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Letter to the Editor

Heterogeneous Genetic Background of Left Ventricular Hypertrabeculation/Noncompaction

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In a recent article, Sasse-Klaassen *et al.*, reported about mapping of a novel gene locus for familial, autosomal dominant left ventricular hypertrabeculation / noncompaction (LVHT) to chromosome 11p15 (Sasse-Klaassen, S. *et al.*, 2004). The article raised a number of comments and concerns.

Hypertrabeculated parts not necessarily locate in akinetic regions or hypertrophied segments. LVHT also has been found in well contracting left ventricles (Ichida, F. *et al.*, 1999) and also in left ventricles with normal thickness of the compacted layer.

LVHT cannot only be attributed to an arrest of the myocardial development during embryogenesis. In single cases LVHT has been reported to develop during adulthood (Finsterer, J., & Stöllberger, C. 2001). The authors themselves present an individual (IV-7) who developed LVHT during adulthood. Additionally, various other pathogenetic concepts, like "dissection" of the myocardium due to malfunction of gap junctions, frustrate attempt of hypertrophy to compensate for myocardial impairment, hyper-vascularization of the subendocardial myocardial layer, transformation of microinfarcts due to impaired oxidative metabolism or impaired microvascular supply, or adaptation of the impaired myocardium to move large stroke volumes at low heart rate and low pressure, have been proposed.

In addition to Barth syndrome, dystrobrevinopathy, and *cypher/ZASP* gene mutations (Sasse-Klaassen, S. *et al.*, 2004; Bleyl, S.B. *et al.*, 1997), LVHT has been found in patients with Becker muscular dystrophy (deletion of exons 45 to 48 of the dystrophin gene, duplication), myotonic dystrophy type 1 (CTG repeat expansion of 300 in the *DMPK* gene), mitochondrial disorder (m.3243A>G, m.3460G>A, m.8391A>G mtDNA mutations), myoadenylate deaminase deficiency (C34T substitution in exon 2 of the *AMPD1* gene), and other rare genetic disorders, like MIDAS syndrome, Roifman syndrome, Melnick Needles syndrome, DiGeorge syndrome, nail patella syndrome, Noonan syndrome, and 5q deletion syndrome (Stöllberger, C. *et al.*, 2002).

The patients did not undergo neurological investigations, although it has been shown that LVHT is associated with neuromuscular disorders in up to 82 % of the cases (Stöllberger, C. *et al.*, 2002). Most frequently LVHT occurs in mitochondrial disorders.

Since no mutations were found in the two candidate genes *MLP* and *SOX6*, it would be interesting to know if also other candidate genes were investigated for re-arrangements. The authors mention in the method section, that they also looked for Cypher/ZASP mutations. Unfortunately, no results of these investigations are presented. Are there any mutated genes located in the region of interest, which are associated with neuromuscular disorders or cause a secondary mitochondrial defect?

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There is a discrepancy between the number of investigated individuals in the results section (n=33) and those given in the illustration of the pedigree (n=34).

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