Apical Hypertrophic Cardiomyopathy: Truly a Benign Entity or Not Benignly a True Entity?

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Hypertrophic cardiomyopathy is one of the most common genetic cardiac disorders, its prevalence approximating 0.2% in the general population [1]. Apical hypertrophic cardiomyopathy, a variant with predominant apical involvement, is most common in Japan where it accounts for about 25% of primary hypertrophic cardiomyopathy cases [2]. Outside of Japan, this condition is far less frequent. Keren et al. [3] were the first to report the clinical characteristics, hemodynamics and imaging study findings in a large group of non-Japanese patients with AHC. Similar to Japanese patients, the subjects studied by Keren and co-workers were characterized hemodynamically by a non-obstructive physiology and morphologically by hypertrophy primarily confined to the left ventricular apex. The authors postulated that the unique morphology and the resulting hemodynamics were probably genetically determined. The clinical course of the patients in this study was generally uneventful, but since this was not a longitudinal study (mean follow-up was less than 2 years) the authors were unable to evaluate the prognosis of AHC in this cohort.

Although primary hypertrophic cardiomyopathy is an important cause of congestive heart failure, its most dreaded complication is that of sudden death, most often caused by malignant ventricular arrhythmias [4]. Lacking long-term natural history studies, and due to the relative rarity of AHC in countries other than Japan, the prognosis of this variant has generally been assumed to be benign [2]. This assumption was based primarily on the experience of the Japanese.

In this issue of *IMAJ*, Abinader et al. [5] report the clinical course of 11 patients with AHC – characterized by the typical electrocardiographic and morphologic abnormalities described by Keren et al. [3]. The patients were followed for 5–20 years. The article by Abinader's team sheds new light on the natural history of this condition. Of the 11 patients, 2 (18%) developed symptomatic ventricular arrhythmias. The first patient with sustained monomorphic VT had an apical aneurysm despite no angiographic evidence of coronary artery disease. The second patient with VT presented with cardiac arrest. Although this patient had a non-Q anterior wall infarction and a diseased left anterior descending artery, the monomorphic morphology of the VT suggests that ischemia may not have been the sole cause of the arrhythmia, but rather the trigger for a re-entrant tachycardia originating in the diseased apex. In keeping with the findings of Abinader et al., a recent report from Japan has also raised concern that patients with AHC are prone to life-threatening arrhythmias [6].

How can the apparent discrepancy between past reports of the benign prognosis of AHC be reconciled with more recent observations of a propensity to malignant arrhythmias? Obviously, one answer might be that previous studies of AHC were too small and lacked follow-up of adequate duration, so that clinical event rates were underestimated. However, considering current understanding of the genetics of hypertrophic cardiomyopathy [7], this explanation is probably over-simplistic. Left ventricular morphology independently predicts the risk of sudden death [8], but it is obvious that in some patients at high risk for sudden death the gross morphologic abnormalities of the left ventricle and hemodynamic parameters such as subaortic obstruction may be modest or even absent [1,9]. Moreover, hypertrophic cardiomyopathy cannot be considered a single entity defined simply by anatomic and hemodynamic findings, but is rather a heterogeneous disorder of diverse genetic causes, where genotype is an important determinant of outcome. For example, patients with troponin T mutations have only mild hypertrophy but severe myocyte disarray and high rates of sudden death at a young age [10]. These data stress the importance of assessing the phenotypic risk for sudden death in asymptomatic patients with hypertrophic cardiomyopathy – not only by clinical and morphologic criteria (such as family history or hypertrophy evaluated by echocardiography) but also by histologic parameters and by genotype. It is conceivable that in AHC too the genotype is of prognostic importance. The variable prevalence and prognosis of AHC in different parts of the world suggests that this syndrome, classically defined and diagnosed morphologically, may not represent a single entity. It is plausible that different mutations in one gene or more determine the typical left ventricular morphology of AHC but simultaneously lead to varying degrees of microscopic abnormalities and thus to a heterogeneous patient population in terms of risk for sudden death.

An obvious limitation of the report by Abinader et al. [5], acknowledged by the authors, is the small sample size. Nevertheless, their observations as well as those of others [6] suggest that a complacent approach to all patients with AHC may be unsafe. As for primary hypertrophic cardiomyopathy, additional studies are needed to elucidate the genetic basis of this syndrome, to define

AHC = apical hypertrophic cardiopathy
VT = ventricular arrhythmia

the role of laboratory testing for sudden death-risk stratification, and to outline optimal strategies of management.

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