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Management of Myotonia Congenita in Pregnancy

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Abstract

Myotonia congenita is a rare autosomal recessive disorder of skeletal muscle. Affected individuals experience periods of prolonged muscle contraction due to dysfunction of the CLC-1 chloride ion. These prolonged muscle contractions can interfere with normal labor and delivery. The stress associated with delivery put women at increased risk of myotonic crisis, a debilitating state during which the muscles cannot relax. There is little published on the management of women with myotonia congenita during pregnancy and delivery. Here we examine the case of a gravid female with myotonia congenita, discuss the risks associated with delivery and how to reduce risk to provide a safe delivery for these women. Additionally, we identify a novel mutation associated with the condition.

Keywords: Thomsen's disease; CLCN-1 gene; Myotonic crisis

Introduction

Myotonia congenita is an autosomal recessive hereditary disorder of skeletal muscle that leads to periods of prolonged muscle contraction. It is caused by a mutation in the CLCN-1 gene. This gene codes for the major chloride channel in skeletal muscle, ClC-1 [1]. Impairment of ClC-1 leads to prolonged repolarization of skeletal muscle, presenting clinically as delayed muscle relaxation. Physical and emotional stresses are known triggers for myotonic events and little is published on delivery planning in the patient with myotonia congenita. Presented here is the case of a woman with known myotonia congenita during pregnancy and the specific concerns associated with delivery in these patients.

Patient Presentation

The patient is a 36 year-old primigravida who initially presented for routine obstetric care. She reported a long history of musculoskeletal symptoms originating in childhood. Most notably, she had difficulty initiating movement after periods of prolonged inactivity due to muscle stiffness. The stiffness improved after repetitive movement. Her symptoms were exacerbated by stress and cold. She had been affected since childhood and her mother first noted difficulty walking at age two.

The patient had been diagnosed with a muscular disorder as a child but there was some question as to the exact diagnosis. She had undergone electromyography and was evaluated by another neurologist five years prior to presentation. The results of this work up were suggestive of myotonia congenita but no firm genetic diagnosis had been made.

Her history revealed she was born in Iran to parents who were first cousins. No other family members were affected. Genetic testing of the CLCN-1 gene locus was performed given high clinical suspicion for myotonia congenita. The results revealed she was homozygous for a novel mutation in the CLCN-1 gene. This mutation, c. 1355C>T, results in change in the amino acid sequence (p.452Pro>Leu) of the chloride ion channel and is therefore suspected to be pathogenic.

Amniocentesis was performed due to advanced maternal age. Results revealed fetal karyotype 46 X,Y. No further genetic testing was performed. The current pregnancy did not seem to affect the patient's clinical status. She reported no increase in symptoms. Mode of delivery had been discussed extensively during prenatal care. The patient was concerned that the stress of labor and risk of decreased body temperature at the time of delivery would incite a myotonic crisis. Myotonic crisis is a prolonged contraction of skeletal muscles usually lasting 2-3 minutes that can impair movement and in severe cases affect respiration, resulting in respiratory failure. Due to these concerns, she opted for the controlled circumstances of a cesarean delivery. As her medical condition put her at increased risk during vaginal delivery, both cesarean and vaginal delivery was considered. The patient experienced spontaneous preterm labor at 35 weeks 6 days and a male 2583 gram neonate with Apgars of 9 and 9 at 1 and 5 minutes, respectively, was born by primary cesarean delivery without complication. She did not experience myotonic crisis and her post-operative course was uncomplicated.

Based on the results of genetic testing, the patient was counseled that her child would be a carrier of the pathogenic mutation. The father was also of Iranian descent but there was no known consanguinity. As he was asymptomatic, the probability of an affected child was extremely low. Following the birth of the infant genetic testing confirmed carrier status. No other mutations were identified, thus the infant is thought to be an asymptomatic carrier.

Discussion

Myotonia congenita is characterized by impaired muscle relaxation due to a mutation in the skeletal muscle chloride channel. It is a rare disease with a prevalence of 1:23,000 to 1:50,000 [1]. During normal muscle contraction, chloride ions function to repolarize the cell membrane. This leads to muscle relaxation and prepares the muscle cells for subsequent depolarization and contraction. With mutations in this channel, muscle groups can sustain prolonged contraction causing muscle stiffness. Symptoms are relieved after repetitive movement due to an increase in chloride ion concentration with each consecutive motion.

The CLCN-1 gene codes for the affected chloride channel. The CLCN-1 gene is located on chromosome 7q35 and organized into 23 exons which together help form the 18 alpha-helices that form the

transmembrane ion channel [2]. Over 130 different mutations have been identified. The pattern of inheritance can be either dominant or recessive, known as Thomsen and Becker variants respectively. Due to incomplete penetrance and variable expressivity, the phenotypic presentation can vary greatly even within families. In the recessive form of the disease, compound heterozygosity is common with different mutations inherited from each parent leading to an affected child.

Worsening of disease has been reported both during menstruation and pregnancy. This is thought to be secondary to hormonal effects on chloride channel function [1]. Some women remain stable throughout pregnancy while others may have mild to severe worsening of symptoms. Treatment is geared towards decreasing stress and encouraging exercise. Medical therapies are available for those with severe symptoms. Mexiletine, an antiarrhythmic drug, has demonstrated efficacy in symptom reduction [1]. Dosing begins at 150 mg twice daily and can be titrated as needed to a maximum of 300mg three times daily [3]. Acetazolamide, a carbonic anhydrase inhibitor, is also helpful in some patients; dosing ranges from 125 mg twice daily to 250 mg three times per day [3]. Additional treatment options include procainamide (125-1000 mg/day), quinine (200-1200 mg/day) and phenytoin (300-400 mg/day) [3]. All of these medications are pregnancy class C, with the exception of pnenytoin. Phenytoin is class D and associated with congenital malformations, thus it should not be used in pregnancy. The class C medications should only be used if the benefits of treatment outweigh potential risk to the fetus.

Special care should be taken to ensure a safe delivery. There is concern that the stress of vaginal delivery may precipitate a myotonic crisis making it difficult for the woman to be repositioned or push effectively during the second stage of labor. Successful vaginal delivery is documented in case reports [4]. Assisted vaginal delivery may help to alleviate some of the physical stress, but there is little evidence to support routine assisted delivery. Both spinal and epidural anesthesia can be used for pain control [4,5].

Cesarean delivery can also be safely performed. The largest risk comes with administration of general anesthesia in the case of emergent cesarean delivery. Depolarizing paralytics such as succinylcholine are contraindicated, as there is the potential for triggering a dangerous hyperthermic reaction similar to malignant hyperthermia [6]. Propofol can also precipitate myotonic crisis [6,7] and should be avoided in these patients. Thus, if cesarean delivery is indicated, regional anesthesia is preferred. If emergency cesarean is necessary, it is critical to adjust anesthesia administration accordingly. Careful pre-operative planning is essential to avoid preventable complications.

Conclusion

A rare condition, myotonia congenita can lead to complications during pregnancy and delivery in affected women. With careful delivery planning many of the potential problems can be avoided. There is little evidence to support either vaginal or cesarean delivery in these patients. Management varies with each case based on symptom severity and discussion between patient and provider. Appropriate anesthesia planning and avoidance of medications that may precipitate myotonic crisis are paramount to patient safety during labor and delivery.

Declaration of Interests

The authors report no conflicts of interest.

References

1. Lossin C, George AL (2008) Myotonia Congenita. Advances in Genetics 63: 25-55.
2. Brugoni R, Kapetis D, Imbrici P, Pessia M, Canioni E, et al. (2013) A large cohort of myotonia congenita probands: novel mutations and a high frequency mutation region in exons 4 and 5 of the CLCN1 gene. J Hum Genet 58: 581-587.
3. Duno M. Colding-Jorgensen E (2011) Myotonia Congenita. GeneReviews, University of Washington, Seattle.
4. Farrow C, Carling A (2007) Successful spinal blockade in a parturient with myotonia congenita. Int J Obstet Anesth 16: 89-90.
5. Basu A, Nishanth P, Ifaturoti O (2009) Pregnancy in Women with Myotonia Congenita. Int J Gynecol Obstet 109: 62-63.
6. Bandschapp O, Iaizzo PA (2013) Pathophysiologic and anesthetic considerations for patients with myotonia congenita or periodic paralyses. Pediatr Anesth 23: 824-833.
7. Gorthi S, Radbourne S, Drury N, Rajagopalan C (2013) Management of pregnancy with Thomsen's disease. Eur J Obstet Gynecol Reprod Biol 170: 293-296.