2 (12.5%) patients had an isolated nonspecific intraventricular conduction defect. The corrected QT interval was normal in all patients.

The mexiletine dose used was 325 (200-600) mg/d, and the mean treatment duration was 46 [2-181] months. According to subjective evaluation as per normal practice, mexiletine was considered ineffective in controlling myotonia in 31%, partially effective temporarily (reason for stopping) in 50%, and very effective in 19%, who remain on this treatment to date. In none of the patients was it stopped due to cardiac complications; 25% had gastrointestinal upset that did not require medication withdrawal.

During treatment there were no significant cardiovascular events such as syncope, pacemaker requirement, atrioventricular block, bundle-branch re-entry ventricular tachycardia, or sudden cardiac death. On serial ECGs, the onset of left anterior fascicular block was documented in 1 patient, and in another patient, right bundle branch block, which was initially rate-dependent and then later became established during treatment.

After stopping treatment, during follow-up of the cohort, 2 pacemakers were implanted: 1 for symptomatic sinus node dysfunction and another in an asymptomatic patient with onset of first-degree atrioventricular block and complete bundle branch block with pathological prolongation of the HV interval on the electrophysiology study done as standard. There were 4 deaths (25%), 2 due to stroke, 1 due to pneumonia, and 1 due to severe respiratory failure.

In conclusion, the long-term use of mexiletine to improve myotonia in patients with DM1 without severe conduction defects on baseline ECG, even at high doses, does not appear to be associated with an increased cardiac risk and shows evidence of modest effectiveness. The limitations inherent to the retrospective nature of this cohort study must be taken into account when evaluating the results, which should be supported with a prospective study.

**CONFLICTS OF INTEREST**

There are no potential conflicts of interest.


**AUTHORS’ CONTRIBUTIONS**

R. Salguero-Bodes: study conception, data collection, analysis, and manuscript writing. A. Ruiz-Curiel: data collection, analysis, manuscript review. Remaining authors: participation in conception and critical review of the manuscript.

**FUNDING**

None.

**REFERENCES**


1885-5857 © 2021 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

**Dilated cardiomyopathy and mild limb girdle muscular dystrophy caused by the p.Gly424Ser genetic variant in the fukutin gene**

*Miocardiopatía dilatada y distrofia muscular de cinturas leve causada por la variante genética p.Gly424Ser en fukutina*

To the Editor,

Dystroglycanopathies are a heterogeneous group of autosomal recessive disorders with a broad clinical spectrum. They include congenital muscular dystrophy, limb girdle muscular dystrophy (LGMC), and dilated cardiomyopathy (DCM). They are characterized by hypoglycosylation of α-dystroglycan, which is essential for muscle integrity. Fukutin is one of the proteins involved in its glycosylation and in the pathophysiology of the dystroglycanopathies. We report the first case described in Europe of a patient with DCM and LGMC who is homozygous for the p.Gly424Ser genetic variant in the fukutin gene (FKTN) and provide histological confirmation of the resulting abnormality.

A 28-year-old man consulted due to limb weakness and myalgia, with no cardiac symptoms. He showed a 4/5 strength loss in the lower limbs, pseudohypertrophy of the triceps surae and gastrocnemius, atrophy of the quadriceps, positive Gower’s sign (use of the upper limbs to get up), and elevated creatine kinase (CK; 6220 U/L). Electromyography showed moderate myopathy in all 4 limbs. Electrocardiography revealed sinus rhythm, a short PR interval, and negative lateral Q and T waves, whereas echocardiography showed DCM with 30% left ventricular ejection fraction.
After ruling out coronary heart disease, we began treatment with carvedilol and enalapril. The workup was completed with a genetic study of the dystrophin gene, which was normal. Written consent was obtained from the patient for the presentation and publication of this article, including the images. Approval was also received from the institutional ethics committee.

The patient was cardiologically and neurologically stable for 15 years. At 43 years of age, he started showing progressive dyspnea on moderate exertion and was admitted with heart failure and in cardiogenic shock. Electrocardiography (figure 1A) revealed biatrial enlargement, left anterior fascicular block, and lateral Q waves. Echocardiography (figure 1B) showed DCM with severe dysfunction (20% left ventricular ejection fraction) and akinesia in inferolateral segments. He received optimal neurohormone treatment and underwent automatic defibrillator implantation. Due to unfavorable progression, he required a heart transplant 6 months later. In a histological study, the explanted heart showed extensive biventricular fibrosis.

Five years after the transplant, the patient’s myopathy was stable but his CK levels were still elevated (figure 1C). He was referred to the inherited heart disease unit, where a family study was performed. His first-degree relatives were healthy and without myopathy, except his father, who had nonobstructive hypertrophic cardiomyopathy (HCM) (maximum septal thickness...


Figure 2. Histology of the triceps surae muscle. A: (hematoxylin and eosin) muscle fibers with slight variability in the diameter and the occasional internalized nuclei. B: (immunohistochemistry) slight reduction in laminin α2. C: severe reduction in α-dystroglycan vs a healthy control (D).
A genetic study performed using next-generation sequencing with a panel of 18 genes (figure 1D) failed to identify any pathogenic variant associated with HCM.

A genetic study performed with next-generation sequencing of the proband (DCM panel, 96 genes) identified the homozygous variant c.1270G>A, p.Gly424Ser in FKTN. His parents were heterozygotic carriers of this variant. A biopsy of the triceps surae muscle revealed mild muscle involvement, with immunohistochemistry confirming a severe deficit in α-dystroglycan and a slight reduction in laminin α2; the remainder of the study was normal (figure 2).

Funding

No funding has been received to perform this study.

Authors' Contributions

J.M. Larraña-Moreira and R. Barrialas-Villa performed the design, figures, and drafting of the manuscript. P. Blanco-Arias helped to perform the genetic study and critical analysis. B. San Millán-Tejado assisted with the histological study, figure 2, manuscript revision, and critical analysis. G. Barge-Caballero and M.G. Crespo-Leiro helped in the manuscript drafting and critical analysis.

CONFLICTS OF INTEREST

P. Blanco-Arias is an employee of Health in Code S.L. The other authors do not declare conflicts of interest.


1Unidad de Cardiopatías Familiares, Complejo Hospitalario Universitario de A Coruña (CHUAC), A Coruña, Spain
2Instituto de Investigación Biomédica de A Coruña (INIBIC). A Coruña, Spain
3Facultad de Medicina, Universidade da Coruña (UDC), A Coruña, Spain
4Servicio Galego de Saúde (SERGAS), Spain
5Área de Neurología, Health in Code S.L., A Coruña, Spain
6Servicio de Anatomía Patológica, Neuropatología, Hospital Álvaro Cunqueiro, Vigo, Pontevedra, Spain
7Unidad de Insuficiencia Cardíaca Avanzada y Trasplante Cardíaco, Complejo Hospitalario Universitario de A Coruña (CHUAC), A Coruña, Spain
8Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain

Corresponding author:
E-mail address: c.larranaga88@gmail.com
(J.M. Larraña-Moreira).

Available online 11 June 2021

REFERENCES


https://doi.org/10.1016/j.rec.2021.04.015
1885-5857 © 2021 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.