Case Report: Congenital Myasthenia Gravis- A case for newborn screening?

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Background

Myasthenia gravis is an autoimmune neuromuscular junction disorder which can result in involuntary muscle weakness. It commonly affects various muscular groups involving the eyes, face, arms, legs, and even muscles used for breathing. Most often Myasthenia Gravis affects adults, but it can occur in the pediatric population. Congenital Myasthenia Gravis (CMG) has a broad and variable presentation with many potential differential diagnoses. In rare cases, CMG can present in the first years of life with a fatigable weakness and a severe respiratory failure. In the more common, benign cases, presentation can occur later in life. Here, we present an interesting case of CMG in a male neonate. Through our findings we aim to make the case to introduce a more focused CMG genetic analysis within newborn screening testing as to avoid potential detrimental outcomes, improve quality of life, and decrease the financial burden on the families and healthcare system.

Case Presentation

Our case begins with a term male neonate, who shortly after birth required resuscitation with positive pressure ventilation, then blow-by for five minutes after his delivery. Shortly after at 16 hours he became apneic with subsequent respiratory failure requiring transfer to the NICU where he was intubated and ventilated. During his stay in the NICU, the patient required a total of three days of mechanical ventilation, followed by CPAP for one day. The patient was able to tolerate oral feeds on the ninth day of life. Upon genetic testing, no inborn errors of metabolism were identified on his newborn screening, and his echocardiogram, CT and MRA imaging studies of the brain were normal. He did however display prolonged focal discharges on his EEG in the right frontal region, raising concern for seizure risk. Over the course of the next four years, he met few motor milestones, experiencing episodes of respiratory failure on six occurrences. During the next three years, the patient was tested for muscular dystrophy, spinal muscular atrophy, and inborn errors of metabolism, however no conclusive diagnosis could be reached. Eventually genetic testing revealed the diagnosis of congenital myasthenia gravis, displaying signature mutations in RAPSN, N88k and 373del. Pyridostigmine treatment was initiated, allowing proper development, milestone achievement, and physical activities such as walking, and running with minimal fatigue, without further respiratory failure.

Discussion & Conclusions

Congenital Myasthenia Gravis is due to mutations in genes involved in the production of proteins required in signaling at the neuromuscular junction. These genetic mutations, resulting in single or multiple different defective proteins, effect various locations at the junction such as the

presynaptic membrane, synaptic basal lamina, or the postsynaptic membrane. Available diagnostic panels and whole exome sequencing have allowed further classification of and expanded our understanding of CMG. However, a more rapid and accurate diagnosis of CMG is crucial and can reduce mortality and improve quality of life if caught early. Successful treatment of CMG is feasible, but requires life-altering, and lifelong medical treatment that should be initiated as soon as possible. A focused panel should be included in newborn screening to prevent delay in treatment, harm to the patient, and undue financial burden on families.