CASE REPORT

Becker congenital myotonia in black African with molecular findings

Simon Azonbakin1*, Diane Adovoekpe1, Marius Adjagba1, Jules Alao2, Gratien Sagbo2, Constant Adjien3 and Anatole Laleye1

Abstract

Background: Congenital myotonia is a congenital disorder that affects skeletal muscles with myotonia. Affected muscles show stiffness and pain sometimes. The two major types of myotonia congenita are known as Thomsen disease and Becker disease. These conditions are distinguished by the severity of their symptoms and their patterns of inheritance. The causative factor is mutations in CLCN1 gene. Myotonia congenita is rarely reported in black especially in black African.

Case presentation: This is a case report of Becker Congenital Myotonia in a 36-year-old male from Benin. The symptoms arose at the age of 7 years with regular and progressive course and muscles pains. Electromyogram, blood sampling, laboratory investigations and muscles biopsy confirm the diagnostic with molecular finding.

Conclusion: The authors report a case of Becker congenital myotonia in a black African with molecular confirmation. Mexiletine was used as symptomatic agent with good results.

Keywords: Myotonia, Congenital, Becker disease, CLCN1 gene, Mexiletine

Introduction

Myotonia congenita is a disorder that affects skeletal muscles. Beginning in childhood, patients with this condition experience muscle tensing that prevent muscles from relaxing normally. Although myotonia can affect any skeletal muscles, including muscles of the face and tongue, it occurs most often in the legs. Myotonia causes muscle stiffness that can interfere with movement. In some patients, the stiffness is very mild, while in other cases it may be severe enough to interfere with walking, running, and other activities of daily life. These muscle problems are particularly noticeable during movement following a period of rest. The two major types of myotonia congenita are known as Thomsen disease and Becker disease. These conditions are distinguished by the severity of their symptoms and their patterns of inheritance. Becker disease usually appears later in childhood than Thomsen disease and causes more severe muscle stiffness, particularly in males [1]. People with Becker disease often experience temporary attacks of muscle weakness, particularly in the arms and hands, brought on by movement after periods of rest. They may also develop mild, permanent muscle weakness over time. This muscle weakness is not seen in people with Thomsen disease. Myotonia congenita is estimated to affect 1 in 100 000 people worldwide [2]. Both forms of the disease are caused by varied mutation in the CLCN1 gene on the long arm of chromosome 7 [1]. This gene codes for the voltage-gated chloride channel (CIC-1). Becker myotonia is rarely reported in back especially in black African. We report on a case of Becker congenital myotonia in a black African with atypical presentation and a molecular confirmation.
Case presentation

K.E. 36-year-old male born to non-consanguineous parents was seen for medical genetic evaluation after numerous visits in Rheumatology and Neurology services for muscles pains and enlargement. The symptoms arose at the age of 7 years with regular and progressive course. Family history was positive since two other cases segregated in the siblings (Fig. 1). No history of toxic and auto-immune nor inflammatory disease was present. The physical examination disclosed generalized muscular enlargement predominating on neck, scapular, trunk and upper arms muscles (Figs. 2 and 3), movements limitation, muscles’ fasciculation and myotonia after usages and movements. Heart and chest clinical evaluation was unremarkable. Electromyogram, blood sampling, laboratory investigations and muscles biopsy were performed on the patient. From this index case, some family members illustrated on the family tree were recruited. Biochemical analyses showed slight increase in creatine phosphokinase at 404 UI/l (normal < 200 UI/l), normal blood level of potassium and sodium per crises and post crises. On the electromyogram, a burst of myotonia signs was observed. Light microscopy of the muscle biopsy revealed the presence of an inequality in the gauge of the fibers between them, but the blocks are not oriented perfectly both longitudinally and transversely. There are some nuclear centralizations with some of these nuclei having a chain aspect. No abnormal proliferation of interstitial connective tissue. Electronic Microscopy shows a non-significant abnormality especially of rough reticulum (Figs. 4 and 5).

Fig. 1 Family pedigree with the molecular finding

Fig. 2 Neck, arms and thoracic muscular hypertrophy

Fig. 3 Neck, arms and back muscular hypertrophy

Fig. 4 Optic microscopy of the muscle: discrete abnormalities without specific character
Genomic DNA was extracted from blood using standard techniques and sequencing of the 23 exons of the \textit{CLCN1} gene was performed (ABI 3130 XL Genetic Analyzer, Applied). Two heteroallelic \textit{CLCN1} missense novels mutations were detected in the index case as well as her two affected siblings. A first one, c. 1025 C > T p.Pro342Leu (p.P342L) (exon 9), was inherited from maternal lineage and a second one, c. 1480 T > C p.Phe494Leu (p.F494L) (exon 14) coming probably from paternal lineage (Fig. 6). The father was not available since he deceased few months before molecular testing. This case is suggestive of congenital myotonia with recessive pattern inheritance. Mexiletine was proposed to reduce muscles stiffness frequencies with 200 mg per day for all of the affected patient. The patient II2 was severely affected like the proband. On the other hand, patient II3 experienced only slight symptoms of myotonia at lower limbs.

\textbf{Discussion}

Myotonia congenita is a rare muscle disease characterized by sarcolemma over-excitability inducing skeletal muscle stiffness. The case report is compatible with congenital disease since it started early in youth and several cases were presented through generations.
Myotonia is acceptable regarded the symptoms reported by the family and the signs showed by the proband at electromyogram evaluation. These included muscle stiffness when stimulated, difficulty in relaxing contracted muscles and abnormal enlargement of the muscles and burst of myotonic electric manifestations [3].

The two main types of myotonia congenita are Thomsen disease, which begins in infancy, and Becker disease, which usually begins between the ages 4 and 12. Thomsen disease is inherited in an autosomal dominant manner and Becker disease, the more common form, is inherited in an autosomal recessive manner [4, 5]. Taking into account the onset age, the fact that parents were normal allows us to conclude in favor of Becker disease. The family bears at clinical and electro-testing stages myotonia congenita type Becker disease [1, 2]. In respect with clinical presentation, and myopathy epidemiology, we tried to exclude other dystrophynopathies such as Duchene muscular disorder, Becker muscular disorder and Limb girdle muscular disorders with creatine phosphokinase dosage, other canal disorders with blood electrolytes like Westphal disease [6, 7]. The reported condition could not be mistaken for other myotonia especially the dystrophic myotonia. This occurred in mature adult with autosomal inheritance pattern. Affected patients have myotonia, cataracts and cardiac conduction defects. In affected men, hormonal changes may lead to early balding and infertility. There are two major types of myotonic dystrophy (type 1 and type 2). Their signs and symptoms overlap, although type 2 tends to be milder than type 1. The muscle weakness associated with type 1 particularly affects the lower legs, hands, neck, and face. Muscle weakness in type 2 primarily involves the muscles of the neck, shoulders, elbows, and hips. Both types are autosomal dominant and genes that are involved are DMPK for the type 1 and CNBP in type 2 [8]. Molecular confirmation was a very good help since manifestations were predominant in upper limbs instead of lower limbs as generally reported. Furthermore, molecular finding was consistent with an autosomal recessive inheritance profile which is reasonably expected [9, 10]. Our patient benefited from symptomatic treatment with mexiletine since this molecule showed good results in some patients that suffered from Becker myotonia congenita [11].

Studies on Becker's myotonia remain very rare. In sub-Saharan Africa, we had noted cases in Tanzania, Nigeria and South Africa [12–14]. In general, the symptomatology was globally that found in our case. Within 15 Norwegian families, about 8 different mutations were found, thus reflecting the genetic heterogeneity of the disease [15]. Also, most of the mutations were compound heterozygous as in our case.

**Conclusion**

This case of Becker myotonia in a Beninese's family was the first well-documented case in the country. This was caused by two heteroallelic CLCN1 missense novels mutations in the index case as well as her two affected siblings. The therapeutic approach was favorable.

**Abbreviations**

CLCN1: Chloride voltage-gated Channel; CNBP: Nucleic Acid-Binding Protein; DMPK: Myotonic Dystrophy Protein Kinase.

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**Author contributions**

SA and DA have done the initial consultation and the coordination of different steps of the treatment. MA had coordinated the different step of genetic analysis. JA had done the genetic consultation. CA had done the neurological exam, GS and AL had supervised all the steps of the treatment. All authors have read and approved the manuscript.

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**Availability of data and materials**

The patient date is available in the Teaching Hospital de la Mère et de l’Enfant (CHU MEL).

**Declarations**

**Ethics approval and consent for publication**

The patient has authorized us to share their information for a scientific interest. Consent information paper was signed by the patient.

**Consent for publication**

The patient has given us the permission to publish his data.

**Competing interests**

The authors declare that they have no competing interests.

**Author details**

1Laboratoire d’Histologie, Biologie de la Reproduction, Cytogénétique et Génétique médicale, Faculté des Sciences de la Santé- Université d’Abomey-Calavi, Godomey, Benin. 2Unité d’Enseignement et de Recherche en Pédiatrie, FSS, Cotonou, Bénin. 3Unité d’Enseignement et de Recherche en Neurologie, FSS, Cotonou, Bénin.

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