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Letter to the Editor

RYR2 Deletion and Left Ventricular Noncompaction

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In a recent article, Campbell *et al.*, (2015) reported about a 20 years old female carrying a novel exon-3 deletion in the *RYR2* gene, which manifested phenotypically with exertional syncope, polymorphic ventricular tachycardia, and left-ventricular hypertrabeculation / noncompaction (LVHT). We have the following comments and concerns.

How can the authors be sure that ventricular arrhythmias were due to the RYR2 deletion? Arrhythmias may be also caused by LVHT, a structural myocardial abnormality frequently associated with ventricular arrhythmias and sudden cardiac death (Miyake, C. Y., & Kim, J. J. 2015). Additionally, coronary heart disease may cause arrhythmias. Was coronary angiography normal?

Five syncopes were described in the presented patient. Since LVHT is frequently associated with stroke / embolism, ischemic embolic stroke has to be excluded by cerebral MRI (Stöllberger, C. *et al.*, 2011). Was there ever a cerebral MRI carried out before implanting the implantable cardioverter defibrillator (ICD)? Were ever thrombi within the intertrabecular spaces detected on echocardiography or cardiac MRI? Did she ever experience an embolic event outside the brain? Syncope may be also due to epilepsy. How were seizures excluded? There is no mentioning of the carotid ultrasound. Was carotid artery stenosis excluded as a cause of syncope?

As many others, the authors suggest that there is a causal link between the RYR2 deletion and LVHT (Campbell, M. J. *et al.*, 2015). However, a causal relation between LVHT and any of the mutated genes so far reported has never been proven. Arguments against a causal relation, are that LVHT is associated with mutations in more than 30 different genes (*RYR2*, *TAZ*, *dystrophin*, *DMPK*, *α-DTNA*, *RYR1*, *ITGA7*, *MYH7B*, *LAMP2*, *GAA*, *GBEI*, *MADD*, *COL7A1*, *MMACHC*, *PMP22*, *FXN*, *β-globin*, *PLEC1*, *GLA*, *NKX2-5*, *MYH7*, *LDB3/ZASP*, *ACTC1*, *TNNT2*, *MYBPC3*, *TPM1*, *TNNI3*, *LMNA*, *SCN5A*, *HCN4*, *NNT*, *glycyl-tRNA-synthetase*, mtDNA genes and nDNA genes encoding for the mitochondrial proteome (SDH) or mitochondrial tRNAs (Finsterer, J., & Zarrouk-Mahjoub, S. (015), that LVHT occurs only in a small number of mutation carriers, and that family members of a patient with LVHT often present without cardiologic disease or clinical heterogeneity including cardiac abnormalities other than LVHT, such as hypertrophic cardiomyopathy, dilative cardiomyopathy, or arrhythmias. An argument for a causal relation is the simultaneous occurrence of the mutation and LVHT in several family members, which was not the case in the presented family.

According to the presented data the patient developed LVHT between age 16 and 17y (Campbell, M. J. *et al.*, 2015). Thus, LVHT has to be interpreted as acquired (Finsterer, J., & Stöllberger, C. 2012). Acquired LVHT has been particularly described in athletes, pregnant females and neuromuscular disorders (NMDs) ((Finsterer, J., & Stöllberger, C. 2012; Gati, S *et al.*, 2014). Was the patient pregnant between ages 16 and 17y? Was she ever investigated for a NMD? Did she ever complain about symptoms indicative of a NMD? Was creatine-kinase ever elevated? Was she ever seen by a neurologist familiar with NMDs? Was she ever carrying out extreme sport?

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Overall, this interesting case shows that work-up for syncope may lead to the detection of LVHT, that thromboembolism originating from meshwork thrombi and epilepsy need to be excluded in LVHT patients with recurrent syncopes, and that LVHT may be acquired even in patients not being athletes, pregnant, or affected by a NMD. The presented patient challenges the assumption that LVHT is congenital in each case.

REFERENCES

1. Campbell, M. J., Czosek, R. J., Hinton, R. B., & Miller, E. M. (2015). Exon 3 deletion of ryanodine receptor causes left ventricular noncompaction, worsening catecholaminergic polymorphic ventricular tachycardia, and sudden cardiac arrest. *American Journal of Medical Genetics Part A*, *167*(9), 2197-2200.
2. Miyake, C. Y., & Kim, J. J. (2015). Arrhythmias in left ventricular noncompaction. *Cardiac electrophysiology clinics*, *7*(2), 319-330.
3. Stöllberger, C., Blazek, G., Dobias, C., Hanafin, A., Wegner, C., & Finsterer, J. (2011). Frequency of stroke and embolism in left ventricular hypertrabeculation/noncompaction. *The American journal of cardiology*, *108*(7), 1021-1023.
4. Finsterer, J., & Zarrouk-Mahjoub, S. (2015). Considerations about the genetics of left ventricular hypertrabeculation/non-compaction. *Cardiology in the Young*, *25*(7), 1435-1437.
5. Finsterer, J., & Stöllberger, C. (2012). Acquired, familial noncompaction and eccentric hypertrophic cardiomyopathy associated with metabolic myopathy and epilepsy. *International journal of cardiology*, *160*(1), 73-75.
6. Gati, S., Papadakis, M., Papamichael, N. D., Zaidi, A., Sheikh, N., Reed, M., ... & Sharma, S. (2014). Reversible de novo left ventricular trabeculations in pregnant women: implications for the diagnosis of left ventricular noncompaction in low-risk populations. *Circulation*, *130*(6), 475-483.