Possible New Syndrome: Left Ventricular Noncompaction, Partial Agenesis of the Corpus Callosum, and Developmental Delay in a Brazilian Child

Dionisia A.C. Lamonica,1 Dagma V.M. Abramides,1 Luciana P. Maximino,1 Mariana G. Gejão,1 Greyce K. da Silva,1 Amanda T. Ferreira,1 Renata H. Furlan,2 Célia M. Giacheti,3 Plínio A. Barros-Neto,4 and A. Richieri-Costa2*

1Departamento de Fonoaudiologia, FOB-USP, Bauru, SP, Brazil
2Departamento de Genética Médica, HRAC-USP, Bauru, SP, Brazil
3Departamento de Fonoaudiologia UNESP, Marília, SP, Brazil
4CentroCard, Bauru, SP, Brazil

Received 31 July 2008; Accepted 4 February 2009

We report on the clinical, neuropsychological and language characteristics of a boy with left ventricular noncompaction cardiomyopathy (LVNC), agenesis of the splenium of the corpus callosum, minor anomalies of face and limbs, mild mental retardation, and speech and language disabilities. The occurrence of pilomatricoma (calcifying epithelioma) may be part of the clinical spectrum or a fortuitous finding. Compared to other related conditions with LVNC suggests that this is a “new” unique pattern MCA/MR syndrome. © 2009 Wiley-Liss, Inc.

Key words: left ventricular noncompaction cardiomyopathy; mental retardation; speech/language disorders

INTRODUCTION

Noncompaction cardiomyopathy, also known as (LVNC) or left-ventricular hypertrabeculation/noncompaction is a type of cardiomyopathy manifested by heart failure, arrhythmias, and embolic events [Engberding and Bender, 1984a,b; Chin et al., 1990]. The main echocardiographic signs include excessive trabeculations and deep intertrabecular recesses, in which blood flows within the intertrabecular recesses as shown by color Doppler imaging. The noncompacted myocardium preferentially involves the apex and the mid lateral and inferior wall of the left ventricle showing a classical two-layered structures [Engberding et al., 2007]. LCNV may be associated with other congenital heart defects [Burke et al., 2005; Friedman et al., 2007]. Its association with extra-cardiopulmonary anomalies is rare [Tunaoglu et al., 2003], except in patients with 1p36 deletion [Battaglia et al., 2008]. We report a boy with LCNV, structural anomalies of the corpus callosum, developmental delay, and a skin nevus associated with pilomatricoma which may be a “new” syndrome.

How to Cite this Article:
with two episodes of cardiac arrhythmia leading to cardiac arrest. The diagnosis of noncompaction cardiomyopathy was made by color Doppler echocardiography. Neuropsychological development and language acquisition were delayed. He had recurrent respiratory infections until 3 years of age, and exercise intolerance which has persisted. Brain magnetic resonance imaging performed at age 30 months showed abnormal shape of the anterior part of the corpus callosum (genu) with partial agenesis of the posterior portion (splenium) (Fig. 2). When examined at age 10 years, he weighed 25 kg (<10th centile), and had a height of 137 cm (50th centile), with head circumference of 53 cm (50th centile), inner canthal distance 3.4 cm (>50th centile), outer canthal distance 9.3 cm (>50th centile). He had mild mental retardation, severe language disabilities, long and thin face, myopia, deep set eyes, short palpebral fissures, high nasal bridge, mild malar hypoplasia, open bite, incisors diastema and long neck.

Behavior and cognitive assessment was performed through Child Behavior Checklist (CBCL), Raven’s Progressive Matrices and the Wechsler Intelligence Scale for Children-III (WISC-III), the Mesulan Cancel Test, and the Illinois Test of Psycholinguistic Abilities (ITPA). Patient’s performance showed mild intellectual deficit [VIQ (68), PIQ (61), and FSIQ (62)]. Speech and language
evaluation showed poor verbal communication. Syntax, morphology, semantics, phonology and pragmatics were impaired, and receptive oral language was better than expressive language. Graphic spatial disorganization associated with cognitive impairment, attention deficit and hyperactivity result in impaired proficiency for reading accuracy, arithmetic difficulties, and poor writing performances.

Conventional cytogenetic (550 bands) analyses were normal. Genomic DNA from the patient and normal individuals were hybridized to slides containing triplicates of ~3,500 large insert clones evenly spaced at ~1 Mb density over the full genome. The clones were provided by the Wellcome Trust Sanger Institute (UK), and are fully described in the Ensembl Genome Database. Array production, DNA labeling and hybridization have been previously described [Rosenberg et al., 2006]. Target imbalances were determined based on log 2 ratios of the average of the replicates, and sequences were considered as amplified or deleted when outside the ±0.33 range. No submicroscopic deletions or duplications were detected. Echocardiographic color Doppler (Fig. 5) showed thickening of the left ventricular wall with a two-layered structure: a compacted epicardial layer and a non-compacted layer with numerous and prominent trabeculations (LVNC). Left ventricular diastolic diameter (d) was 4.9 cm (normal 3.2–4.5 cm). Color Doppler imaging showed blood flowing from the ventricular cavity into the intertrabecular recesses.

**DISCUSSION**

Noncompaction of the left ventricular myocardium is a heterogeneous condition viewed as an isolated type of unclassified myocardiopathy [Engberding and Bender, 1984a,b]. It is attributed to the developmental arrest of normal endocardium and myocardium embryogenesis resulting in excessive trabeculations and deep intertrabecular recesses [Chin et al., 1990; Engberding et al., 2007]. The isolated form of LVNC occurs in the absence of other structural heart disease, and the other form occurs in association with other congenital heart defects [Ichida et al., 2001; Markiewicz-Loskot et al., 2006; Xia et al., 2008]. Clinical and genetic heterogeneity have been clearly demonstrated since autosomal dominant, recessive, and X-linked genes have been implicated as causal agents [Digilio et al., 1999; Sasse-Klaassen et al., 2004; Brady et al., 2006; Xing et al., 2006; Stöllberger and Finsterer, 2007; Finsterer et al., 2008; Moric-Janiszewska and Markiewicz-Loskot, 2008; Vijayvergiya et al., 2008]. LVNC has been frequently reported in association with several neuromuscular disorders [Bleyl et al., 1997; Finsterer et al., 2005; Stöllberger and Finsterer, 2005; Spencer et al., 2006; Finsterer et al., 2007a,b; Stöllberger et al., 2007].

Left ventricular noncompaction has been occasionally reported within the clinical spectrum of several malformation syndromes such as X-linked microphthalmia with linear skin defects syndrome [Kherbaoui-Redouani et al., 2003], the autosomal dominant noncompaction cardiomyopathy, bradycardia, pulmonary stenosis, atrial septal defect and heterotaxy syndrome [Wessels et al., 2008], in some numeric chromosome abnormalities such as Turner syndrome [van Heerde et al., 2003], trisomy 13 [McMahon et al., 2005], mosaic trisomy of chromosome 22 [Wang et al., 2007]; and in few structural chromosomal anomalies [Kanemoto et al., 2006; Thienpont et al., 2007; Battaglia et al., 2008; Wessels et al., 2008] especially, the 1p36 deletion syndrome. This condition is characterized by distinct craniofacial features, micro-brachycephaly, developmental delay, mental retardation, hypotonia, seizures, brain anomalies, heart defects, and minor limbs anomalies such as brachy/camptodactyly and short feet [Battaglia, 2005; Battaglia et al., 2008]. However, in some individuals with the 1p36 microdeletion the clinical manifestations seem to be more complex and variable, and LVNC is not an obligatory finding [Tan et al., 2005; Robinson et al., 2008; Rudnik-Schöneborn et al., 2008].

Recently, Kanemoto et al. [2006] reported on a patient with LVNC, callosal agenesis, and severe developmental delay who presented a microdeletion involving the region 1q43, confirming that the association of LVNC and callosal agenesis seems to be rare.

In the patient here described, mild mental retardation is associated with language disorder consisting of a typical pattern of speech impairment, restricted vocabulary that results in secondary manifestation due to callosal involvement, since structural anomalies of the corpus callosum are clearly implicated in critical aspects of language processing [Paul et al., 2003; Brown et al., 2005]. Another finding in our patient refers to pilomatricoma, a tumor of hair follicle matrix cells that has been reported in chromosomal and microdeletion syndromes such as Turner syndrome [Noguchi et al., 1999; Wood et al., 2008], trisomy 9 [Matsuura et al., 2002], Sotos syndrome ['Tatton-Brown et al., 2005; Gilberte et al., 2008], Rubinstein–Taybi syndrome [Cambiaghi et al., 1994; Kalyoncu et al., 2006]. The whole clinical picture of the patient here described, as well as the evaluation through CGH-array clearly excludes the syndromes above mentioned.

We propose that this patient may represent a new syndrome consisting of LVNC with partial callosal agenesis, mental retardation, severe speech/language delay, pilomatricoma, and minor limb anomalies and resulting from the involvement of multiple
ACKNOWLEDGMENTS

The senior author (A.R.-C.) is indebted for CNPq support (Grant: 470996/2006-4 and 301926/2007-7). We would like to thanks Dr. Carla Rosenberg who performed the CGH-array study.

REFERENCES


