Letter to the Editor

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Genetic background of left ventricular hypertrabeculation/non-compaction with stroke

With interest we read the article by Markiewicz-Loskot et al. on a 3-year-old female in whom heart failure at age 10 months led to the diagnosis of restrictive cardiomyopathy and left ventricular hypertrabeculation (LVHT)/non-compaction.1 The study raises concerns.

Left ventricular hypertrabeculation is not exclusively congenital. In single cases it has been described as an acquired phenomenon.2–4 In a single patient, it even disappeared after treatment of heart failure.5 How was restrictive cardiomyopathy diagnosed? Did the patient show a restrictive filling pattern on echocardiography? Did the restrictive filling pattern resolve during follow-up? Did extension and morphology of LVHT change over time?

In the discussion, it is mentioned that the patient suffered from cerebral embolism. At which age and which territory was affected? How do the authors know that the origin of embolism was the heart and not the aorta or the carotid or vertebral arteries? Did stroke occur before or after detection of LVHT and before or after initiation of oral anticoagulation (OAC)? Was there atrial fibrillation when stroke occurred? Which was the indication for OAC? Was OAC given for severely reduced systolic function, for atrial fibrillation, or for LVHT? Though reported in single cases, we did not find an increased risk of thromboembolism when comparing 62 LVHT patients with sex-, age-, and systolic function-matched controls.6

Though initially described in children, it is still a matter of discussion if LVHT is indeed more prevalent in children compared with adults. Meanwhile, LVHT has been described in all age groups, including nonagenarians.7 Furthermore, there is no age-dependent typical pattern of LVHT regarding clinical, echocardiographic, or neurological findings.7

On the basis of small case series and case reports, it was initially believed that LVHT has a high mortality. Follow-up studies on larger cohorts of LVHT patients, however, showed that the mortality in these patients is not uniformly high but dependent on the cardiac and neurological comorbidity.8,9 In a study on 86 adult LVHT-patients, we calculated a mortality of 5.3%/year (unpublished) Predictors of mortality, in this study, were advanced age, presence of neuromuscular disorder (NMD), exertional dyspnoea, oedema, heart failure, left anterior hemiblock, and reduced systolic function.

In up to 80% LVHT is associated with NMDs, such as dystrophinopathies, dystrobrevinopathies, myotonic-dystrophy, zasopathy, myoadenylate-deaminase deficiency, Charcot-Marie-Tooth disease, mitochondrial disorder, Barth syndrome, laminopathy, Friedreich’s ataxia, or Pompe’s disease.10 Was the described patient seen by a neurologist and was there any indication of a NMD?

The genetic background of LVHT is far more heterogeneous than indicated in the discussion. Left ventricular hypertrabeculation was not only associated with mutations in the tafazzin (G4.5, TAZ), DTNA (dystrobrevin), and lamin A/C genes, but also with mutations in the cypher/ZASP, GAA, DMPK, AMPD1, mitochondrial, frataxin, CSX, and PMP22 genes.10 So far, LVHT was not associated with mutations in the FKBP1A gene.11 Additionally, LVHT has been described in patients with Turner’s syndrome, Ohtahara syndrome, Roffman syndrome, Noonan syndrome, Nalpataella syndrome, Melnick needles syndrome, MIDAS syndrome, DiGeorge syndrome, Beals–Hecht syndrome, congenital adrenal hyperplasia, distal 4q-trisomy/distal 1q-monosomy, distal 5q-deletion, trisomy-11, and trisomy-13.11

In conclusion, LVHT has a highly heterogeneous genetic background. Left ventricular hypertrabeculation requires comprehensive cardiac and neurological investigations and as long as there is no profound evidence for OAC in LVHT per se, it should be restricted to classical indications, such as atrial fibrillation, severe heart failure, or severe atherosclerosis.

References


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