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Editorial

The Expanding Spectrum of FLNC Cardiomyopathy

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Mutations in gene encoding filamin C (FLNC) have been historically associated with hypertrophic cardiomyopathy (HCM) and myofibrillar myopathy [1]. Subsequently, several variants have been associated with other cardiomyopathy phenotype, including dilated cardiomyopathy (DCM) and arrhythmogenic left ventricular cardiomyopathy (ALVC) [2]. In particular, FLNC variants have been associated with a peculiar left ventricular phenotype, with diffuse non-ischemic fibrosis, and ventricular arrhythmias potentially leading to sudden cardiac death [3].

Recently, FLNC variants have been found in patients with restrictive cardiomyopathy (RCM) [4].

The contribution of a genetic pathogenesis to RCM has not been completely elucidated. Moreover, the knowledge about relevant mutations and genes implicated in this condition is limited due to the rarity of the disease, in particular in pediatric patients.

Girolami et al. described a case of a 7-year-old girl diagnosed with RCM after a comprehensive clinical evaluation. In particular, the patient showed a negative family history for sudden cardiac death and cardiomyopathies, no extra-cardiac manifestations, electrocardiogram and echocardiography revealing bi-atral enlargement. In addition, due to increased pulmonary vascular resistance at cardiac catheterization, the patient had been evaluated for heart transplantation.

The patient underwent clinical exome, which evidenced a de novo variant c.6527_6547dup (p.Arg2176_2182dup) in the FLNC, classified as likely pathogenic according to the American College of Medical Genetics [5].

Currently, it is not completely understood why different FLNC mutations are responsible for different clinical entities. It has been observed that missense mutation leads to HCM, while truncating mutation to DCM or ALVC [2]. Occasionally, missense mutations in FLNC have recently shown co-segregation with RCM in two Caucasian families [6].

FLNC encodes for the protein filamin C, which is localized at the level of the Z-bands and the intercalated disc. It is known to be involved in the sarcomeric organization and in the intercellular adhesion [7,8]. The identification of FLNC variants has significant implication for management strategies since they have been associated with increased sudden cardiac death risk and poor outcome [2].

This case report highlights the importance of performing exome sequencing to identify rare genetic variants, in order to guide therapy and offer genetic counselling to the family.

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