Myopathy And Cardiomyopathy Due To A Desmin Indel

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Abstract:- In a recent article, Schirmer et al. reported about a four-generation family, in which the index case presented with myopathy and cardiomyopathy (CMP) requiring heart transplantation (HTX), and three members with sudden cardiac death (SCD) [1]. In the index case an indel mutation in the desmin gene was made responsible for the phenotype [1]. We have the following comments/concerns.

Keywords:- Desmin, Neuromuscular, Cardiac Involvement, Myofibrillar Myopathy, Phenotype, Heterogeneity

Introduction:-

In a recent article, Schirmer et al. reported about a four-generation family, in which the index case presented with myopathy and cardiomyopathy (CMP) requiring heart transplantation (HTX), and three members with sudden cardiac death (SCD) [1]. In the index case an indel mutation in the desmin gene was made responsible for the phenotype [1]. We have the following comments/concerns.

Desminopathies manifest frequently in the heart with restrictive CMP (rCMP), characterized by bilaterally enlarged atria, a restrictive filling pattern with a deceleration time <150ms, normal or reduced diastolic and systolic ventricular diameters or volumes, but normal systolic function [2]. Did the patient fulfill these criteria or was there myocardial thickening >11mm, suggesting hypertrophic cardiomyopathy?

Since the index patient had undergone orthotopic heart transplantation at age 57y, we should be informed if the explanted heart had undergone patho-anatomic histological, immune-histological, and biochemical investigations. Was desminopathy visible on these investigations?

At age 16y the patient was suspected to have had myocarditis [1]. Was myocarditis suspected upon an endo-myocardial biopsy or upon cardiac MRI (cMRI) with contrast medium? Endo-myocardial biopsy typically shows inflammatory cells and other histological and immune-histological abnormalities. Myocarditis on cMRI typically shows myocardial enhancement 15 minutes after application of the contrast medium (late gadolinium enhancement (LGE)) [3]. Was LGE visible at that time in the index patient?

Interestingly, the mutation caused marked intra-familial phenotypic heterogeneity [1]. How to explain that only the index patient manifested in the skeletal muscles and the myocardium? Is it conceivable that myopathy in the three family members with SCD was subclinical or only mildly manifesting?

How severe was myopathy in the index patient? Was he still able to ambulate independently at the time of HTX or did he require a walker or even a wheel chair? Since it is well documented that immunosuppressive therapy, required life-long after HTX, may be myotoxic [4], we should be informed...
if myopathy in the index case deteriorated after HTX. Did degree of progression of muscle disease increase after HTX?
Since the mutation was classified as only “likely pathogenic” it would be interesting to know if the authors suspected another mutation in other genes responsible for the phenotype? Why was the desmin gene chosen for sequencing? Why was no panel investigation carried out?
This interesting article could profit from presentation of more extensive clinical data, from a more precise characterization of the CMP, from post-hoc examination of the explanted heart, from a detailed description of the immunosuppressive regimen and its effect on the progression of myopathy.

References:


