Letter to the Editor

In a recent article, Hirano et al. reported about Ebstein’s anomaly, non-compaction/left ventricular hypertrobraculation (LVHT), and ventricular septal defect (VSD) in a single patient carrying a MYH7 mutation [1]. We have the following comments and concerns.

LVHT is frequently associated with neuromuscular disorders (NMDs) or chromosomal defects [2]. MYH7 mutations may be even associated with muscle disease [3]. Was the described MYH7 mutation also manifesting in the skeletal muscle as has been previously reported [3,4]? Were family members carrying the MYH7 mutation also investigated for muscle disease?

LVHT has been repeatedly reported in association with MYH7 mutations [4-11]. In an adult with mild myopathy LVHT was associated with the c.5566G>A mutation [4]. In a patient with bicuspid aortic valve and LVHT, cardiac abnormalities were associated with the mutation c.1316T>G [5]. In several members of a family with LVHT the mutation c.842G>C was detected [6]. A pediatric patient with heart failure carried the mutation R369Q [7]. In four LVHT families and 4 sporadic cases the mutations c.818_IG_A, Arg243His, Asp239del, Phe252Leu, Arg1359Cys, and Ala1766Thr, were detected [8]. In a 26yo female with LVHT the mutation Tyr350Asp was reported [9]. A 7day-old boy undergoing surgical repair for VSD and LVHT carried the insertion c.2010-2031ins [10]. In a family with LVHT, atrial septal defect (ASD) II and Ebstein’s anomaly the mutation Tyr283Asp was detected [11]. MYH7 mutations associated with LVHT were also reported by Hoedemaekers et al. 2010 [12]. LVHT associated with MYH7 mutations may be already detected upon intra-uterine ultrasound [13].
LVHT is frequently associated with embolism, ventricular arrhythmias, and heart failure. Was the history in this particular patient positive for heart failure, embolism, arrhythmias, palpitations, syncope, or sudden cardiac death (SCD)? Was a cerebral MRI carried out to rule out subclinical embolic stroke? Were any other family members screened for LVHT? Did any arrhythmia occur in any of the three LVHT patients?

The presented pedigree in table 2 is confusing since it does not show Ebstein’s anomaly in the index patient’s sister unlike the description in the case presentation. Additionally, the pedigree indicates LVHT in the father which is not described in the text.

Why did heart failure persist in the index patient? Was it due to coarctation or LVHT? Was a left-right shunt present prior to closure of the VSD? Did the father also present with a VSD, LVHT, ASD, and coarctation? Did the sister of the index patient present with ASD and coarctation?

How do the authors explain that the MYH7 mutation manifested with LVHT, Ebstein’s anomaly, and VSD in the two children but only with LVHT in the father? Absence of Ebstein’s anomaly and VSD in the father could be an argument in favour of assessing the mutation as non-pathogenic or that it was not fully penetrant? Did the father have a history of stroke or embolism, syncope, or heart failure?

Overall, this interesting presentation could profit from providing more detailed information about findings in the presented patients. MYH7 mutations may be also associated with complex LVHT irrespective if they go along with or without muscle disease.

References

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