JACC: CASE REPORTS VOL. 29, 2024

HEART FAILURE AND CARDIOMYOPATHIES

THE FOUR CORNERS: CLINICAL VIGNETTE CORNER

Inferolateral Fibrosis in a Nonhypertrophic Left Ventricle

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ABSTRACT

A 62-year-old recreational cyclist presented with transient loss of consciousness and common electrocardiographic findings. Despite absence of left ventricular hypertrophy, multidisciplinary evaluation and a positive family history led to the diagnosis of non-classical Fabry disease. This case emphasizes the added value of multidisciplinary analysis of nonspecific findings to diagnose a rare disease. (JACC Case Rep. 2024;29:102735) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

CASE PRESENTATION

A 62-year-old male cyclist with 35 years of experience reported an episode of transient loss of consciousness during a high-intensity ride. He described the event as a brief blackout without prodromal symptoms or loss of postural tone and reported no chest pain or palpitations. Following this incident, he continued cycling 32 km twice weekly and participating in weekly group rides of ~80 km. His history included a presumed tonic-clonic seizure at 46 years of age. At 59 years of age, he experienced a traumatic fall, possibly due to transient loss of consciousness, during a 140-km bike race, necessitating intensive care unit admission. Family history revealed pacemaker implantation in his brother (at 58 years of age) due to multiple syncopal episodes, attributed to complete atrioventricular (AV) block.

Despite normal cardiopulmonary findings during physical evaluation (blood pressure: 140/80 mm Hg; 60 bpm), resting electrocardiogram showed sinus rhythm, first-degree AV-block, and new left-axis deviation and

TAKE-HOME MESSAGE

- Multidisciplinary evaluations and thorough family history assessments can identify a rare presentation of Fabry disease, such as typical inferolateral fibrosis without hypertrophy.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received June 20, 2024; revised manuscript received September 9, 2024, accepted September 23, 2024.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2024.102735

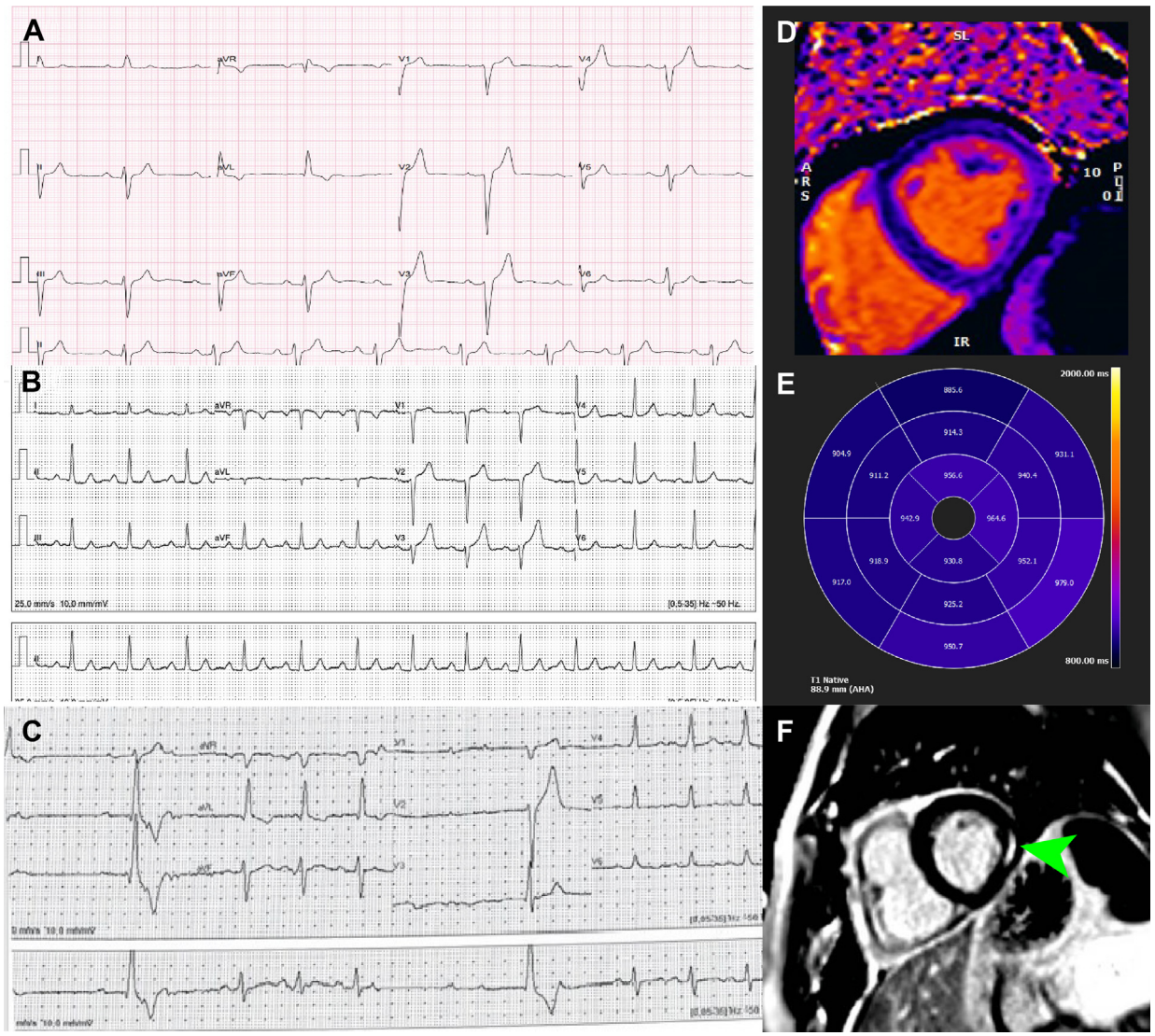
ABBREVIATIONS AND ACRONYMS

AV = atrioventricular

GLA = alpha-galactosidase A

left bundle branch block (**Figures 1A and 1B**). Echocardiography showed normal biventricular size, function, and valve function (Video 1, Supplemental Figure 1). Rhythm monitoring showed multiform premature ventricular contractions, also in couplet, that increased during activity (Supplemental Figure 2). Cardiac magnetic resonance imaging revealed normal cardiac dimensions and function (Video 2) but also basal inferolateral mid-wall fibrosis (**Figure 1F**). Global T1 time was diffusely decreased (**Figures 1D and 1E**); coronary computed tomography showed no coronary artery disease. Multidisciplinary sports cardiology evaluation concluded that, based on similar symptoms and electrocardiogram abnormalities in the patient's brother (**Figure 1C**), a heritable cardiomyopathy was possible. A cardiomyopathy gene panel (59 genes) identified a pathogenic (class 5) variant, c.436>T, p(Pro146Ser), in the *GLA* (alpha-

FIGURE 1 Cardiac Assessment as Reviewed by the Multidisciplinary Sports Cardiology Team



(A) 12-lead resting electrocardiogram at current presentation showing progressive PQ interval prolongation, new left axis deviation, and new left bundle branch block. (B) Electrocardiogram from admission 3 years earlier as comparison. (C) Electrocardiogram of the patient's brother before pacemaker implantation showing sinus rhythm with similar PR and QRS prolongation and an advanced atrioventricular block followed by ventricular escape beats. (D, E) T1 mapping on cardiac magnetic resonance basal short-axis slice with a T1 polar plot using a color scale, indicating diffusely decreased myocardial T1 values of 934 ms (local cut-off: <1,000 ms). (F) Gadolinium-enhanced magnetic resonance imaging showing inferolateral mid-wall high signal intensity, indicative of fibrosis (green arrow).

galactosidase A) gene, linked to non-classical Fabry disease. Metabolic tests confirmed decreased *GLA* activity (4.4 nmol/h/mg [range: 32-70 nmol/h/mg]) and elevated plasma lyso-ceramide trihexoside (7.8 nmol/L [range: 0.3-0.5 nmol/L]). The patient was advised to avoid peak exercise and started on low-dose beta-blockers as the syncopal mechanism was presumed to be ventricular tachyarrhythmia, not AV block. Regular arrhythmia monitoring was recommended instead of pacemaker implantation. Family screening confirmed the *GLA* variant in the brother.

At 8 months, the patient remained symptom-free. Holter monitoring showed no ventricular tachyarrhythmia episodes; a Medtronic LINQ II was implanted for arrhythmia monitoring. The patient declined Fabry-specific therapy; multiorgan assessments revealed no Fabry-related abnormalities (kidneys, brain).

DISCUSSION

Non-classical Fabry disease in men primarily involves the heart, and often presents in the 5th or 6th decade of life with arrhythmias, conduction abnormalities, or congestive heart failure.[1] Key indicators suggestive of Fabry include pacemakers in family, AV block, inferolateral fibrosis, and lowered T1 times, usually starting with left ventricular hypertrophy on cardiac imaging. Genetic and metabolic testing establish definitive diagnoses.[2] In this case, the presence of inferolateral fibrosis without left ventricular hypertrophy is a rare finding that has not been previously documented in symptomatic male patients.[3] However, there are limited data on how exercise-induced cardiac remodeling affects Fabry disease. Therefore, genetic analyses were driven by the patient's brother's similar presentation, emphasizing the importance of family history. This case further shows the added value of multidisciplinary evaluation for both diagnosing and managing rare cardiac diseases.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS Anderson-Fabry disease, athlete, cardiac magnetic resonance imaging, cardiomyopathy, electrocardiography, genetic cardiac disorders

APPENDIX For supplemental figures and videos, please see the online version of this paper.