Becker’s variant of myotonia congenita in two siblings- A clinico-genetic study

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We report a family of a brother and sister of myotonia congenita, conforming to autosomal recessive transmission (Becker’s variety). To the best of our knowledge, no account of a family of autosomal recessive myotonia (Becker’s disease), has earlier been reported from India.

Key Words: Myotonia congenita, Becker’s variant, trinucleotide repeat

Introduction

Congenital myotonia refers to an uncommon hereditary disease of skeletal muscles that begins in early life and is characterized by myotonia and muscular hypertrophy. The condition may present in autosomal dominant or recessive forms. The former variety is subdivided into Thomsen’s disease and myotonia levior, the latter being milder in manifestation. The recessive form is known as Becker’s disease and both the forms are considered as channelopathies, where the transport of chloride ion is faulty and the genetic locus is assigned to 7q35 chromosome.

Becker’s variant starts with myotonia and muscular hypertrophy imparting it the classic description ‘Herculean features’. Sometimes, this condition is associated with muscular weakness and wasting that is not always clinically detectable. The myotonia ‘warms up’ with repeated activity and the patient walks normally with ease. The disease may progress up to adulthood and thereafter, it remains static and the lifespan usually is not shortened.

We report a family of brother and sister of myotonia congenita, conforming to autosomal recessive transmission (Becker’s variety), where the brother presented with signs of myotonia and muscular hypertrophy, while his asymptomatic sister was found to display almost identical features. The relevant literature in this regard has been reviewed.

Case report

A 16-year-old Hindu male, born of a non-consanguineous marriage complained of difficulty in initiating his gait. The problem used to resolve as he started walking and he stated that if he grasped an object firmly in his hand, releasing it was difficult and the palm maintained the posture of incomplete opening. On direct enquiry he stated that if and when he sneezed, he assumed a grotesque countenance since his eyelids used to be tightly closed and the mouth would remain open along with the contraction of the forehead muscles.

On examination, the thighs, calf muscles and proximal muscles in the upper limbs were hypertrophied and there was evidence of grip, tongue and eyelid myotonia. Getting up from a sitting posture was accomplished with difficulty and initiation of movement was slow which improved as he continued to walk. The forearms were partially wasted and there was no clinical stigmata of dystrophia myotonica, paramyotonia congenita or chondrodystrophic myotonia. On examining his parents and the sister it was observed that the sister was also well built with hypertrophied thigh muscles and there was evidence of grip myotonia. The parents had no neurological abnormality. Considering the autosomal recessive pattern of inheritance and the clinical picture, the diagnosis of Becker’s variety of myotonia congenita was entertained.

Investigations

The serum creatine phosphokinase (CK) in the proband was in the range of 690 IU/L (normal value: 20-200 IU/L), while that in his sister was 48 IU/L. The serum potassium level was normal in the fasting state as also after a heavy carbohydrate meal, excluding thereby the possibility of periodic paralysis. Electromyographic studies in both the sibs showed normal motor unit potentials with complete recruitment pattern and the typical repetitive discharges of varying amplitude and frequency along with the classical dive-bomber’s sound, indicating myotonia. Muscle biopsy was avoided since the subjects refused it. The electrocardiogram and glucose tolerance test were within normal limits while the lateral view of the skull did not show small pituitary fossa or hyperostosis frontalis interna that could suggest dystrophia myotonica. Thyroxine, triiodothyronine and thyroxin stimulating hormones were within normal limits in both of them.
Genetic testing and detection of trinucleotide repeat (CTG) repeats in DNA

To detect the polymorphic CTG repeats in the 3'-untranslated region of myotonin protein kinase gene, expansion of which causes myotonic dystrophy, polymerase chain reaction (PCR) was carried out using synthetic oligonucleotide primers, flanking the repeat region. The amplified PCR products were separated on 6% denaturing polyacrylamide gel (for normal allele detection) or 0.8% agarose gel with appropriate DNA markers (for expanded allele detection). Separated DNA was transferred on to Hybond-N+ membrane by capillary transfer method and hybridized with 32P-dCTP labeled oligonucleotide, washed and autoradiographed with Kodak X-ray film. Sizes of the repeats were determined from the appropriate markers.

Discussion

The brunt of Becker’s disease falls on the lower limbs, probably as a result of work hypertrophy, since the quadriceps and other muscles are in a continual state of contraction. The cranial musculature is also frequently involved, where classically there is visible myotonia of the eyelids after the patients is asked to open the eyes following forceful closure. Serum CK is elevated two to three times and serum potassium is normal during and between attacks.

Both the dominant and the recessive forms of myotonia congenita are linked to CLCN-1 gene on chromosome 7q35 encoding the skeletal muscle chloride channel and the differences between the two types of myotonia are probably caused by different mutations of the same gene suggesting that the diseases are allelic. Sun et al reported two sibs and a first degree cousin from a consanguineous marriage who demonstrated wasting of muscles and muscular contracture instead of muscular hypertrophy. Attempts to identify trinucleotide repeat expansion in both the varieties of myotonia congenita have turned negative. Sunohara et al described a family where five subjects suffered from myotonia and that conformed to the autosomal dominant variety of the disease. The present study is to the best of our knowledge, the first family of Becker’s variety of myotonia congenita that is being reported from India. We propose that the members of the family of every child presenting with myotonia should undergo detailed screening clinically and be tested for trinucleotide repeats, since congenital myotonia, in comparison to myotonic dystrophy or congenital myotonic dystrophy carries better prognosis and the subjects may live up to adult life.

References
