From the Symptoms of an Undiagnosed Mother to the Infant with Congenital Myotonic Dystrophy

Tanısız Annenin Semptomlarından Konjenital Myotonik Distrofili Bebeğe

Congenital Myotonic Dystrophy

Nazlı Dilay Gültekin, Fatma Hilal Yılmaz, Hüseyin Altunhan, Rahmi Örs
Neonataloji BD, Necmettin Erbakan Üniversitesi, Konya, Türkiye

Öz

Konjenital myotonik distrofi (KMD) neonatal dönemde, hipotoni, respiratuar yetmezlik ve beslenme problemleri ile bulgu veren klinik spektrumu geniş bir hastalıktır. Aile öyküsü tanıda önemli olmakla birlikte neonatal dönemde bebeğin tanı alması annenin ya da nadiren babanın tanı almasını sağlayabilir. Burada neonatal dönemde hipotonisite ve solunum yetmezliği ile prezente olan erkek hastada, annenin halsizlik, kas ağrısı ve çok uyuma şikayetlerinden yola çıkılarak genetik analizle KMD tanısına varıldı. Vakamızda olduğu gibi, hipotonik bebeklerde yalnızca aile öyküsünün derinleştirilerek KMD tanısının daha erken konabileceği akılda tutulmalıdır.

Anahtar Kelimeler

Konjenital Myotonik Distrofi; Hipotonik İnfant; Polihidroamniyoz; Dismorfik Yüz; Solunum Yetmezliği

Abstract

Congenital myotonic dystrophia (CMD) is a disorder with a wide clinical spectrum, characterized by hypotonia, respiratory failure, and nutritional challenges in the neonatal period. Although familial history is important in the diagnostic process, diagnosing the infant in the neonatal period may, conversely, lead the mother, or rarely the father, to be diagnosed. Here, a male infant presenting with hypotonicity and respiratory failure in the neonatal period was diagnosed with CMD through genetic testing by looking at the complaints of fatigue, muscle pain, and hypersomnia in the mother. As in our case, it should be kept in mind that CMD can be diagnosed at an early stage only by focusing on the familial history in hypotonic infants.

Keywords

Congenital Myotonic Dystrophia; Hypotonic Infant; Polyhydramnios; Dysmorphic Face; Respiratory Failure

DOI: 10.4328/JCAM.4997 Received: 24.03.2017 Accepted: 05.04.2017 Printed: 01.02.2017 J Clin Anal Med 2017;8(suppl 1): 58-60
Corresponding Author: Nazlı Dilay Gültekin, Neonataloji BD, Necmettin Erbakan Üniversitesi, Meram Tıp Fakültesi, 42060, Konya, Türkiye.
T: +90 3322236697 F.: +90 3322236182 E-Mail: dilayyenihan@hotmail.com

Introduction

Congenital myotonic dysthropia (CMD) is a neuromuscular disorder with an autosomal dominant hereditary transmission. In CMD, a disorder with a prevalence of 1/100,000 across the world, facial dysmorphic signs, such as fishmouthing, long face, ptosis, and temporal muscle atrophy are remarkable findings seen at the time of delivery. Patients with CMD present with severe hypotonia, talipes equinovarus, artrogryposis, weakened weeping and sucking, and respiratory failure. Congenital cataracts, thyroid dysfunction, and cardiac involvement are also seen among cases with CMD, but more rarely [1,2]. CMD develops as a result of the repetition of the myotonic dystrophy protein kinase (DMPK) gene in chromosome 19q13 due to the increased cytosine-thymine-guanine (CTG) trinucleoid in the 3' untranslated region. In such patients, the repetition of CTG is generally found to be more than 1,000 [2], and the mortality is between 30-40% in the neonatal period [3]. Here, we aimed at presenting how an infant with the complaints of hypotonicity and respiratory failure during the neonatal period was diagnosed with CMD by focusing on the infant's symptomatic, but previously undiagnosed, mother.

Case Report

Our case was born at term to a 23-year-old mother as the second living infant after the second pregnancy through cesarean section, and the infant's Apgar scores were 5 and 7 at minutes 1 and 5, respectively. Resuscitated in the delivery room, the patient was taken to the neonatal department after the intubation. The patient's parents with non-kinship also had a 2-year-old healthy daughter. The prenatal history of the patient revealed polyhydramnios. While the patient's weight, head circumference, and height were 2750 gr (25-50 p), 35 cm (90 p), and 48 cm (50-75 p) respectively, the physical examination also revealed prominent root of nose, antraverted nostrils, higher palate, retrognathia and micrognathia, and inverted-V-shaped upper lip (Figure 1). The cardiological and gastrointestinal systems examination of the patient conducted following intubation and mechanical ventilation were within normal limits. On the neurological examination, hypotonicity and hyperlacticity in all extremities were present, and no deep tendon reflexes were recorded in the lower extremities. Bilateral talipes echinovarus deformity was observed, and metabolic tests of the patient with syndromic presentation were detected to be normal. Investigated in terms of hypotonicity, the level of creatine kinases (CK) (85 U/L) was at normal level. Cranial magnetic resonance imaging (MRI) demonstrated subdural hemorrhage on the right parietal region. The speech defects in the patient's mother drew attention. Although previously evaluated many times in the neurology and psychiatry departments due to the complaints of hypersomnia and fatigue, the mother had not been diagnosed with anything. On physical examination, the mother displayed myotonic findings such as masklike face and difficulty in relaxation after gripping fingers (Figure 2). After performing electromyography (EMG), myotonic discharges were determined in the mother, and so the patient was genetically evaluated in terms of CMD. As a result of the genetic testing, at least 50 CTG repeat size was detected in an allele of the myotonic dystrophia protein kinase (DMPK) gene, and the patient was diagnosed with CMD. The patient was supported with mechanical ventilation for 20 days during the hospital stay. On day 58, the patient was discharged with oral feeding and without supplemental oxygen.

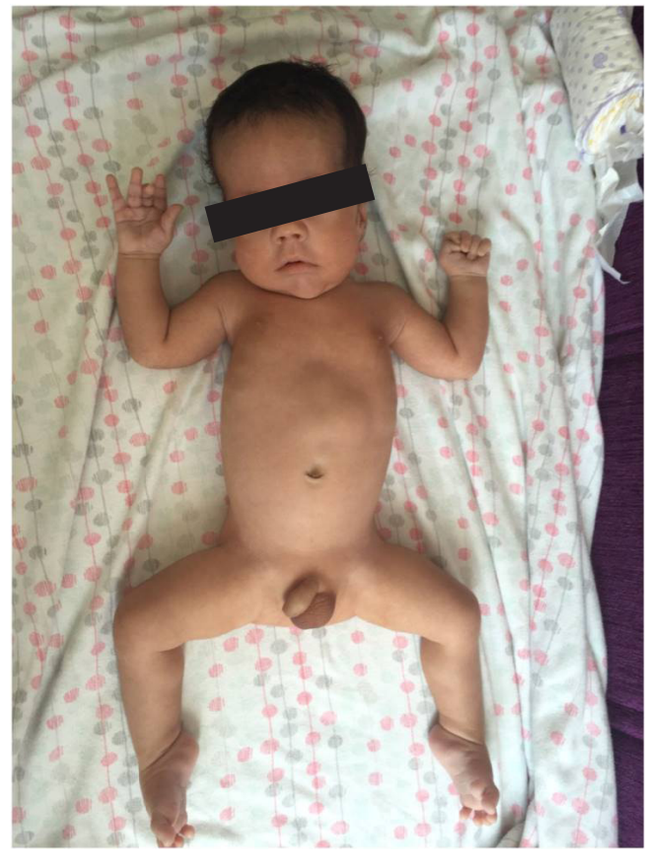

Figure 1. Floppy infant with bilateral talipes echinovarus deformity

Figure 2. Patient's mother showing masklike face and infant with antraverted nostrils, retrognathia and micrognathia, and inverted-V-shaped upper lip

Discussion

The clinical features of CMD were first described by Hans Steinert et al. at the beginning of the 1900s [4]. There are two different forms of the disease, both characterized by muscle weaknesses, myotonia, and cataracts. Various genetic differences are observed between type 1 myotonic dystrophy (MD), the most severe form seen at birth or in childhood, and type 2 MD seen during adulthood. While the repetition of CTG is observed in the DMPK gene in type 1 MD, the repetition of cytosine-cytosine-

thymine-guanine (CCTG) repeat expansion occurs in zinc finger protein 9 (ZNF9) gene in type 2 MD. Our case was a type 1 MD patient with a 50 repeat expansion of CTG in the DMPK gene. In patients affected by the condition in the neonatal period, respiratory failure stemming from the weakness of respiratory muscles is one of the most significant challenges. The existence and severity of respiratory failure define the prognosis. While the mortality rate due to respiratory failure is almost 25% in patients needing mechanical ventilation for more than 30 days, the rate increases up to 40% in infants seriously affected by CMD [5]. In our patient, the need for ventilation ceased at the 26th day after birth.

Whilest the congenital form is generally seen in the infants of symptomatic mothers with multisystemic involvement, serious complaints can also be observed in the neonatal period in the infants of mothers with mild symptoms who are not yet diagnosed. Consistent with the literature, the mother of our patient diagnosed with type 1 MD and needing long-term ventilation had yet to be diagnosed. The most commonly encountered cardiac defects in type 1 MD patients are conducting abnormalities, with the rate of 40%. Minor conducting defects can be detected via electrocardiography (ECG) alone. Because CMD is a disorder with a progressive course, the use of an implantable cardioverter defibrillator or pacemaker is proposed in order to prevent sudden cardiac death often seen in such patients [6]. Even though the ECG performed on our patient did not reveal any conducting defect, the patient was followed up by the pediatric cardiology department. In addition, studies have illuminated the association between the width of CTG repetition size in type 1 MD patients and the prevalence and progression of cardiomyopathy. For this reason, the detection of CMD cases at an early stage is important to prevent disease progression by properly following up these patients through ECG.

Even if it is not observed in the neonatal period, myotonia is detected in all cases prior to 11 years of age [5]. The earlier the symptoms of CMD began in the mothers, the more CMD risk increases in the infants. In our patient's mother, myotonia symptoms had been present since her infancy. In a study, Esplin et al. assumed MD as an important cause in idiopathic polyhydramnios. In cases with idiopathic polyhydramnios and fetal swallowing dysfunction, myopathy due to X linked myopathy, congenital myotonic dystrophy, and congenital myopathy are three neuromuscular disorders to be ruled out [7]. In our patient, the history of polyhydramnios also drew attention to such an association, and such signs as the dysarthria detected in the mother, masklike face, marked muscle weakness increasing with pregnancy, and fatigue were the guiding lights for the diagnostic approach to the infant. As with our patient, the fact that while a mild form of the disease is present in the mother, a severe form of CMD is observed in the infant and this demonstrates that tissue mosaicism and other genetic factors are also effective in determining the severity of disease phenotype. In the study performed by Cobo et al., it was shown that the risk of developing CMD is higher during the neonatal period in cases where the number of maternal alleles is more than 300 repetitions [8]. While the congenital form of CMD is observed in only 10% of the infants with less than 300 CTG repetitions, 60% of the infants of mothers with more than 300 repetitions were congenitally affected by the condition [8]. However, more than half of the affected mothers are not diagnosed with myotonic dystrophy or have no other complaints. As in our patient, diagnosing the infant with CMD is generally a factor leading to the diagnosis of the mother.

In infants whose mothers present with the clinical signs of a muscle disorder, the diagnosis can be achieved in a shorter period through genetic testing with no need for detailed tests. Genetic tests lead to certain diagnosis and are more cost-effective. The techniques such as electromyography (EMG) and muscle biopsy used to diagnose muscle disorders are insufficient in the diagnosis of CMD during the neonatal period. Although effective to demonstrate myopathic potentials, EMG is not useful because myotonic discharges are not observed during the neonatal period [2]. The assessment of muscle biopsy with different stainings is important in the diagnosis of CMD; however, these unconventional procedures are uncommon in most laboratories [9]. If muscle biopsy is evaluated properly, then the increase in the number of central nucleus, atrophy of type 1 bindings, clusters of pyknotic cells, and angular fibers can be observed.

Among the problems anticipated in the follow-up period of the patients with CMD, retardation in psychomotor development, growth retardation, nutritional deficiencies, and constipation are frequently observed [10]. Therefore, patients with CMD should be followed up by other training departments.

In conclusion, CMD can be diagnosed at an early stage in infants with the help of detailed familial histories. Investigating the mother with reference to the diagnosis of the infant can give clues as to the prognosis of the condition. With this report, we aimed to emphasize the importance of observation and history as a cost-effective diagnostic procedure; more-recently developed techniques or technologies are not necessarily required or effective.

Competing interests

The authors declare that they have no competing interests.

References

1. Campbell C. Congenital myotonic dystrophy. J Neurol Neurophysiol 2012; S7:1.
2. Bass N, LotzeT.E, Miller G. Hypotonia and Neuromuscular Disease in the Neonate in Fanaroff and Martin's Neonatal-Perinatal Medicine. 10th ed. Saunders Elsevier; Philadephia 2015; 950-63.
3. 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.
4. Thornton C.A. Myotonic Dystrophy. Neurol Clin 2014; 32:705-19.
5. Volpe JJ. Neuromuscular disorders: Muscle involvement and restricted disorders. In: Neurology of the Newborn. 5th ed. Saunders Elsevier; Philadephia 2008. p. 801.
6. Nigro G, Papa AA, Politano L. The heart and cardiac pacing in Steinert disease. Acta Myol 2012;31(2):110–6.
7. Esplin MS, Hallam S, Farrington PF, Nelson L, Byrne J, Ward K. Myotonicdystrophy is a significantcause of idiopathicpoly- hydramnios. Am J Obs Gynecol 1998; 179: 974-7.
8. Cobo AM, Poza JJ, Martorell L, Lopez de Munain A, Emparanza JI, Baiget M. Contribution of molecular analyses to the estimation of the risk of congenital myotonic dystrophy. J Med Genet 1995;32:105–8.
9. Campbell C, Levin S, Siu VM, et al. Congenital myotonic dystrophy: Canadian population-based surveillance study. J Pediatr 2013; 163:120-5.
10. Domingues S, Alves Pereira C, Machado A, Pereira S, Machado L, Fraga C, Oliveira A, Vale I, Quelhas I. Congenital myotonic dystrophy in a Neonatal Intensive Care Unit: caseseries. Arch Argent Pediatr 2014;112:18-22.

How to cite this article:
Gültekin ND, Yılmaz FH, Altunhan H, Örs R. From the Symptoms of an Undiagnosed Mother to the Infant with Congenital Myotonic Dystrophy. J Clin Anal Med 2017;8(suppl 1): 58-60.