Congenital Myotonic Dystrophy

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Introduction

Congenital myotonic dystrophy is a rare autosomal dominant disease, which begins to show its symptoms in the intrauterine period and differs significantly from myotonic dystrophy of adults. The major feature differentiating it from the adult type is hypotonia, instead of myotonia. It was first discribed by Vanier in 1960. The diagnosis is quite easy if there is an index case in the family. The surviving babies are usually mentally retarded in later life. We present a family and their latest offspring with myotonic dystrophy, and discuss issues relevant to the disease.

Case Report

This baby girl was born through vaginal delivery to a non-consanginous 40 year old mother, as her 6th child, after 39 weeks of gestation. Her birthweight was 2150g and her length was 48 cm. The pregnancy of the mother was remarkable for polyhydramnios. On her first physical examination, profound hypotonia, tent-shaped upper lip, bilateral ptosis of the eyelids and retrognathia were noticed (Figure 1). She did not have any findings compatible with arthrogyriposis. Starting immediately after birth, moderate respiratory distress and intercostal retractions were evident. However, arterial blood gases were within acceptable limits and peripheral oxygen saturation as measured by pulse oximeter was in the range of 90-95%. On her chest x-ray, both diaphragms were elevated, decreasing the expansion space of the lungs. However, the aeration of the lungs were satisfactory. (Figure 2). She was given free oxygen by hood and recovered within 2 days, after which she was started on oral feeding. From the 3rd to 6th days, she had moderate feeding difficultly with gastric desiduals, but recovered from the 7th day onwards and on the 12th day of life, she was feeding completely on breast milk by oral route. A cranial ultrasonography was found to be normal. Family history revealed that her mother had myotonic findings. The baby had 2 brothers and a sister with similar findings at birth. Therefore PCR and Southern blot test was performed on her DNA, obtained from peripheral blood. The test confirmed that she had an allele with more than 1600 CTG repeats on chromosome 19q13.3. Her mother was found to be homozygous for this disease and the number of CTG

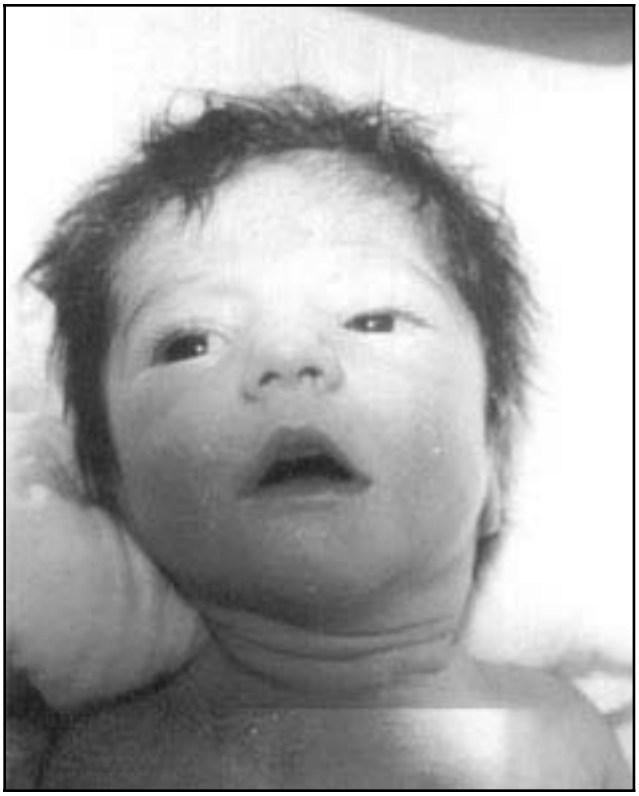

Figure 1. General appearance of the child.

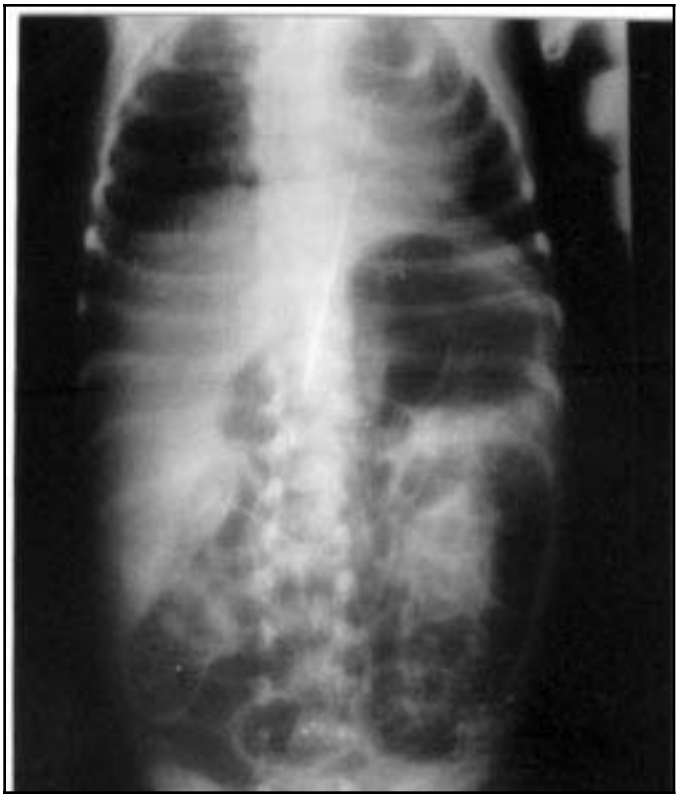

Figure 2. Bilateral elevated diaphragms.

repeats in the mother was 300. After the mother was diagnosed as a carrier of the disease, all of her offsprings were screened and the diagnoses reached. One of her brothers and one sister, 16 and 20 years old respectively, were mentally retarded, and the number of CTG repeats in each of them were 470. One of her sisters and one of her brothers had died at the age of 3 months and 1 day. One of her brothers, who was 14 years old, was seemingly normal, but he had a shorter allele with 58 repeats. He is expected to manifest the disease later in life. The baby was discharged on the 10th day of life. Although the importance of follow-up was emphasized, the family was lost to follow-up.

Discussion

Congenital myotonic dystrophy (CMD) is an autosomal dominant disease, inherited almost always through the mother. Neonatal mortality is about 15-20%.[1] The disease affects all the muscles in the body starting from the intrauterine period. This results in decreased swallowing and decreased body movements, leading to polyhydramnios.[2] In the immediate newborn period, hypotonia, hyporeflexia, respiratory distress, feeding difficulties, fascial diplegia, elevation of the diafragma and arthrogyriposis may be seen.[3] The respiratory distress and feeding difficulties resolves within the first weeks. Serum CPK levels and nerve conduction velocities are normal. The electromyographic (EMG) findings are not specific in the neonatal period and become typical after the age of 2-3 years.[4] Therefore, EMG is not required in the investigation of the case. In 80% of cases, ventricular dilatation is also seen,[5] but it was not seen in our case and her cerebral sonography was found as normal. Although she might not be aware of, active myotonia is evident in the mother and she can not open her eyelids once she closes them tightly or open her fists, once they are clenched.[6] The mother of this case had similar findings but she seemed to be content with her life. The mother was found to be homozygous for congenital myotonic dystrophy which is a very rare finding.[7]

Myotonic dystrophy is associated with an increase in the number of specific (CTG) trinucleotide repeats in the unstable region of the mytonoic dystrophy gene, which is located at chromosome 19q13.3. The mutation is dynamic and the number repeats and the severity of the disease increase with successive offsprings, i.e. the "anticipation" phenomenon. The number of repeats is also correlated with the age at onset of the disease. This gene encodes a protein kinase, which affects the function of sodium-potassium channels on the cell membrane.[8] Determination of the number of repeats from a DNA sample of a woman can be used to estimate the likelihood of transmitting severe congenital myotonic dystrophy. However, somatic mosaicism can also occur, in which case the extent of repeat expansion varies from tissue to tissue. In this case, the baby had an allele which had 1600 CTG repeats and the number of repeats were much more than that of the mother and siblings.

All the children who survive are mentally retarded in later life. The mean IQ of these patients is about 50 to 65.[3] This finding was also evident in the brother and sister of this case.

Although the family had been offered genetic counselling before and after this pregnancy, they refused to use contraceptive methods, prenatal diagnosis and therapeutic abortion because of their religious beliefs.

The treatment of these children is an ethical decision, which should take into consideration the concerns of the family and the physician. Adequate nutrition and ventilation should be ensured until the baby is able to perform these functions on his/her own. Assisted ventilation, tube feedings, and gastrointestinal prokinetics may be used. If muscle and joint deformities develop,they can usually be managed in a non-surgical approach.[9] The problems in the neonatal period and in later life incurs a heavy burden to the children, to the family and to the society. Genetic counselling is an essential part of the management.

References

1. Volpe JJ. Neuromuscular disorders: Muscle involvement and restricted disorders. In: Neurology of the Newborn. 4th edition. Philadelphia: W.B. Saunders, 2000, pp. 671-714.
2. Dunn LJ, Diereker LI. Recurrent hydramnios in association with mytonia dystrophica. Obstet Gynecol 1973; 42: 104-6.
3. Hageman A, Gabreels F, Liem KD et al. Congenital myotonic dystrophy: a report on 13 cases and a review of the literature. J Neurol Sci 1993;115: 95-101.
4. Kuntz NL. Clinical and electrophysiological profile of congenital myotonic dystrophy. Ann Neurol 1984; 19: 931-4.
5. Regev R, de Vries LS, Heckmatt JZ, et al. Cerebral ventricular dilation in congenital myotonic dystrophy. J Pediatr 1987; 111: 372-6.
6. Roig M, Balliu PR, Navarro C et al. Presentation, clinical course and outcome of the congenital form of myotonic dystrophy. Pediatr Neurol 1994; 11: 208-13.
7. Martorell L, Illa I, Arosell J,. et al. Homozygous myotonic dystrophy: clinical and molecular studies of three unrelated cases. J Med Genet 1996; 33: 783-5.
8. Ptacek LJ, Johnson KJ, Griggs RC. Mechanisms of disease: genetics and physiology of the myotonic muscle disorders. N Eng J Med 1993; 328: 482-9
9. O'Brien TA, Harper TS. Course, prognosis and complications of childhood-onset myotonic dystrophy. Dev Med Child Neurol 1984; 26: 62-7.