ACC.17™

847
JACC March 21, 2017
Volume 69, Issue 11

Heart Failure and Cardiomyopathies

EXTENDED REMISSION AND LATE RE-DECOMPENSATION OF DILATED CARDIOMYOPATHY ASSOCIATED WITH A NOVEL RIBONUCLEIC ACID BINDING MOTIF PROTEIN 20 (RBM20) MUTATION

Poster Contributions
Poster Hall, Hall C
Saturday, March 18, 2017, 9:45 a.m.-10:30 a.m.

Session Title: Advances in HCM, PPCM and Other Cardiomyopathies
Abstract Category: 13. Heart Failure and Cardiomyopathies: Clinical
Presentation Number: 1201-287

Authors: *Rodrigo Mendirichaga, Celso De La Cruz Luque, Jeffrey Smith, Rhanderson Cardoso, Nanette Bishopric, University of Miami Miller School of Medicine, Miami, FL, USA*

Background: Dilated cardiomyopathy (DCM) is the most common cause of heart failure in the young, and is familial in at least 1/3 of cases. Autosomal dominant mutations in RNA-binding motif protein 20 (RBM20), located on chromosome 10, account for ~3% of DCM. RBM20 is a cardiac-enriched RNA binding protein that regulates alternative splicing of a number of genes, including TTN, CAMK2D and MYH7, which are themselves implicated in cardiomyopathy. Mutations in RBM20 are highly penetrant and confer early onset aggressive disease. The exact relationship between RBM20 cellular functions and the penetrance and onset of DCM remain to be established.

Methods: The proband was diagnosed with DCM at age 16, when he presented with NYHA class IV heart failure. He required 3 months of left ventricular assist device (LVAD) support, after which he experienced myocardial recovery on carvedilol. Fourteen years later, he presented with acute biventricular failure leading to LVAD re-implantation and orthotopic heart transplantation. Notably, his mother was diagnosed with DCM at age 36 and similarly recovered with carvedilol, enjoying a 25 year disease-free interval, before acutely progressing to end-stage heart failure requiring heart transplantation.

Results: Sequence and deletion/duplication analysis of 76 candidate genes unveiled a novel heterozygous variant in RBM20 (2749 G>A, E917K), resulting in a non-conservative amino acid substitution (glutamate to lysine) likely to impact secondary protein structure. The E917K variant was not present in 60,706 unrelated individuals from the Exome Aggregation Consortium. No other definitive disease-related mutations were identified. No deletions or duplications of the 60 nuclear-encoded genes were detected by exome hybridization array.

Conclusions: We report a DCM family with a novel mutation in RBM20 and an unusual clinical course characterized by early onset of heart failure, prolonged remission, and sudden recurrence of biventricular failure 14 and 25 years after initial presentation. The prolonged interval between early and late disease manifestations suggests the possibility of distinct age-dependent mechanisms in the origin of this cardiomyopathy.