Image

Hypertrophic Cardiomyopathy in Monozygotic Twins

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Male monozygotic twins (MT), age 19 years, with obstructive hypertrophic cardiomyopathy (HCM), symptoms (exertional dyspnea) started around age 13 years, and similar clinical presentation (a grade 3/6 systolic murmur heard in the left lower sternal border, typical ECG signs of left ventricular hypertrophy). In both patients, there were echocardiographic moderate left atrial enlargement, massive septal hypertrophy (>30mm) and severe resting outflow tract gradient, without significant differences betweem them. Some discordances were observed in two-dimensional images (Figure 1). Color Doppler showed marked septal coronary branchs in twin G (Figure 2), which was not found in twin V. Twin G evoluted to medical refractory NYHA III/IV functional class and was referred to a surgical myectomy.

Hypertrophic cardiomyopathy is a primary disease of the myocardium caused by mutations in genes coding for sarcomeric proteins[1], and the phenotype can be influenced by modifiers genes[2] and environmental factors. Then, the clinical and morphological manifestations of the disease are variable, from absence of symptoms to heart failure, even among mutation carriers of a given family. MT are considered genetically identical (causing and modifiers genes), and phenotypic discordances have been credited to the action of environmental factors. In MT with HCM, it would be expected similar expression of the disease, as observed by Maron et al[3], with limited discordances. However, the cases reported in the literature do not support this view. There are reports of MT pairs with concordant[3-6] and discordant[4,7] phenotypes. In general terms, our patients showed similar manifestations of the disease, but there were some diverse echocardiographic and clinical findings.

The cases reported here and the literature review bring more questions than answers about the pathogenetic mechanisms of hypertrophic cardiomyopathy. There is not a reasonable explanation to understand the contrasting situation existing between MT pairs with very similar findings and pairs with absolutely different expression of the disease, including symptoms, extent and distribution of the hypertrophy, outflow obstruction, age of presentation and outcome.

Can we assume that the genetic background is absolutely identical in MT? they develop from a separation of the embryonic cells of a single embryo at the two-cell stage, but human twinning can also occur at a developmental stage as late as 7 days of gestation, and this timing can determine placental anastomoses and umbilical differences, exposing the developing twins to variable intrauterine environments[8]. In addition, there are studies of genetic mechanisms that may result in phenotypic, genotypic, and epigenetic differences between MT[9], but those phenomena are rare and cannot be assumed as a major cause of the discordances under discussion.

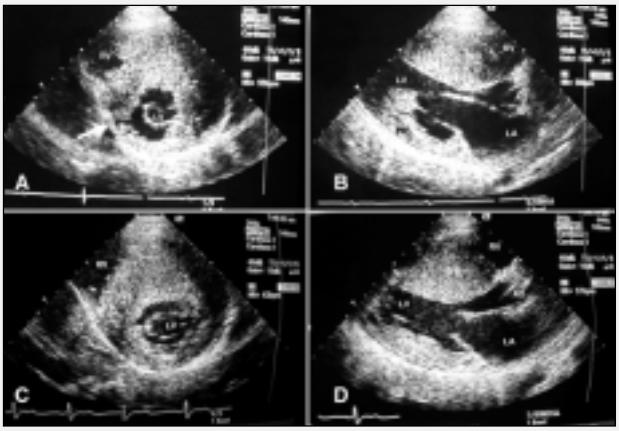

Fig. 1 · A and B) two-dimensional echocardiogram of twin V; C and D) two-dimensional echocardiogram of twin G. In A and C (short axis), the LV hypertrophy is more difuse in twin G. Note a displasy in the inferior wall of twin V (arrow). In B and D (long axis), similar IVS thicknesses are showed but the PW is more hypertrophied in twin G. RV· right ventricle cavity; LA· left atrium; AO· aorta; LV· left ventricle cavity; IVS· interventricular septum; PW· posterior wall.

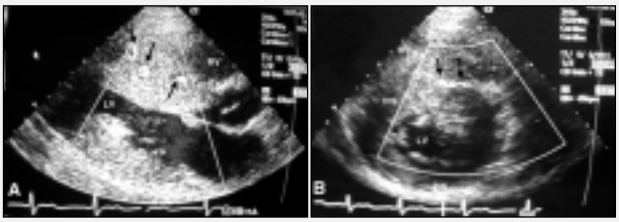

Fig. 2 – A) twin G, long axis. Enlarged septal coronary branchs are showed with color Doppler (arrows). B) twin G, short axis. An enlarged perforating septal branch is showed with color Doppler (arrows).

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