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A case of Limb girdle muscular dystrophy type 4 C

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Introduction

Limb-girdle muscular dystrophies (LGMD) are a group of progressive hereditary myopathies that predominantly affect the muscles of the hip and shoulder girdles.[1]Distal muscle involvement is a late feature of the condition. Most cases of LGMD are of autosomal recessive inheritance but some families express an autosomal dominant trait.[2] We present a genetically confirmed case of limb-girdle muscular dystrophy type 4C.

Case Report

A 13-year-old boy presented with progressive lower limb weakness since the age of 3 years. He was born as a second child of second degreeconsanguineous parents. His elder sister had died at the age of 9 years following a similar progressive neurological disease. There were no complications in the antenatal and perinatal periods. He had age-appropriate development until 3 years of age.

At the age of three, he developed difficulty in standing from a squatting position. His symptoms were progressed gradually and by 4 years of age, he found it difficult to climb staircases. He required walking aids by 5 years and became wheelchair-bound by 9 years of age. His upper limb functions were preserved until 10 years of age and started to decline gradually, predominantly involving proximal muscle groups. Despite other neurological disabilities, his cognitive functions remain well.

Examination revealed affected lower limbs more than the upper limbs with marked proximal muscle involvement. There was no calf hypertrophy or fasciculation. Tendon reflexes were preserved in the early part of the illness and later on, they were diminished. There were no extraocular muscle involvements. Since the age of 3, he was investigated extensively at tertiary care hospitals in Sri Lanka but there was no conclusion until 13 years.

Laboratory tests performed at the beginning of the illness showed increased transaminases (AST 96 U/l) and elevated CPK concentration (3084U/l). Because of elevated CPK, he has been suspected of having a myopathic disorder since then. On clinical grounds, he was managed as a child with Duchenne Muscular Dystrophy (DMD). However, the first, electromyography (EMG) done at the age of 4 years revealed a normal denervation pattern and decreased duration of motor unit potentials (MUP), which is considered as the most sensitive and specific parameter for myopathy in conventional EMG was not observed. Repeat EMG was carried out at the age of 9 years and that was also inconclusive. Mutational analysis for Duchenne Muscular Dystrophy (DMD), Spinal Muscular Atrophy (SMA), and late-onset Pompe disease was negative. Both ECG and 2D Echo revealed no cardiac involvement.

At the age of 13 years, the child was sent to India for further investigations. AppGen Sanger validation test was done in view of limb-girdle muscular dystrophy using bidirectional Sanger sequencing. His FKTN gene harbours homozygous missense mutation c.1256T>A; p(Ile419Asn). Both parents had heterozygous missense mutations of the same gene.

Discussion

The limb-girdle muscular dystrophy (LGMD) manifests with progressive weakness of pelvic and shoulder girdle muscles. Except for having few cases of autosomal dominant and sporadic patterns, usually, LGMDs have an autosomal recessive inheritance. There are sixteen genetic types of LGMD are described at present.1 LGMDs with autosomal dominant inheritance are named as LGMD type 1, and those with autosomal recessive inheritance are named as LGMD type 2. Distinct genetic forms have been identified under two main types of LGMD and they are sub-classified using alphabetical letters. The autosomal dominant forms ((LGMD 1A to LGMD 1G)

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are milder compared to autosomal recessive forms (LGMD 2A to LGMD 2M).2

The clinical features usually start in late childhood involving pelvic or shoulder girdle. Thereafter it remains static for long period with a mild degree of disability related to proximal muscle weakness. Although the confinement to a wheelchair is a late finding in LGMD, in this child it was an early feature. The rate of progression differs between different pedigrees however is almost similar within a kindred.[1] Unlike other muscular dystrophies, cardiomyopathy and intellectual impairment are unusual in LGMDs.

Diagnosis of LGMDs is challenging and time-consuming as seen in this case, it took almost a decade to come to a diagnosis. Elevated CPK, characteristic EMG pattern, and muscle biopsy features may aid the diagnosis of muscular dystrophy, however, none of these investigations are specific enough to arrive at a definitive diagnosis.[3] Specific mutational analysis is the gold standard in the diagnosis.[4]

Management of LGMDs involves a multidisciplinary team and primarily consists of supportive therapy. In order to optimize muscle strength and joint flexibility, it is advisable to perform an exercise and physical therapy. Some studies have shown a beneficial effect of coenzyme Q but there is no convincing evidence in it to be used routinely.[5]Gene therapy for LGMDs is under the research level.

Conclusion

In conclusion, in this case report, we present a child with a rare degenerative neurological illness. One of the striking features in this case is the time taken to arrive at the definitive diagnosis since the initial presentation due to many limitations.

References

1. Kleigman M. Nelson Textbook of Paediatrics 20th edition, Vol -2 In: Harvey B. Sarnat Limb-Girdle Muscular Dystrophies. 2015;609.4 :2982-2983

2. Meena AK, Sreenivas D, Sundaram C, Rajasekhar R, Sita JS, et al. Sarcoglycanopathies: a clinico-pathological study. Neurology India. 2007 Apr 1;55(2):117.

3. Sharma MC, Mannan R, and Singh NG et al. Sarcoglycanopathies: An enigmatic form of muscular dystrophy: A report of 7 cases. Neurol India 2004; 52: 446-9.

4. Thompson R et al, Limb girdle muscular dystrophies – international collaborations for translational research, Nat Rev Neurol. 2016 May 12 (5): 294 -309

5. Folkers K, Simonsen R. Two successful double-blind trials with coenzyme Q10 (vitamin Q10) on muscular dystrophies and neurogenic atrophies. Biochim-Biophys Acta 1995; 1271: 281-6.