (AChR Ab), most infants of myasthenic mothers are asymptomatic. A higher ratio of fetal to adult AChR Ab antibodies can lead to neonatal transient myasthenia gravis in 10-15% of infants. The fetal AChR inactivation syndrome described in the 3 brothers results from inactivation of the fetal subunit during a critical period of fetal development. Mothers with a previously affected child have a 100% risk of recurrence with subsequent children. Infants with transient neonatal myasthenia gravis should be examined for speech impairment and hearing loss at follow-up. The term *transient* neonatal myasthenia gravis is not entirely appropriate for these patients.