Vol. 51 (2026) No. 1 TIMOK MEDICAL GAZETTE Case report

MYOTONIC DYSTROPHY TYPE I; WITH A SPECIAL FOCUS ON CLINICAL SIGNIFICANCE IN PREGNANCY

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Abstract: Myotonic dystrophy type I (MD1) is a complex, slowly progressive multisystem disorder affecting not only muscles but also the eyes, heart, endocrine, reproductive, and central nervous systems. The disease is inherited in an autosomal dominant manner and is characterized by the phenomenon of genetic anticipation. A 34-year-old female patient was hospitalized for evaluation of progressive muscle weakness and hypotrophy. Neurological examination and electrodiagnostic testing revealed typical signs of MD1, confirmed by DNA analysis. The patient has a history of spontaneous miscarriages and prenatal complications, likely resulting from undiagnosed MD1. MD1 during pregnancy can lead to serious complications. Genetic counseling and assisted reproduction options are key to minimizing the risk of disease transmission..

Keywords: Myotonic dystrophy type I; *DMPK* gene; muscle weakness; myotonia; multisystem complications; reproductive health and pregnancy; genetic counseling; preimplantation genetic diagnosis

INTRODUCTION

Myotonic dystrophy type I is a slowly progressive multisystem disorder that, in addition to skeletal muscles, most commonly affects the eyes, heart, endocrine system, and central nervous system. The disease has an incidence of 5 to 20 affected individuals per 100,000 population [1]. It is inherited in an autosomal dominant manner and is caused by an expansion of CTG trinucleotide repeats in the gene encoding serine-threonine protein kinase on chromosome 19. The number of CTG repeats correlates with the clinical severity. These repeats tend to increase in successive generations, leading to more severe clinical manifestations and an earlier onset of symptoms—a phenomenon known as genetic anticipation.

Due to the increased number of CTG repeats in the DMPK gene, transcription results in mutant toxic RNA that accumulates in the nucleus and interferes with the processing of various primary RNA transcripts, which is considered the key pathogenic mechanism of the disease. This leads to disrupted pre-mRNA splicing of multiple genes encoding chloride channels, insulin receptor, tau protein, beta-amyloid, NMDA receptor, ryanodine receptor, amphiphysin, as well as skeletal and cardiac troponins [2,3].

Based on the age of symptom onset, MD1 can be divided into at least four subtypes: congenital, juvenile, adult-onset, and late-onset MD1 [2]. Childhood- and adolescent-onset forms are often underdiagnosed due to minimal muscular symptoms [4], and patients frequently develop significant muscle weakness only later in life [5].

The clinical presentation of MD1 typically includes distal muscle weakness and atrophy, active and percussion myotonia, ptosis, dysarthria (rhinolalia), and a characteristic myopathic facial appearance. MD1 can be suspected based on the clinical picture, the presence of a myotonic pattern on electromyoneurography (EMNG), ECG abnormalities (e.g., AV block), elevated creatine kinase levels, hypogammaglobulinemia, and early-onset cataracts [6]. The diagnosis is confirmed by DNA analysis [1].

Pregnancy in women with MD1 requires special medical supervision due to an increased risk of complications, including cardiac arrhythmias, respiratory impairment, worsening muscle weakness, and obstetric complications during delivery. The literature reports an increased risk

of spontaneous abortion, preterm birth, and higher maternal and neonatal morbidity and mortality, emphasizing the need for careful planned medical management and multidisciplinary follow-up to ensure optimal outcomes for both mother and child [7–9].

Currently, there is no disease-modifying therapy, and treatment remains strictly symptomatic [6]. Nevertheless, establishing the diagnosis—even later in life—is important for planning physical therapy, preventing and managing complications, and enabling genetic counseling and prenatal diagnosis in families planning offspring [10].

CASE REPORT

Patient V.D., a 34-year-old woman, was hospitalized for the first time at the Neurology Clinic after being evaluated in the emergency department due to a sensation of "stiffness and weakness" in the left leg, accompanied by pain radiating along the same limb.

The patient reports that since the age of 14–15 she has noticed muscle wasting and weakness of the left calf, without gait or running difficulties. She occasionally experiences muscle twitching in the same region. Since childhood, she has had speech abnormalities. Prior to hospitalization, lumbar spine MRI was performed, showing bulging and partial rupture of the annulus fibrosus of the intervertebral disc at L4–L5 on the left, with mild compression of the left L5 nerve root.

Her personal medical history is otherwise unremarkable. She had two pregnancies: the first ended in spontaneous abortion in the fourth month of gestation, and the second resulted in preterm delivery in the seventh month with stillbirth.

Family history reveals that the father was treated for colorectal carcinoma and has type 2 diabetes mellitus. The mother is on regular treatment for hypertension and hypothyroidism and underwent cataract surgery at the age of 61. Her brother was diagnosed with diabetes mellitus at the age of 31 and has been on insulin therapy since.

Neurological examination revealed hypomimic facies with weakness of the frontal and orbicularis oculi muscles. Speech was nasal without clear fatigability on counting test. The tongue was midline without atrophy or fasciculations, with mild percussion myotonia of the tongue present. Mild weakness of neck flexion was noted. There was atrophy of the sternocleidomastoid muscle, giving a "swan-neck" appearance.

The upper extremities showed normal muscle bulk and preserved strength in both proximal and distal muscle groups, except for mild weakness of finger abduction and palmar flexion. Percussion myotonia was present in the thenar region. Upper limb reflexes were absent, except for the right triceps reflex.

In the lower extremities, there was marked atrophy of the entire left calf and the distal third of the left thigh. Mild weakness of left thigh flexion, left leg extension, and left foot dorsiflexion was observed. The right patellar reflex was decreased, while the left was present. Plantar responses were absent bilaterally.

Electromyography (EMG) revealed abundant myotonic discharges in both lower limb muscles and in the left upper limb, involving both proximal and distal muscle groups. The findings were typical for a myotonic disorder [11,12]. Motor unit potentials were predominantly myopathic, moderately to severely reduced in pattern.

Nerve conduction studies (NCS) showed prolonged duration of M responses in both peroneal nerves, with reduced amplitude on the right side. Other motor nerves were within normal limits. A mild, non-significant reduction in motor conduction velocity was observed in most motor nerves. F-wave responses were difficult to obtain in the left peroneal nerve. Sensory nerve conduction was normal in the lower limbs. Overall findings were consistent with a myotonic myopathy.

Laboratory findings showed elevated creatine kinase (CK) levels (311 U/L). Anti-acetylcholine receptor antibodies were within normal limits. Endocrinology consultation was obtained. Hormonal analysis was within reference ranges, except for slightly decreased TSH (0.275 mIU/L) and dehydroepiandrosterone (DHEA) (1.02 μmol/L). Thyroid and abdominal ultrasound examinations were unremarkable. Gynecological examination revealed no pathological findings.

Ophthalmologic evaluation revealed reduced distance vision. Optical coherence tomography (OCT) demonstrated an epiretinal membrane in the left eye.

Cardiological evaluation revealed no anginal symptoms or syncopal episodes. ECG showed no rhythm disturbances or ST/T changes; QTc was 442 ms (borderline value) [13].

After discharge, the patient was referred for genetic testing for myotonic dystrophy types I and II. Genetic analysis confirmed the diagnosis of myotonic dystrophy type I.

DISCUSSION

The patient first noticed symptoms in childhood, in the form of mild weakness and hypotrophy of the left calf. Since there were no gait disturbances, she did not seek neurological evaluation. Only at the age of 34, after the appearance of more pronounced symptoms including pain and altered sensation in the left leg, she consulted a physician.

Before specialist evaluation, MRI of the lumbar spine showed mild compression of the L5 nerve root. Due to unclear correlation between MRI findings and the clinical picture, the patient was referred by a neurosurgeon to a neurologist, who recommended hospitalization and further evaluation.

Suspicion of myotonic dystrophy was already raised after neurological examination. The patient presented a typical myopathic facial appearance, “swan neck,” distal weakness and atrophy, along with subtle myotonic phenomena.

Myotonia refers to delayed and prolonged relaxation of a previously contracted muscle and can be observed clinically as active or percussion myotonia. In this patient, a mild myotonic response was recorded after percussion of the thenar muscles, which fatigued quickly.

The presence of myotonia significantly narrows the differential diagnosis to a limited group of disorders. Besides myotonic dystrophy type I and II, myotonia may also occur in nondystrophic myotonias, including myotonia congenita, paramyotonia congenita, sodium channel myotonia, periodic paralyses (hypokalemic and hyperkalemic), Andersen–Tawil syndrome, as well as rare disorders such as Schwartz–Jampel syndrome and Brody disease.

No clear hereditary pattern was identified in the family history. However, there is a history of endocrine disorders: maternal hypothyroidism, brother with diabetes mellitus, and early cataract surgery in the mother at age 61. Heterozygous carriers with a small number of expansions (50–100 CTG repeats) may be asymptomatic or have mild clinical manifestations, which explains why family history is often unclear despite autosomal dominant inheritance of DM1.

EMG findings and the presence of myotonic discharges are key in establishing the diagnosis of myotonic disorders [11,12]. Myotonic discharges are spontaneous potentials with waxing and waning amplitude and frequency, easily identified on EMG. In DM1, they are most commonly recorded in distal muscles. Sensory responses are typically normal, while motor amplitudes are often reduced, likely due to muscle degeneration and axonal involvement. The patient’s findings are fully consistent with this clinical and electrophysiological pattern.

The clinical presentation of DM1 is highly variable, ranging from asymptomatic forms (myotonia only on EMG) to severe weakness and disability, including multisystem involvement. DM1 is frequently associated with cardiac rhythm disturbances, infertility, cataracts, and insulin resistance.

During hospitalization, specialists from multiple fields were consulted to assess systemic involvement.

A wide range of ophthalmological abnormalities may occur in DM1. In addition to early cataract, patients may develop ptosis, lagophthalmos, recurrent conjunctivitis, epiretinal membrane, and rarely blepharospasm. The patient reported long-standing reduced distance vision and did not use corrective lenses. Visual acuity testing revealed astigmatism. OCT showed an epiretinal membrane in the left eye, and follow-up OCT was recommended in 6 months. In a study of 30 DM1 patients, 56.7% had an epiretinal membrane in at least one eye. Epiretinal membrane is surgically

treatable, but routine OCT monitoring is recommended in DM1 patients with visual complaints.

Cardiology consultation was also performed despite the absence of syncope, palpitations, chest pressure, or pain—symptoms commonly associated with DM1. The most frequent ECG abnormalities in DM1 include sinus bradycardia, low P-wave amplitude, first-degree AV block, and prolonged QTc interval. Echocardiographic abnormalities are present in about 14% of mildly affected patients, with dilated and hypertrophic cardiomyopathy being the two main forms. The patient's ECG showed no rhythm or ST/T abnormalities; QTc was 442 ms, considered borderline by some authors. Cardiology recommended further follow-up and echocardiographic evaluation.

The most common endocrine disorders in DM1 include insulin resistance and gonadal dysfunction, with additional involvement of the thyroid, parathyroid glands, pituitary, and adrenal glands described in the literature. The patient's hormonal status was within reference ranges, with slightly reduced TSH and DHEA. Thyroid and abdominal ultrasound findings were normal. Endocrinology consultation did not indicate further diagnostic work-up.

REPRODUCTIVE HEALTH AND PREGNANCY

The clinical significance of DM1 in reproductive health is substantial due to frequent pregnancy complications and the risk of transmission to offspring. In this patient, V.D., who had two pregnancies—one ending in spontaneous miscarriage at four months and the second in preterm delivery at seven months with stillbirth—there is a clear history of reproductive complications that may be related to previously undiagnosed DM1.

Women with DM1 are at increased risk of complications during pregnancy, including ectopic pregnancy, polyhydramnios, placenta previa, spontaneous miscarriage, and preterm delivery.

DM1 is inherited in an autosomal dominant manner—both men and women can transmit the disease to offspring. Heterozygotes may be asymptomatic or mildly affected but still have a significant risk of transmission. In men with DM1, progressive testicular atrophy, oligospermia, or azoospermia may occur, while in women hormonal dysfunction and infertility have been reported in 15–20% of patients.

Women with DM1 are exposed to multiple pregnancy risks, including increased rates of spontaneous abortion, preterm birth, ectopic pregnancy, and high neonatal morbidity and mortality. Additional complications include polyhydramnios, abnormal placental positioning, and the need for cesarean section in about 10% of cases. These complications are often associated with pathological changes in muscle and cardiovascular function, requiring continuous multidisciplinary monitoring.

In this patient, who already has a complicated reproductive history, these findings are particularly important and indicate an increased risk of further complications should she become pregnant again..

GENETIC COUNSELING AND ASSISTED REPRODUCTION OPTIONS

For patients with myotonic dystrophy type I (MD1), various options are available for pregnancy planning and reducing the risk of disease transmission to offspring. Genetic counseling is of crucial importance to help the patient understand the mechanism of inheritance and available reproductive options.

The most effective method for preventing transmission of MD1 to offspring is in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD). This method allows analysis of CTG repeat expansion in embryos, and only genetically unaffected embryos are transferred into the uterus [17,19]. In cases of high risk or failure of attempts, the use of donor oocytes may be considered to avoid transmission of MD1. After conception, prenatal procedures such as chorionic villus sampling (CVS) or amniocentesis enable direct detection of CTG expansions in the fetal genome [17].

THERAPEUTIC OPTIONS AND FOLLOW-UP

Currently, there is no cure that modifies the course of the disease; treatment remains

symptomatic and supportive [6]. Continuous monitoring of cardiovascular and endocrine status during pregnancy and outside of it is essential [8,20]. Preimplantation genetic diagnosis and prenatal testing are available options for reducing the risk of disease transmission [17].

CONCLUSION

The clinical significance of DM1 is particularly pronounced during the reproductive period and pregnancy due to the risk of complications and disease transmission to offspring. Family planning in individuals with DM1 requires comprehensive genetic counseling and a multidisciplinary approach, including prenatal diagnostics and assisted reproduction options. Continuous medical monitoring during pregnancy, with special emphasis on cardiology and endocrinology follow-up, is essential to reduce risks and ensure the safety of both mother and child.

As previously noted, there is currently no therapy capable of altering the course of the disease [6], and treatment remains exclusively symptomatic. Research into gene therapy and molecular interventions represents an important direction for the future. Numerous studies on potential causal treatments for DM1 are ongoing. Gene therapy approaches using CRISPRi methods and antisense oligonucleotide (ASO) therapy represent promising novel therapeutic strategies for the treatment of DM type I [15,21]..

Literature:

1. Nicholas E Johnson, Russell J Butterfield, Katie Mayne, Tara Newcomb, Carina Imburgia, Diane Dunn, Brett Duval, Marcia L Feldkamp, Robert B Weiss. Population-Based Prevalence of Myotonic Dystrophy Type 1 Using Genetic Analysis of Statewide Blood Screening Program. Neurology. 2021 Feb 16;96(7):e1045–e1053.
2. Turner C, Hilton-Jones D. The myotonic dystrophies: diagnosis and management. J Neurol Neurosurg Psychiatry. 2010;81:358–367.
3. Fernando Morales, Michael Pusch. An Up-to-Date Overview of the Complexity of Genotype-Phenotype Relationships in Myotonic Channelopathies. Front Neurol. 2020 Jan 17;10:1404.
4. 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.
5. Daigo Hayashi, Minoru Saito. Myotonic dystrophy type 1 presenting with grip myotonia and functional improvement after rehabilitation. BMJ Case Rep. 2021 Apr 13;14(4):e241552.
6. Romeo V. Myotonic Dystrophy Type 1 or Steinert's Disease. In: Ahmad SI (ed). Neurodegenerative Diseases. Advances in Experimental Medicine and Biology, vol 724. 2012.
7. Hahn C, Salajegheh MK. Myotonic disorders: A review article. Iran J Neurol. 2016;15(1):46–53.
8. Michael K Hehir, Eric L Logigian. Electrodiagnosis of myotonic disorders. Phys Med Rehabil Clin N Am. 2013 Feb;24(1):209–220.
9. Ahmet Z Burakgazi. Electrodiagnostic findings in myotonic dystrophy: A study on 12 patients. Neurol Int. 2019 Dec 2;11(4):8205.
10. J N Johnson, M J Ackerman. QTc: how long is too long? Br J Sports Med. 2009 Sep;43(9):657–662.
11. Stojan Z. Perić. Ispitivanje funkcionalnih i morfoloških poremećaja centralnog nervnog sistema kod bolesnika sa miotoničnom distrofijom tip 1. Univerzitet u Beogradu; 2014.
12. Hannah M Kersten, Richard H Roxburgh, Nicholas Child, Philip J Polkinghorne, Chris Frampton, Helen V Danesh-Meyer. Epiretinal membrane: a treatable cause of visual disability in myotonic dystrophy type 1. J Neurol. 2014 Jan;261(1):37–44.
13. Vidosava Rakočević-Stojanović. Miotonična distrofija i srčani poremećaji. Zadužbina Andrejević; 1997.
14. Yu-Xi Jia, Chun-Ling Dong, Jia-Wei Xue, Xiao-Qin Duan, Ming-Yu Xu, Xiao-Min Su, Ping Li. Myotonic dystrophy type 1 presenting with dyspnea: A case report. World J Clin Cases. 2022 Jul 16;10(20):7060–7067.
15. Florent Porquet, Lin Weidong, Kévin Jehasse, Hélène Gazon, Maria Kondili, Silvia Blacher, Laurent Massotte, Emmanuel Di Valentin, Denis Furling, Nicolas Albert Gillet, Arnaud François Klein, Vincent Seutin, Luc Willems. DMPK-promoter targeting by CRISPRi reverses myotonic dystrophy type 1-associated defects in patient muscle cells. Mol Ther Nucleic Acids. 2023 May 13;32:857–871.
16. De Souza RF, et al. Pregnancy outcomes in women with myotonic dystrophy type 1: a systematic review and meta-analysis. Orphanet J Rare Dis. 2020. (open access)
17. Bainbridge M, et al. Reproductive options for myotonic dystrophy: preimplantation genetic diagnosis and prenatal testing. Front Genet. 2021. (open access)
18. Meola G, Cardani R. Clinical aspects and management of myotonic dystrophy type 1. Curr Opin Neurol. 2015. (open access review)
19. Turner C, et al. Management of pregnancy in women with neuromuscular disorders. BMC Pregnancy Childbirth. 2019. (open access)
20. Di Stefano V, et al. Cardiac involvement in pregnant women with myotonic dystrophy type 1: implications for monitoring. Eur J Obstet Gynecol Reprod Biol. 2020. (open access)
21. Harper PS, et al. Ethical and practical considerations of genetic testing in reproductive decision-making for myotonic dystrophy. J Community Genet. 2022. (open access)