A Cardiomyopathy in a Patient With Limb Girdle Muscular Dystrophy Type 2A

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Limb girdle muscular dystrophy (LGMD) is a muscular dystrophy with predominantly proximal distribution of weakness that spares the distal, facial, and extraocular muscles early in the course of the disease. Cardiac muscle may be affected, which may manifest as hypertrophic/dilated cardiomyopathy and cardiac dysrhythmias. Significant cardiac involvement has been documented frequently in LGMD2C-F, 2I, and LGMD1B forms of the disease, rarely in the LGMD1C and 2B subtypes, and thus far have not been reported in type 2A. We report a presentation of severe cardiomyopathy in an adult with muscular dystrophy type 2A.

A 23-year-old black man was seen in hospital with complaints of decreased exercise tolerance, dyspnea on exertion, orthopnea, and some presyncopal episodes for several weeks. The patient’s LGMD was diagnosed at the age of 21 years. No family history of similar problems was noted. Physical examination at the time revealed decreased strength in the shoulder girdle area, with inability to raise the arm over the head. Laboratory data at the time showed a creatinine kinase of 4263 U/L and serum troponin of 0.77 ng/mL. ECG revealed sinus rhythm with bifascicular block. The patient’s blood was then sent for genetic testing, which demonstrated CAPN3 sequencing alteration (Athena Diagnostics, Inc).

When seen by cardiology, he was noted to be alert and oriented, afebrile, and normotensive. On physical examination he was noted to have jugular venous distension, with cardiac examination significant for a grade III/VI holosystolic murmur at the left lower sternal border, with a displaced point of maximal impulse. ECG revealed normal sinus rhythm, right bundle-branch block, and left anterior fascicular block. Laboratory tests revealed a BNP of 541 pg/mL, with negative cardiac enzymes. His other laboratory tests were found to be within normal limits. No family history of similar problems was noted. Physical examination at the time revealed decreased strength in the shoulder girdle area, with inability to raise the arm over the head. Laboratory data at the time showed a creatinine kinase of 4263 U/L and serum troponin of 0.77 ng/mL. ECG revealed sinus rhythm with bifascicular block. The patient’s blood was then sent for genetic testing, which demonstrated CAPN3 sequencing alteration (Athena Diagnostics, Inc).

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Discussion

Significant cardiac involvement has been rarely documented in LGMD1C, 2A, and 2B, whereas it is relatively common in LGMD2C, 2D, 2F, 2I, and LGMD1B. This may manifest as hypertrophic/dilated cardiomyopathy and cardiac dysrhythmias. LGMD1B patients often exhibit findings of both cardiomyopathy and dysrhythmia.1

LGMD2A (calpainopathy) is found as a result of a mutation of chromosome 15 in the CAPN3 gene encoding the proteolytic enzyme calpain-3.2 Calpain-3 (p94) belongs to the calpain family of soluble intracellular cysteine proteases, the majority of which are activated by a calcium-dependent mechanism. Calpain-3 is not, however, calcium activated, with this expression existing almost solely in muscle, being anchored by titin within the I-band of the sarcomere, at the M line and N2 line.2 The exact mechanism behind the pathogenesis of LGMD2A is unclear, but it is the most common LGMD of the autosomal recessive variety, comprising ≈30% of cases.

Previous reports have not revealed associated cardiac manifestations in patients with LGMD2A. One postulation to explain this finding is that, despite CAPN3 transcripts being present, there is a lack of calpain 3 expression in adult cardiomyocytes.3 Our patient clearly exhibits CAPN3 sequencing alteration on genetic testing and is now diagnosed with LGMD2A (calpainopathy) is found as a result of a mutation of chromosome 15 in the CAPN3 gene encoding the proteolytic enzyme calpain-3.2 Calpain-3 (p94) belongs to the calpain family of soluble intracellular cysteine proteases, the majority of which are activated by a calcium-dependent mechanism. Calpain-3 is not, however, calcium activated, with this expression existing almost solely in muscle, being anchored by titin within the I-band of the sarcomere, at the M line and N2 line.2 The exact mechanism behind the pathogenesis of LGMD2A is unclear, but it is the most common LGMD of the autosomal recessive variety, comprising ≈30% of cases.

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Disclosures

None.

References


KEY WORDS: cardiomyopathy ■ genetics
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Circ Heart Fail. 2013;6:e12-e13
doi: 10.1161/CIRCHEARTFAILURE.112.971424
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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