Open Access

OBM Genetics

LIDSEN Publishing Inc.

Original Research

Congenital Phenotypes and DMPK CTG Repeat Number in Mothers/Children with Myotonic Dystrophy Type 1

Kosuke Shigematsu [1, *], Yukiko Mikami [1], Mamiko Shinsaka [1], Masanobu Kinoshita [2], Yasushi Takai [1]

1. Department of Obstetrics and Gynecology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan; E-Mails: s_kosuke@saitama-med.ac.jp; with_bluewing@yahoo.co.jp; mamiko.shinsaka88@gmail.com; yastakai@gmail.com
2. Department of Neurology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan; E-Mail: m.kinoshita@mizuhokai1981.jp

* **Correspondence:** Kosuke Shigematsu; E-Mail: s_kosuke@saitama-med.ac.jp

Academic Editor: Fabrizio Stasolla

OBM Genetics
2023, volume 7, issue 1
doi:10.21926/obm.genet.2301179

Received: June 29, 2022
Accepted: March 24, 2023
Published: March 28, 2023

Abstract

Myotonic dystrophy type 1 (DM1) is an autosomal dominant genetic disease often resulting in more severe symptoms in affected children. The number of CTG repeats is reportedly related to congenital myotonic dystrophy 1 (CDM) severity. In this study, we aimed to clarify whether the number of CTG repeats can predict the severity of symptoms in children with CDM. This retrospective study examined 14 women with DM1 and their 14 children diagnosed with CDM. There were 11 CDM and 3 non-CDM patients. The correlation between the mother and child's CDM onset and CTG repeat numbers was analyzed. The mean CTG repeat numbers in women who bore a child with CDM (detected polyhydramnios during pregnancy; hypotonia, respiratory insufficiency, or suckling failure at birth; bilateral facial weakness; delayed motor and mental development; talipes; and other contractures) were significantly lower compared to those who bore a non-CDM child (620 ± 450 vs. 933 ± 57, respectively). However, there was no significant difference in the mean CTG repeat numbers between the children with and without CDM (1,617 ± 323 vs. 1,789 ± 428, respectively). Our results suggest that CDM cannot be predicted based on the CTG repeat number of the mother or child.

© 2023 by the author. This is an open access article distributed under the conditions of the Creative Commons by Attribution License, which permits unrestricted use, distribution, and reproduction in any medium or format, provided the original work is correctly cited.

Keywords
Congenital; DNA repeat expansion; myotonic dystrophies; myotonic dystrophy 1; pregnancy

1. Introduction

Myotonic dystrophy type 1 (DM1) is an autosomal dominant genetic disorder characterized by myotonia and muscular dystrophy. DM1 is a multisystemic disorder that affects the skeletal muscles and smooth muscles, eyes, heart, endocrine system, and central nervous systems. The expansion of a cytosine causes DM1–thymine–guanine (CTG) trinucleotide repeat sequence present in the 3' untranslated region of the dystrophia myotonica protein kinase (*DMPK*) gene on chromosome 19q13.3.

Symptoms of DM1 are known to manifest earlier and with greater severity in children than in parents [1-4]. This is because of the anticipation phenomenon, in which the mutant allele expands during the almost exclusively maternal gametogenesis process, and the next generation inherits an extended CTG repeat sequence.

Congenital myotonic dystrophy type 1 (CDM1) is a severe form of DM1 that presents as marked muscle weakness from birth [5-7]. Studies have reported that 2%-55% of children born to mothers with DM1 develop CDM1 [6-8]. CDM1 is typically associated with several CTG repeats >1000, although some cases have been reported with 730-1000 repeats [9, 10]. DM1 can be diagnosed prenatally; however, reports on predicting whether a child may have CDM are scarce.

Thus, this study aimed to clarify whether the CTG repeat number of the fetus or mother could be used to predict the development of CDM in the child. We examined the CTG repeat numbers in mothers and their children, the pregnancy course, DM1 severity in the mother, and outcomes in children with DM1 borne by mothers with DM1. We analyzed the prognostic factors associated with CDM risk in children.

2. Materials and Methods

2.1 Editorial Policies and Ethical Considerations

The study protocol was approved by the Ethics Committee (IRB no. 1741-IV) of Saitama Medical Center of Saitama Medical University, and the principles of the Declaration of Helsinki performed the study. The methodology of this study was explained to the adult participants, and written voluntary consent was obtained. For study participants unable to provide consent due to being a minor or due to the effects of DM1, the study plan was explained to a dependent, parent, or child (who was at least 20 years old) before the enrolment of participants who provided consent by proxy. Further, informed consent was obtained from the parent or legal guardian if the participant was a minor. Only those who provided written consent by any of the methods above were included in the study, and patients who could not provide consent or did not understand the nature of the study were excluded.

2.2 Methods

This retrospective study included Japanese patients with DM1 who visited the Department of Neurology at Saitama Medical Center between November 2017 and August 2019. Among them, women aged 20–70 years with their children who also had been diagnosed with DM1 were selected as candidates.

Patients whose pregnancy and postpartum course for both the mother and child could not be obtained by medical records or interview and patients whose CTG repeat count or other information could not be obtained were excluded. In addition, patients whose children died during pregnancy or after birth without being diagnosed with DM1 were also excluded.

We obtained information regarding pregnancy and children, which is not usually recorded in the medical records of neurology, from questionnaires filled out by the patients. If available, we supplemented this information with the patient's obstetric and pediatric medical records. For mothers, data regarding the age at DM1 symptom onset and diagnosis, CTG repeat number, age at CTG repeat measurement, and Muscular Impairment Rating Scale (MIRS) score were obtained from medical records. Details of their pregnancy and labor history (including obstetrical complications [Yes/No], obstetrical abnormalities [Yes/No], delivery mode, placental abnormalities [Yes/No], and threatened preterm labor [Yes/No] [defined as threatened preterm labor appearing in medical records or diagnosed as preterm labor by the attending physician]) were obtained from questionnaires, and those in recent cases were confirmed or completed by medical records. For children, information regarding gestational age at delivery, time of diagnosis, birth weight, birth and the neonatal period, presence of survival, and CTG repeat number were obtained from medical records. The information regarding the course of motor development was obtained mainly from questionnaires.

If the study participants had no prior CTG repeat number test, they were tested after providing consent. In participants who underwent CTG repeat number testing at another facility, consent was obtained from the participant or an adult family member in writing before the information was requested from the facility. Further, when medical information obtained from questionnaires was insufficient to elucidate the condition or symptoms of the mothers and their children, more information was requested from other medical facilities that provided medical care to participants after obtaining written consent.

CDM was defined as a case with genetically confirmed DM1 who dies or requires hospitalization or medical intervention in the newborn period (first month of life) due to at least one of the following symptoms: polyhydramnios in pregnancy, hypotonia, respiratory failure, bilateral facial weakness, delayed motor and mental development, talipes and other contractures, and inadequate lactation at birth, as described in other reports [2, 11].

To elucidate the clinical characteristics of children diagnosed with CDM, the participants were divided into two groups: those with and without CDM. A Student's *t*-test was performed to compare the mean values between these two groups when they have equal variances, a Welch's *t*-test was performed to compare the mean values between the groups when they have unequal variances, and a Mann–Whitney *U* test was used to compare the median values between the groups when they are not normally distributed. Proportions within these two groups were compared using a Fisher's exact test. Correlation analysis was performed to examine the correlation between the variables.

Multivariable logistic regression analysis assessed the prognostic factors associated with CDM in children. Statistical analysis was performed using JMP Pro, version 16.2.0, software (SAS Institute Inc., Cary, NC, USA). A p-value of <0.05 was considered significant.

3. Results

Fourteen mothers and their 14 children were enrolled in the study. Among the 14 children, eleven children (79%) were diagnosed with CDM (CDM group). The other three children (21%) were diagnosed with DM1 during development (non-CDM group). Characteristics of the enrolled mothers are presented in Table 1. Data regarding the characteristics of the children at their time of birth are displayed in Table 2. Cases with the same numbers as in Tables 1 and 2 represent the mother and her child, respectively.

Table 1 Characteristics of the maternal participants.

No.	CTG repeat number	Age at CTG repeat measurement (years)	Pregnancy and labor history[†]	MIRS	Age at symptom onset (years)	Age at diagnosis (years)	Age at childbirth (years)	Placental abnormalities	Threatened premature labor	Premature rupture of membranes	Cesarean section
1	100	38	2 SM	3	26	37	37	none	yes	yes	yes
2	200	38	none	3	25	38	38	none	yes	yes	yes
3	600	27	1 SM	4	14	28	27	none	yes	none	yes
4	1000	39	none	4	25	40	41	none	yes	yes	yes
5	146	36	1 EP	2	30	36	36	none	yes	yes	yes
6	600	39	1 SM, 1 EP	4	25	39	39	yes	yes	yes	yes
7	100	38	none	4	33	34	32	none	none	none	none
8	600	43	none	3	30	40	40	none	yes	yes	yes
9	1000	49	1 SM, 1 TB	5	44	49	34	none	none	none	none
10	1370	47	1 TB (id)	4	40	47	23	none	none	none	none
11	1000	55	none	5	47	55	27	none	none	none	none
12	900	56	1 TB	4	45	48	26	none	none	none	none
13	900	46	2 TB (id and died at 9 yo[‡])	5	23	25	24	none	none	none	yes
14	1100	48	1 TB	5	28	30	26	none	none	none	none

[†]Except for applicable delivery of the child with DM1.

[‡]Died of DM1.

Abbreviations: EP; ectopic pregnancy, id; infant death, MIRS; Muscular Impairment Rating Scale, SM; spontaneous miscarriage, TB; term birth.

Table 2 Characteristics of the pediatric participants.

No	CTG repeat number	Diagnosis	Gestational weeks of delivery	Birth weight (g)	Polyhydr-amnios	Respiratory insufficiency	Hypotonia	Bilateral facial weakness	Delayed motor and mental development	Suckling failure	Talipes and other contractures	Current age (years; as of Sep 2020)
1	1625	CDM	32	1977	yes	yes	yes	yes	yes	yes	yes	2
2	1300	CDM	25	738	yes	yes	yes	yes	yes	yes	-	4
3	1800	CDM	35	2654	yes	yes	-	yes	yes	yes	yes	5
4	2100	CDM	29	1102	none	yes	yes	yes	yes	yes	yes	7
5	1800	CDM	32	1588	yes	yes	yes	yes	yes	yes	yes	10
6	1600	CDM	37	2030	yes	yes	yes	yes	yes	yes	yes	9
7	1000	CDM	40	3200	yes	yes	-	yes	yes	yes	yes	11
8	1600	CDM	36	2154	yes	yes	yes	yes	yes	yes	yes	12
9	1500	CDM	31	1694	yes	yes	yes	yes	yes	yes	yes	23
10	2066	CDM	40	3400	yes	yes	-	yes	yes	yes		34†
11	1300	DM1	40	2900	none	none	none	none	none	none	none	36
12	2100	DM1	39	2180	none	none	none	none	none	none	none	37
13	1966	DM1	>37	3200	none	yes	-	none	none	-	none	37
14	1400	CDM	37	2850	none	-	-	yes	yes	yes	yes	38†

Cases with the same numbers in Tables 1 and 2 represent the mother and her child, respectively.

†Died at age 34 and 38 years.

Unknown items are represented as a "-" sign.

The mean CTG repeat number (standard deviation, SD) of mothers included in this study was 686 (417), and the mean age at the onset of DM1 symptoms was 31.0 (9.6) years. No significant correlation was observed between the CTG repeat number and the mean age at the onset of DM1 symptoms ($p = 0.1603$).

Placenta previa, a reported complication of DM1 pregnancies [12, 13], occurred in only one participant (7.1%). Other reported complications were as follows: polyhydramnios in nine participants (64.3%), threatened premature labor in seven (50.0%), premature rupture of membranes in six (42.9%), and end of pregnancy due to premature delivery in seven (50.0%). The study participants' median gestational age at delivery (range) was 36.5 (25-40) weeks. Polyhydramnios was observed in all participants who experienced threatened premature labor; however, one participant whose pregnancy continued to 40 weeks developed polyhydramnios without symptoms of threatened premature labor.

The most common symptoms in children with CDM were respiratory insufficiency, suckling failure, bilateral facial weakness, and delayed motor and mental development observed in 11 children (92%). This was followed by talipes and other contractures, polyhydramnios, and hypotonia, observed in nine (75%) and seven (58%) children, respectively.

An examination of the clinical course of the offspring after childhood demonstrated that symptoms of DM1 emerged with increasing age even in those without CDM, and the individuals eventually exhibited motor and neurodevelopmental disorders. Two participants died at the age of 34 and 38 years; however, the other included individuals who are currently outpatients (median age as of October 2021, 12.5 [range, 1-38] years).

Children in the CDM group were delivered prematurely; however, no significant difference was noted in the mean number of gestational weeks at delivery between the CDM and non-CDM groups (34.0 (4.7) and 38.7 (1.5) weeks, respectively, $p = 0.1221$).

The mean CTG repeat numbers identified in mothers were significantly lower in CDM than in non-CDM groups ($p = 0.0462$), and the number of CTG repeats in mothers was significantly increased in their children ($p < 0.0001$). However, there was no significant difference between CDM and non-CDM groups in those children. Further, no significant difference in the mean maternal age at symptom onset and diagnosis was observed. However, the mean maternal age at delivery was significantly higher in CDM than in non-CDM groups ($p = 0.0445$). Similarly, the mean period from the maternal symptom onset to delivery was significantly higher in CDM than in non-CDM groups ($p = 0.0318$) (Table 3).

Table 3 Comparison between the congenital myotonic dystrophy (CDM) group and non-CDM group.

	Congenital myotonic dystrophy group (n = 11)	Non-congenital myotonic dystrophy group (n = 3)	p-value
Maternal CTG repeat number, times, mean (SD)	620 (450)	933 (58)	0.0462
Child CTG repeat number, times, mean (SD)	1,617 (323)	1,789 (428)	0.4580

Maternal age at symptom onset, years, mean (SD)	29.1(8.0)	38.3 (13.3)	0.1463.
Maternal age at diagnosis, years, mean (SD)	38.0 (6.3)	42.7 (15.7)	0.6606
Maternal age at delivery, years, mean (SD)	33.9 (6.1)	25.7 (1.5)	0.0445
Period from symptom onset to delivery, years, mean (SD)	4.8 (10.9)	-12.7 (11.8)	0.0318
History of spontaneous miscarriage or infant death†, number (%)	5 (45.5%)	1 (33.3%)	0.6154

†The patient died at an age < 1 year.

Abbreviations: SD; standard deviation.

Results of the multivariate logistic regression analysis of factors associated with CDM in children are presented in Table 4. The results of the multivariate analysis showed that all the factors expected to be involved in the development of CDM were not risk factors.

Table 4 Multivariate analysis of factors associated with congenital myotonic dystrophy (CDM).

Factor	Odds ratio	95% confidence interval	p-value
Maternal CTG repeat number	1.002	0.995 to 1.008	0.6070
Child CTG repeat number	0.998	0.992 to 1.003	0.4406
Period from symptom onset to delivery	1.177	0.945 to 1.465	0.0530

4. Discussion

To the best of our knowledge, this is the largest study in Japan to assess mothers and children who were both diagnosed with DM1. Similar studies of this scale are rare, even outside of Japan. In this study, no significant correlation was found between the number of CTG repeats in mothers and their children, and the presence of a high number of repeats did not lead to an early diagnosis of CDM. However, anticipation was confirmed by the number of CTG repeats in children who were significantly increased compared to those in their mothers.

However, our institution's 0% mortality rate of children with CDM differs from previous reports that children with CDM have a poor prognosis [3, 13]. The present analysis suggests that CDM's prognosis is unrelated to CTG repeats and that other factors may be involved. Our study findings revealed critical information regarding pregnancy, childbirth, neonatal management of women with DM1, and the suitability of prenatal diagnosis in pregnant women with DM1, despite the limited number of study participants.

DM1 severity is commonly correlated with the number of CTG repeats in the *DMPK* gene [11, 14]. CDM is considered an early-onset and severe form of DM1 [3, 4, 11]. However, in the present study,

no significant increase in the CTG repeat number was observed among children with CDM compared to those without CDM (Table 3). The lack of difference between children with and without CDM may have been due to the small number of children without CDM included in the study. Further, the three individuals without CDM were diagnosed with relatively severe DM1 because they presented DM1 symptoms during childhood, which may have affected the results. The children in this study had a CTG repeat number of ≥1,000.

The proportion of children with CDM versus DM1 in this study was greater than previously reported [6, 8]. We believe that this difference may be due to various factors; for example, severe cases of DM1 are easier to diagnose than milder cases, the absence of paternally inherited cases in this study, and the referral of several pregnant women with DM1 complications from other regions to our hospital, as it is the largest perinatal center in Japan.

The present study revealed no significant correlation between CTG repeat number and age at symptom onset or age at diagnosis, which indicated that elevated repeat numbers did not result in an earlier symptom or diagnosis. This may be because the timing of DM1 diagnosis was influenced by the severity of symptoms and how individuals perceived the disease.

The present study's mean maternal age at delivery was significantly higher. The period from the maternal symptom onset to delivery was significantly higher in CDM cases than in non-CDM cases. In other words, most DM1 children with CDM were born several years after the maternal symptom onset, whereas most DM1 children without CDM were born >10 years before the symptom onset (Table 3). It might be because women with mild DM1 may have been pregnant earlier and uneventfully delivered DM1 children without CDM. On the other hand, DM1 is often associated with infertility, abnormalities during pregnancy, miscarriage, and premature delivery [13, 15-19]. Japanese cases of polyhydramnios during pregnancy or threatened preterm labor that led to a diagnosis of DM1 have been reported [18, 20]. However, our study also revealed that it is difficult to predict whether fetuses would present with CDM in cases without polyhydramnios despite being diagnosed with DM1 based on the expanding CTG repeat number.

Barbé et al. [21] suggested that high levels of methylation upstream and downstream of the CTG repeat were better correlated with CDM onset than with the CTG repeat number. We anticipate that developing testing strategies other than the CTG repeat number will be necessary for identifying predictors of DM1 severity in children [22, 23].

In our study, CTG repeat numbers were significantly higher in all children than in their mothers, and symptoms were more severe in children than in mothers. However, no children died during infancy, and life expectancy was better than expected based on previous reports [3-5, 13, 19]. In our study, the small number of cases and large time gaps between births prevented a detailed statistical analysis of long-term prognoses among pediatric participants. In addition, clinical features during early infancy and thereafter varied greatly between individual cases regardless of CDM diagnosis. Therefore, we cannot assert that there is no hope of long-term survival for children diagnosed with CDM, as has been indicated in prior reports.

5. Limitations

Our study had several limitations, including its single-center retrospective design and disproportional participant composition (primarily patients with CDM) with many potential biases. Therefore, additional multicenter studies with larger cohorts are needed.

As previously described, the tendency of patients with mild symptoms to be overlooked, rather than diagnosed with DM1, may have affected the findings of our study. Furthermore, there is a definite possibility of recruitment/selection bias; the women whose children had died during pregnancy or after birth without being diagnosed with DM1 were excluded and not counted, and of recall bias; much of the information about older mothers and their children are obtained only from questionnaires completed by the mothers themselves, because their obstetric and pediatric medical records are more difficult to access. Therefore, some of the results of our study, especially the proportion of infants with CDM, may not be valid for all DM1 groups.

However, despite the abovementioned biases, even among cases of severe DM1, no children died during infancy. This result indicates that high repeat numbers do not guarantee early mortality. One possible reason for this outcome may be the enhanced management of pregnancies with DM1 to prepare for CDM1 delivery. Thus, for safety reasons, the delivery method was a cesarean section, and the baby was admitted to the neonatal intensive care unit immediately after delivery [13, 24]. We believe that our hospital's remarkably low number of neonatal deaths was secondary to these proactive measures. It may be worth discussing if the caesarian section should be recommended in case of genetic diagnosis of DM1, regardless of the maternal or fetal symptoms.

6. Conclusions

The findings of our study suggest that even when the CTG repeat number of the fetus is determined by prenatal genetic testing, extreme care must be taken when using this information to determine the future of the pregnancy. Multiple articles have already reported difficulties associated with prenatal genetic testing for DM1 [25], and our study supports the position of prior authors. Affected mothers and families should be provided accurate information derived from the latest available evidence and given broad support from obstetricians and clinical genetic specialists, including genetic counselors, pediatricians, and neurologists, to make informed independent decisions.

Acknowledgments

We would like to thank the Neonatology and Anesthesiology Departments of our hospital.

Author Contributions

Kosuke Shigematsu, Yukiko Mikami, and Yasushi Takai wrote the main manuscript text. Mamiko Shinsaka and Yukiko Itaya collected the data, and Kosuke Shigematsu performed the data analysis. All authors reviewed the manuscript.

Competing Interests

The authors have declared that no competing interests exists.

References

1. Prendergast P, Magalhaes S, Campbell C. Congenital myotonic dystrophy in a national registry. Paediatr Child Health. 2010; 15: 514-518.

2. Campbell C. Congenital myotonic dystrophy. J Neurol Neurophysiol. 2012; S7: 001.
3. Kamsteeg EJ, Kress W, Catalli C, Hertz JM, Witsch-Baumgartner M, Buckley MF, et al. Best practice guidelines and recommendations on the molecular diagnosis of myotonic dystrophy types 1 and 2. Eur J Hum Genet. 2012; 20: 1203-1208.
4. Johnson NE, Heatwole CR. Myotonic dystrophy: From bench to bedside. Semin Neurol. 2012; 32: 246-254.
5. Turner C, Hilton-Jones D. The myotonic dystrophies: Diagnosis and management. J Neurol Neurosurg Psychiatry. 2010; 81: 358-367.
6. Campbell C, Levin S, Siu VM, Venance S, Jacob P. Congenital myotonic dystrophy: Canadian population-based surveillance study. J Pediatr. 2013; 163: 120-125.
7. Bosemani T, Jasien J, Johnston MV, Huisman TA, Poretti A, Northington FJ. Neonatal neuroimaging findings in congenital myotonic dystrophy. J Perinatol. 2014; 34: 159-160.
8. Lagrue E, Dogan C, De Antonio M, Audic F, Bach N, Barnerias C, et al. A large multicenter study of pediatric myotonic dystrophy type 1 for evidence-based management. Neurology. 2019; 92: e852-e865.
9. Redman JB, Fenwick Jr RG, Fu YH, Pizzuti A, Caskey CT. Relationship between parental trinucleotide GCT repeat length and severity of myotonic dystrophy in offspring. JAMA. 1993; 269: 1960-1965.
10. Martorell L, Cobo AM, Baiget M, Naudó M, Poza JJ, Parra J. Prenatal diagnosis in myotonic dystrophy type 1. Thirteen years of experience: Implications for reproductive counselling in DM1 families. Prenat Diagn. 2007; 27: 68-72.
11. Ho G, Cardamone M, Farrar M. Congenital and childhood myotonic dystrophy: Current aspects of disease and future directions. World J Clin Pediatr. 2015; 4: 66-80.
12. Awater C, Zerres K, Rudnik-Schöneborn S. Pregnancy course and outcome in women with hereditary neuromuscular disorders: Comparison of obstetric risks in 178 patients. Eur J Obstet Gynecol Reprod Biol. 2012; 162: 153-159.
13. Rudnik-Schöneborn S, Zerres K. Outcome in pregnancies complicated by myotonic dystrophy: A study of 31 patients and review of the literature. Eur J Obstet Gynecol Reprod Biol. 2004; 114: 44-53.
14. Overend G, Légaré C, Mathieu J, Bouchard L, Gagnon C, Monckton DG. Allele length of the DMPK CTG repeat is a predictor of progressive myotonic dystrophy type 1 phenotypes. Hum Mol Genet. 2019; 28: 2245-2254.
15. Endo T, Baba T, Sugio A, Morishita M, Takahashi M, Akashi Y, et al. A myotonic dystrophy 1 patient complicated with placental adherence after miscarriage of one dichorionic diamniotic twin following her tenth in vitro fertilization and embryo transfer. Arch Gynecol Obstet. 2012; 286: 1605-1608.
16. Meola G. Clinical aspects, molecular pathomechanisms and management of myotonic dystrophies. Acta Myol. 2013; 32: 154-165.
17. Johnson NE, Hung M, Nasser E, Hagerman KA, Chen W, Ciafaloni E, et al. The impact of pregnancy on myotonic dystrophy: A registry-based study. J Neuromuscul Dis. 2015; 2: 447-452.
18. Yee C, Choi SJ, Oh SY, Ki CS, Roh CR, Kim JH. Clinical characteristics of pregnancies complicated by congenital myotonic dystrophy. Obstet Gynecol Sci. 2017; 60: 323-328.
19. Dorcier LM, Coatleven F, Madar H, Sentilhes L. Abnormally invasive placentation in a woman with congenital myotonic dystrophy. Int J Gynaecol Obstet. 2018; 140: 376-377.

20. Shin YJ, Kim DJ, Park SY, Chung JH, Lee YK, Ryu HM. Myotonic dystrophy diagnosed during the perinatal period: A case series report. J Gene Med. 2016; 13: 105-110.
21. Barbé L, Lanni S, López-Castel A, Franck S, Spits C, Keymolen K, et al. CpG methylation, a parent-of-origin effect for maternal-biased transmission of congenital myotonic dystrophy. Am J Hum Genet. 2017; 100: 488-505.
22. Lanni S, Pearson CE. Molecular genetics of congenital myotonic dystrophy. Neurobiol Dis. 2019; 132: 104533.
23. López Castel A, Overby SJ, Artero R. MicroRNA-based therapeutic perspectives in myotonic dystrophy. Int J Mol Sci. 2019; 20: 5600.
24. Hopkins AN, Alshaeri T, Akst SA, Berger JS. Neurologic disease with pregnancy and considerations for the obstetric anesthesiologist. Semin Perinatol. 2014; 38: 359-369.
25. Savić Pavićević D, Miladinović J, Brkušanin M, Šviković S, Djurica S, Brajušković G, et al. Molecular genetics and genetic testing in myotonic dystrophy type 1. BioMed Res Int. 2013; 2013: 391821.