CASE REPORTS

Myotonia Congenita in a Bangladeshi Family

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Summary:

Myotonia congenita, a rarely found hereditary disease has been reported recently in the Department of Neurology, Dhaka Medical College Hospital. A family of a brother and sister with myotonia congenita is reported. Both of them presented with identical features i.e. myotonia and muscular hypertrophy . To the best of our knowledge no account of a family has earlier been reported from Bangladesh with myotonia congenita.

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Introduction:

Congenital myotonia is a rare hereditary disease of skeletal muscles that starts in early life and is characterized by myotonia and muscular hypertrophy. It may be of autosomal dominant (Thomsen's disease) and autosomal recessive form (Becker's disease)[1]. Both are due to chanellopathies, where the transport of chloride ion is faulty and the genetic locus is at 7q35 chromosome[2].

A family has reported of a brother and a sister with myotonia congenita. Both of them presented with identical features i.e. myotonia and muscular hypertrophy.

Case report:

A 20 year young male came to Neurology OPD Dhaka Medical College Hospital with complaints of difficulty in daily movements, which was more at initiation and lessened gradually with activity. This started at the age of 10-12 years as he can remember. He felt tightened/frozen initially for any attempted movement, which gradually lessened with activity.

In addition to this, he complained of very muscular body even he never did any exercises. He also got occasional generalized pains and cramps.

His symptoms did not exacerbate in cold. The patient had no history of any other medical problem. He also had no history of any routine medication use or substance abuse.

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His parents have a history of consanguinity of marriage. His older sister (26 years of age) had exactly same complaints.

Patient had physical therapy for long time, which failed to ameliorate his symptoms.

Physical examination was essentially unremarkable except one characteristic finding of pronounced muscle development despite a lack of exercise.

Percussion myotonia was mildly positive and he had slight difficulty in releasing his grip or opening his eyes after forcefully closing them. He had no temporal wasting, cataracts, testicular atrophy or alopecia. Needle EMG examination was significant for myotonic discharges with characteristic "Dive bomber" sound in the palm (abductor pollicis brevis) and all other muscles. It was more marked in proximal muscles.

The diagnosis was myotonia congenita based on the young age of onset, muscular hypertrophy rather than dystrophy and EMG findings. The characteristic EMG findings confirmed the diagnosis of myotonia, which was more marked proximally than distally. Lack of typical findings of dystrophic features (e.g. muscle wasting, myopathic facies, cataracts and frontal balding) along with myotonic potentials more marked proximally than distally support the diagnosis of myotonia congenita. Distinction of the type of myotonia congenita is based on inheritance. Since he has one more member in his family with same findings, onset of symtoms for both of them was at the age of 10-12 years, and both of his parents were unaffected, Becker type (autosomal recessive form) was most likely.

We started our patient on carbamazepine (100 mg BID). He came for follow up and his symtoms

improved by 50%. His sister is also on same medication, her symptoms also improved.

Discussion:

The myotonias encompass several neuromascular disorders characterized by sustained involuntary contraction of a group of muscles. Myotonias are traditionaly classified into dystrophic and nondystrophic types. Dystrophic myotonias are characterized by the prominence of muscle weakness and wasting, both of which were absent in our patient. Thus, he had a nondystrophic form of myotonia. These disorders include the paramyotonias and myotonia congenita.

Paramyotonia is a rare hereditary (autosomal dominant) nonprogressive muscular disorder. It is characterized by cold-induced myotonic stiffness that is increased with sustained muscle activity (paradoxical myotonia) and may be followed by a variable degree of weakness[3]. There is no wasting (atrophy) or increase in bulk (hypertrophy).These characteristics arise from a sodium channel abnormality, and our patients' clinical picture was not consistent with paramyotonia.

Myotonia congenita is nonprogressive and nondystrophic. Myotonia congeneta exists in two forms. Becker type, sometime called generalized myotonia, is more common version of the disease. It is autosomal recessive, meaning that it requires two copies of the defective CLCNI gene. The second form, Thomsen's disease, is relatively rare and is inherited as an autosomal dominant manner, meaning that it require only one copy of the defective CLCNI gene. Both diseases are caused by mutations in the chloride channel gene (CLCN1) and the criterion of differentiating Thomsen's from Becker's myotonia congenita lies in the mode of inheritance. However, more than 60 mutations have been identified in families with the disorders.[4]

The clinical feature usually begins during the first decade but in rare cases, onset may occur as late as approximately 18 years of age[5]. Worldwide prevalence is 0.2 to 7.3 per 100,000. Finland has unusually high occurrence, at 7.3 per 100,000[6]. The incidence of the disease among Asians is not well established. A literature search produced only two cases reports[7,8] of the disease in two Chinese families in Singapore and few cases reported in India[9, 10, 11]. Both dominant and recessive forms are associated with muscle hypertrophy and produce patients' extremely muscular appearance, classically described in the literature as "Herculean". The myotonia creates a higher level of resistance and movement against resistance which is a stimulus for muscle growth[12].

Myotonia congenita is due to a chloride channel abnormality (channelopathy) in skeletal muscle. Both forms of myotonia congenita are channelopathies caused by several nonsense and missense mutations in the skeletal muscle *CLCN1* gene[3] that has been localized to human chromosome 7q35. [13, 14]

A tale of two ions[12]: Normally, in a relaxed muscle cell, chloride channels in the cell membrane are open, allowing a current of negatively charged chloride ions to pass into the cell. Chloride channel account for most (70% to 80%) of skeletal muscle resting membrane conductance [15]. This creates a negative membrane potential relative to the outside. A nerve cell triggers contraction of the muscle cell by turning the membrane potential from negative to positive. Chemicals from the nerve cells stimulate the opening of sodium channels in the muscles cell, causing an inward current of positively charged sodium ions. When the positive current overcomes the negative (chloride) current, the muscle cell contracts. In muscle cell affected by myotonia congenita, defective chloride channels reduce the entry of chloride into the muscle cell or allow excess sodium to enter. Therefore, just a small amount of sodium influx is enough to change the membrane potential and cause contraction. The contraction is sustained by a buildup of positively charged ions at the muscle cell membrane, and relaxation is delayed[11], so the hyperexitability and repetitive firing of action potentials in myotonia congenita are caused by a low chloride conductance of the sarcolemma [16]. The abnormal chloride conductance maps to a region that contains the skeletal muscle voltage –gated chloride channel gene *CLCN1*[16].

Because myotonia congenita is rare and the underlying CLCN1 mutations are diverse, testing of the disease is limited.

For most people the diagnosis of myotonia congenita is a clinical diagnosis (based on symptoms) with

supportive evidence from the EMG and family history. Another important part of this diagnosis is exclusion of the most common disease, myotonic muscular dystrophy which is caused by a genetic defect on chromosome 19 that is detectable by a commercially available test.

When the chloride channels in the muscles are not working enough, muscles become hyperexcitable because of sodium channels opening. So, a drug that blocks the sodium channels when they are open will counteract the myotonia. Therefore, the therapy target is electrical stabilization of the muscle membrane. Successful therapies include anticonvulsants (such as carbamazepine and phenytoin), acetazolamide, and drugs such as, tocainide hydrochloride, thiazides, anti-arrhythmic mexiletine hydrochloride, quinine, procainamide hydrochloride and beta-adrenergic agents [17].

In comparison to myotonic dystrophy, myotonic congeneta carries better prognosis and the subject may live up to adult life.

Genetic counseling is advised.

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References

1. Becker PE.Heterozygote manifestation in recessive generalized myotonia. Human Genet 1979; 46: 325-9
2. Fahlke C, Beck CL, George Al Jr. A mutation in autosomal dominant myotonia affects pore properties of the muscle chloride channel. Proc Natl Acad Sci USA 1997; 94: 2729-34
3. Bradley W, Daroff R, Fenichel G, Jankovic J. In: Neurology in Clinical Practice Fourth edition. Baumann Heinemann, 2004, pp 2489-2490.
4. Varkey B. Varkey L Muscle hypertrophy in myotonia congenita. J Neurol Neurosurg Psychiatry 2003; 74: 338.
5. www.Rehabinfo Network / Myotonia Congenita
6. Baumann P, Myllyla VVJ. Myotonia congenita in northern Finland: an epidemiological and genetic study. J Med Genet 1998; 35: 293-296.
7. Cheah JS, Toh BHL. Myotonia congenita (Thomsen's disease) in a chinese family. Singapore Med J 1996; 10: 111-116.
8. Chew KTL, Wong Y-S, Teoh H-L, Lim ECH. Myotonia congeneta in a young active man. The Physician and Sports Medicine 2004: 32.
9. Wadia RS, Amin RB, Prayag SV, Chanratare SN, Sardesai HV. Recessive generalized myotonia. Neurology India 1977; 25: 35-7.
10. Prabhakar S, Chopra JS. Autosomal recessive generalized myotonia (A case report). J Assoc Physic Ind 1981; 29: 791-3.
11. Bhattacharyya KB, Sengupta, Basu S, Bhattacharya NP. Becker's variant of myotonia congeneta in two siblings- A clinico-genetic study. Neurol India 2004; 52: 363-364
12. Stimson D. Myotonia congenita, a muscle disease concealed by a muscular physique. MDA publications, QUEST 2001; 8(6)
13. Ptacek LJ. Channelopathies: ion channel disorder as a paradigm for paroxysmal disorders of the nervous system. Neuromuscul Disord 1997; 7: 250-255.
14. Abdalla JA, Casley WL, Cousin HK. Linkage of Thomsen's disease to the T-cell-receptor beta (TCRB) locus on chromosome 7q 35. Am J Hum Genet 1992; 51: 579-584.
15. Kwiecinski H, Lehmann-Horn F, Rudel R. The resting membrane parameters of human intercostal muscle at low, normal and high intracellular potassium. Muscle Nerve 1984; 7: 60-65.
16. Bryant SH, Morales-Aguilera A. Chloride conductance in normal and myotonic muscle fibres and the action of monocarboxylic aromatic acid. J Physiol 1971; 219: 367-383.
17. Weinberg J. Curl LA, Kunci RW. Occult presentation of myotonia congenita in a 15 year old athlete. Am JS ports Med 1999; 27: 529-31.