Limb-Girdle Muscular Dystrophy Type 2C: Case Report

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Authors’ contributions

This work was carried out in collaboration among all authors. Authors OEBA and AR designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OEB and AR managed the analyses of the study. Author OEB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Limb-Girdle muscular dystrophy (LGMD) is a group of inherited disorders that lead to muscle weakness and skeletal muscle wasting involving the muscles around the hips and shoulders. This can cause a gait disturbance, difficulty running or even a complete loss of the ability to walk. The appearance of the disorder, the course and the muscles affected are variable between the different subtypes of the disease. Typically, patients with type 2C Limb-Girdle dystrophy (LGMD2C) start having symptoms early in infancy and lose their ability to walk around the age of 12. Others have less symptomatology and have late expression in adulthood. This disorder can affect the heart muscle in some patients. They can also have osteoarticular and vertebral deformations. The prognosis depends on the muscles often affected by respiratory failure. LGMD2C is caused by a pathogenic mutation in the SGCG gene. We report the case of a 13-year-old child, with a notion of femoral fracture at the age of 5 years and first degree consanguinity in the parents, no similar case in the family, and who presents since 3 years difficulty walking. Clinical examination: walking, positive sign of Gowers, scapula alta, enlarged calves. On the biological level: CPK 6380, LDH 482, PAL 219, ASAT 68, ALAT 103. The electromyogram shows a slowing of the motor conduction speed of the external popliteal sciatic nerve with a slight loss of amplitude. Muscle biopsy objective

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a discreet dystrophic formula with a total absence of expression of gamma sarcoglycans and proteins of the muscle membrane. Gamma glycanopathy is genetically confirmed by the mutation of the δ-SG gene. A cardiac ultrasound was without abnormality.

Keywords: Muscular pathology; immunohistochemistry.

1. INTRODUCTION

Gamma sarcoglycan (GSGC) is one of four transmembrane sarcoglycans (SGC) found on the cell membrane of skeletal muscle. SGCs form a sub-complex closely related to the glycoprotein complex and dystrophin (DAG) (Fig. 1). The presence of SGC is essential for good integrity and perfect muscle contraction. Type 2C limb Girdle dystrophy (LGMD-2C) or severe childhood muscular dystrophy is an autosomal recessive disorder caused by genetic abnormalities in the sarcoglycan gamma gene (SGCG). It clinically resembles dystrophinopathies which are more frequent [1-4]. There is no definitive treatment for LGMD-2C and other muscular dystrophies. Management is mainly physiotherapy and stretching exercises, surgery for orthopedic complications, the use of mechanical and respiratory aids may be necessary to prolong survival and improve quality of life. Cardiological monitoring and emotional support are also necessary [5-9]. The differential diagnoses of LGMD-2C are essentially muscular dystrophies of Duchenne and Becker, hence the interest in immunohistochemical staining of muscle biopsy and molecular genetic analysis [10-12]. In Morocco, the epidemiology of LGMD2C is poorly understood. In this study, we will report the case of a Moroccan child carrying LGMD2C.

2. CASE REPORT

We report the case of a 13-year-old child, 2nd of a brother out of 2, having a notion of femoral fracture at the age of 5 and first degree consanguinity in the parents, no similar cases in the family, and who has had difficulty walking for 3 years. A clinical examination shows walking, a positive sign of Gowers, scapula alta, enlarged
mutations have been described in the gamma sarcoglycan (SGCG) gene, located on chromosome 13 (13q12), which consists of 8 exons (Fig. 3). The SGCG gene sequence is made up of 291 amino acids. Three parts of the extracellular domain of gamma sarcoglycan have a possible critical function, two for assembly with the other sarcoglycans (either beta or alpha), and the putative domain of EGF type. So far, forty mutations have been described in the gamma sarcoglycan gene (2). A truncated gamma sarcoglycan protein without an EGF-like domain (capable of assembling with other sarcoglycans) generates the homozygous del525T mutation [1, 2, 13-15]. LGMD2C is one of the most serious forms, with the highest incidence reported in North Africa following a mutation in the SGCG gene [16]. In Morocco, the epidemiology of LGMD is poorly known, but the prevalence of these disorders is higher in the Moroccan population than in others due to consanguineous marriages, which can reach up to 15% [17]. However, the scarcity of specialized centers prevents patients from benefiting from an immunohistochemical analysis for their diagnosis, treatment and genetic counseling. A study of 26 Moroccan patients reveals that 19 of the 26 patients (73%) were homozygous for the c.525delT mutation, and also reported in other North African populations [18,19]. The prevalence of LGMD-2C is 1/20 492. This prevalence is 1/51 020 among Europeans [19]. The difference observed between the Moroccan population and the others is explained by the high rate of parental consanguinity (15.25%) and the increase in the prevalence of autosomal recessive diseases in Morocco in consanguineous marriages (60%) [17].

3. DISCUSSION

The sarcoglycan gamma (SGCG) gene is located on chromosome 13 (13q12), which consists of 8 exons (Fig. 3). The SGCG gene sequence is made up of 291 amino acids. Three parts of the extracellular domain of gamma sarcoglycan have a possible critical function, two for assembly with the other sarcoglycans (either beta or alpha), and the putative domain of EGF type. So far, forty mutations have been described in the gamma sarcoglycan gene (2). A truncated gamma sarcoglycan protein without an EGF-like domain (capable of assembling with other sarcoglycans) generates the homozygous del525T mutation [1, 2, 13-15]. LGMD2C is one of the most serious forms, with the highest incidence reported in North Africa following a mutation in the SGCG gene [16]. In Morocco, the epidemiology of LGMD is poorly known, but the prevalence of these disorders is higher in the Moroccan population than in others due to consanguineous marriages, which can reach up to 15% [17]. However, the scarcity of specialized centers prevents patients from benefiting from an immunohistochemical analysis for their diagnosis, treatment and genetic counseling. A study of 26 Moroccan patients reveals that 19 of the 26 patients (73%) were homozygous for the c.525delT mutation, and also reported in other North African populations [18,19]. The prevalence of LGMD-2C is 1/20 492. This prevalence is 1/51 020 among Europeans [19]. The difference observed between the Moroccan population and the others is explained by the high rate of parental consanguinity (15.25%) and the increase in the prevalence of autosomal recessive diseases in Morocco in consanguineous marriages (60%) [17].

![Fig. 3. The spectrum of alterations in the exon / intron succession of gamma sarcoglycan](image-url)
4. CONCLUSION

It is concluded that screening for c.525 delT is the first test for muscular dystrophy of belts, with a good cost / benefit ratio in public health strategies, until access to immunohistochemical analysis be generalized. This will be useful not only for patients, prenatal diagnosis and genetic counseling, but also for future clinical trials and new therapeutic approaches.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard, written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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