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Apical hypertrophic cardiomyopathy: A view from the U. S. A.

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The initial reports from Japan in the late 1970s by Sakamoto and associates[1] and Yamaguchi and his colleagues[2,3] describing a form of cardiac disease characterized morphologically by left ventricular hypertrophy confined to the most apical (distal) portion of the left ventricle, aroused considerable interest amongst cardiologists and students of hypertrophic cardiomyopathy throughout the world[4~9]. These early descriptions by Japanese investigators implied that such patients had a variant of hypertrophic cardiomyopathy that was probably unique to Japan. The characteristic clinical hallmarks of this entity—a striking electrocardiographic pattern of giant T-wave inversion and an angiographic silhouette showing diastolic deformation of the left ventricular cavity which resembled a "spade" (i.e., the playing card "ace of spades" reflecting hypertrophy localized to the apex)—were features apparently not often observed in patients with hypertrophic cardiomyopathy living in other parts of the world. In the ensuing decade, much has been written and discussed regarding "apical hypertrophic cardiomyopathy" and a large measure of confusion (much of it still unresolved) has arisen regarding the nature and clinical significance of this entity and its relationship to the overall population of patients with hypertrophic cardiomyopathy. Therefore, this would seem to be an appropriate time to reflect on apical hypertrophic cardiomyopathy in an effort to clarify some of these issues—from the perspective of an investigator working with a large population of patients spanning the broad clinical spectrum of hypertrophic cardiomyopathy in North America.

In Japan, the entity of apical hypertrophic cardiomyopathy comprises an important segment of the overall patient population with hypertrophic cardiomyopathy (i.e., about 25% in some series)[3,10] compared to an estimated $<3\%$ of patients with hypertrophic cardiomyopathy in other parts of the world[9]. Characteristically, apical hypertrophy in Japanese patients is a clinically benign entity[10] without demonstrable genetic transmission[11,12], which is identified predominantly in older

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males[3,12], not infrequently is associated with systemic hypertension[12,13], and rarely results in severe cardiac symptoms or death[3,10,14]. Therefore, this group of patients would appear to be clinically distinct from most other subsets of hypertrophic cardiomyopathy described in Japan[10] or elsewhere[15~18] in which genetic transmission and marked symptoms are common. In Japanese patients with *non*-apical forms of hypertrophic cardiomyopathy the morphologic and clinical features are diverse[10] and largely similar to those of *non*-Asian patients with hypertrophic cardiomyopathy reported in other parts of the world.

At the National Institutes of Health during a seven year period from 1979–1985, we have identified by two-dimensional echocardiography only 23 patients who showed a morphologic variation of this disease in which ventricular hypertrophy was judged to be located *predominantly* in the apical (or distal) portion of the left ventricle below the mitral valve and chordal levels (comprising 2% of almost 1,000 patients studied with hypertrophic cardiomyopathy during this period of time)[9]. In these patients, left ventricular hypertrophy was located sufficiently distal in the ventricle as to appear distinctly different from most other patients with this disease. These patients, while racially diverse, where predominantly Caucasian and only one was of Asian descent. The majority (about 60%) were male and two-thirds experienced significant cardiac symptoms and functional limitation. None had a "spade" deformity of the left ventricle and only four had "giant" T wave inversion. Therefore, most of these patients do not appear to represent the same clinical and morphologic entity as apical hypertrophic cardiomyopathy described by the Japanese. Indeed, we have identified only three patients who closely resemble true apical hypertrophy of the Japanese type with respect to the distribution of left ventricular hypertrophy—i.e., with ventricular hypertrophy totally confined to the true left ventricular apex below papillary muscle level, as viewed echocardiographically in the apical two- and four-chamber cross-sectional planes. Each of these three patients was a young (<40 years old) asymptomatic male; two of the three had typical "giant" T wave inversion on electrocardiogram, but one showed no T wave abnormalities. In contrast to the circumstance in Japan where "giant" T-wave inversion is frequently (though not invariably) associated with apical hypertrophy[1~3,10,19,20], it has been our experience that the electrocardiographic pattern of T-wave inversion is more likely to be associated with a number of other morphologic forms of hypertrophic cardiomyopathy which do not resemble localized apical hypertrophy[4,21].

In addition to this experience at the National Institutes of Health, a number of other investigators from outside of Japan and the Far East have reported about 100 non-Japanese patients with "apical hypertrophic cardiomyopathy" (most as single case reports or as small series of patients)[5~8,22~34]. While the clinical features of these patients were believed by the authors to represent apical hypertrophy of the Japanese type, in our view the vast majority did not actually show the most characteristic features of Japanese patients, i.e., "giant" negative T waves and "spade" deformity of the left ventricle, or definitive echocardiographic evidence of hypertrophy localized to the apex; indeed, only 25 reported non-Japanese patients appear to convincingly meet the criteria of apical hypertrophy as defined by the Japanese[5,7,8,24,27,28,31~34]. Therefore, available evidence would suggest that if a "spade" deformity of the left ventricle and "giant" T wave inversion are pathognomonic features of apical hypertrophic cardiomyopathy, then this must be a relatively rare disease entity outside of Japan.

The reason for the differences in phenotypic expression of hypertrophic cardiomyophathy in Japanese patients as compared to patients from outside of Japan is not well understood. It is possible that this morphologic diversity reflects multiple etiologies for a group of clinical entities which we have come to refer to collectively as hypertrophic cardiomyopathy, largely as a matter of convenience. Hence, apical hypertrophy in Japan could be an etiologically distinct disease

entity, separate in this respect from the more "usual" forms of hypertrophic cardiomyopathy. It is conceivable (but certainly unproven) that genetic, racial or environmental (e.g., dietary) factors distinctive to Japan could account in large measure for these disease variations. It is also worth considering that the apparent increased prevalence of apical hypertrophy associated with "giant" negative T waves in Japan results from the practice in that country of routinely screening large segments of the adult working population for heart disease with electrocardiography. Many asymptomatic individuals with apical hypertrophy could exist in other parts of the world, but are not identified because wide spread electrocardiographic screening is not conducted in their societies.

In conclusion, hypertrophic cardiomyopathy is a relatively rare disease (or group of diseases) with genetic and probably non-genetic etiologies which occurs throughout the world. It is characterized by morphologically diverse patterns of left ventricular hypertrophy ranging from marked diffuse thickening of the ventricular septum and left ventricular free wall to mild hypertrophy of a relatively small portion of the left ventricle[18,35~39]. Apical hypertrophy of the Japanese type is apparently another disease variant that deserves a place in the broad morphologic spectrum of hypertrophic cardiomyopathy. In the 10 years since "apical hypertrophic cardiomyopathy" was first described[1], the experience of a number of investigators throughout the world would suggest that patients who strictly fulfill the clinical and morphologic criteria of this disease entity, as described by Japanese authors, are distinctly uncommon outside of Japan[9]. Hence, while such patients represent a significant proportion of all patients with hypertrophic cardiomyopathy in Japan, they do not constitute a sizeable segment of the disease spectrum in non-Asian parts of the world. At this time, the long-term clinical significance of the apical form of hypertrophic cardiomyopathy is unclear and studies designed to define the natural history of this entity will constitute an important area for future investigation.

References

1) Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y, Hayashi T, Amano K: Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle: Echocardiographic and ultrasono-cardiotomographic study. Jpn Heart J **17**: 611–629, 1976
2) Nishiyama S, Yamaguchi H, Ishimura T, Nagasaki F, Takatsu F, Umeda T, Machii K: Echoardiographic features of apical hypertrophic cardiomyopathy. J Cardiogr **8**: 177–183, 1978
3) Yamaguchi H, Ishimura T, Nishiyama S, Nagasaki F, Nakanishi S, Takatsu F, Nishijo T, Umeda T, Machii K: Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): Ventriculographic and echocardiographic features in 30 patients. Am J Cardiol **44**: 401–412, 1979
4) Maron BJ, Bonow RO, Seshagiri TNR, Roberts WC, Epstein SE: Hypertrophic cardiomyopathy with ventricular septal hypertrophy localized to the apical region of the left ventricle (apical hypertrophic cardiomyopathy). Am J Cardiol **49**: 1838–1848, 1982
5) Abinader EG, Rauchfleisch S, Naschitz J: Hypertrophic apical cardiomyopathy: A subtype of hypertrophic cardiomyopathy. Israel J Med Sci **18**: 1005–1009, 1982
6) Keren G, Belhassen B, Sherez J, Miller HI, Megidish R, Berenfeld D, Laniado S: Apical hypertrophic cardiomyopathy: Evaluation by noninvasive and invasive techniques in 23 patients. Circulation **71**: 45–56, 1985
7) Vacek JL, Davis WR, Bellinger RL, McKierman TL: Apical hypertrophic cardiomyopathy in American patients. Am Heart J **108**: 1501–1506, 1984
8) Bloomberg GB, Henderson MA, Rakowski H, Wigle ED: Apical hypertrophic cardiomyopathy. Circulation **70** (Suppl II): II–335, 1984 (abstr)
9) Louie EK, Maron BJ: Apical hypertrophic cardiomyopathy: Clinical and two-dimensional echocardiographic assessment. Ann Int Med **106**: 663–670, 1987
10) Koga Y, Itaya K, Toshima H: Prognosis in hypertrphic cardiomyopathy. Am Heart J **108**: 351–359, 1984
11) Kishimoto C, Kaburagi T, Takayama S, Yokoyama S, Hanyu I, Takatsu Y, Tomimoto K: Two forms of hypertrophic cardiomyopathy distinguished by inheritance of HLA haplotypes and

left ventricular outflow tract obstruction. Am Heart J **105**: 988–994, 1983
12) Koga Y, Itaya M, Takahashi H, Koga M, Ikeda H, Itaya K, Toshima H: Apical hypertrophy and its genetic and acquired factors. J Cardiogr **15** (Suppl VI): 65–74, 1985
13) Fujiwara S, Umemoto M, Miyamoto Y, Ota A, Arita M, Yokote Y, Nakamura Y, Ueno Y, Nishio I, Masuyama Y: The role of hypertension in apical hypertrophy. J Cardiogr **15** (Suppl VI): 53–64, 1985
14) Sakamoto T, Amano K, Hada Y, Tei C, Takenaka K, Hasegawa I, Takahashi T: Asymmetric apical hypertrophy: Ten years experience. Postgrad Med J **62**: 567–570, 1986
15) Maron BJ, Epstein SE: Hypertrophic cardiomyopathy: A discussion of nomenclature. Am J Cardiol **43**: 1242–1244, 1979
16) Ciró E, Nichols PF, Maron BJ: Heterogeneous morphologic expression of genetically transmitted hypertrophic cardiomyopathy: Two-dimensional echocardiographic analysis. Circulation **67**: 1227–1233, 1983
17) Maron BJ, Nichols PF, Pickle LW, Wesley TE, Mulvihill JJ: Patterns of inheritance in hypertrophic cardiomyopathy: Assessment by M-mode and two-dimensional echocardiography. Am J Cardiol **53**: 1087–1094, 1984
18) Louie EK, Maron BJ: Hypertrophic cardiomyopathy with extreme increase in left ventricular wall thickness: Functional and morphologic features and clinical significance. J Am Coll Cardiol **8**: 57–65, 1986
19) Fujii J, Saihara S, Sawada H, Aizawa T, Koto K: Distribution of left ventricular hypertrophy and electrocardiographic findings in patients with so-called apical hypertrophic cardiomyopathy. J Cardiogr **15** (Suppl VI): 23–33, 1985
20) Morimoto S, Sekiguchi M, Hasumi M, Inagaki Y, Takimoto H, Ohtsubo K, Hiroe M, Hirosawa K, Matsuda M, Komatsu Y: Do giant negative T waves represent apical hypertrophic cardiomyopathy? Left ventriculographic and cardiac biopsy studies. J Cardiogr **15** (Suppl VI): 35–51, 1985
21) Maron BJ, Wolfson JK, Ciró E, Spirito P: Relation of electrocardiographic abnormalities and patterns of left ventricular hypertrophy identified by 2-dimensional echocardiography in patients with hypertrophic cardiomyopathy. Am J Cardiol **51**: 189–194, 1983
22) Tilmant PY, Lablanche JM, Laurent JM, Hethuin JP, Folliot JP, Bertrand ME: Myocardiopathie hypertrophique apicale non-obstructive. Arch Mal Coeur **73**: 1269–1278, 1980
23) Sheikhzadeh A, Ghabusi P, Afraz M-R: Apikale linksventrikuläre Hypertrophie, eine Form der hypertrophen nicht obstruktiven Kardiomyopathie mit extrem grossen negativen T-Wellen. Herz **6**: 369–376, 1981
24) Lock CB, Ng R, Oh V, Ee B, Tan L: Apical hypertrophic cardiomyopathy in an Indian male. Singapore Med J **22**: 298–301, 1981
25) Steingo L, Dansky R, Pocock WA, Barlow JB: Apical hypertrophic nonobstructive cardiomyopathy. Am Heart J **104**: 635–637, 1982
26) Sheikhzadeh A, Ghabusi P: A case of asymmetrical apical hypertrophy which is a form of hypertrophic nonobstructive cardiomyopathy with giant negative T-waves. Jpn Heart J **23**: 843–849, 1982
27) Krishnaraj N, Rajan S, Jayakrishnan TK, Raghuran AR, Moorthy JS, Abraham KA, Subramanyam R: Apical hypertrophic cardiomyopathy. Indian Heart J **34**: 133–137, 1982
28) Bertrand ME, Tilmant PY, Lablanche JM, Thieuleux FA: Apical hypertrophic cardiomyopathy: Clinical and metabolic studies. Eur Heart J **4** (Suppl F): 127–133, 1983
29) Kereiakes D, Anderson DJ, Crouse L, Chatterjee K: Apical hypertrophic cardiomyopathy. Am Heart J **105**: 855–856, 1983
30) McDonnell MA, Tsagaris TJ: Recognition and diagnosis of apical hypertrophic cardiomyopathy. Chest **84**: 644–647, 1983
31) Przybojewski JZ, Blake RS: Hypertrophic nonobstructive apical cardiomyopathy: A case presentation and review of the literature. S Afr Med J **66**: 492–498, 1984
32) Keren A, Takamoto T, Harrison DC, Popp RL: Left ventricular apical masses: Noninvasive differentiation of rare from common ones. Am J Cardiol **56**: 697–699, 1985
33) Panidis IP, Nestico P, Hakki AH, Mintz GS, Segal BL, Iskandrian AS: Systolic and diastolic left ventricular performance at rest and during exercise in apical hypertrophic cardiomyopathy. Am J Cardiol **57**: 356–358, 1986
34) Rovelli EG, Parenti F, DeVizzi S: Apical hypertrophic cardiomyopathy of "Japanese type" in a Western European person. Am J Cardiol **57**: 358–359, 1986
35) Maron BJ, Gottdiener JS, Bonow RO, Epstein SE: Hypertrophic cardiomyopathy with unusual locations of left ventricular hypertrophy undetectable by M-mode echocardiography: Identification

by wide-angle two-dimensional echocardiography. Circulation **63**: 409–418, 1981

36) Maron BJ, Gottdiener JS, Epstein SE: Patterns and significance of distribution of left ventricular hypertrophy in hypertrophic cardiomyopathy: A wide angle, two-dimensional echocardiographic study of 125 patients. Am J Cardiol **48**: 418–428, 1981

37) Shapiro LM, McKenna WJ: Distribution of left ventricular hypertrophy in hypertrophic cardiomyopathy: A two-dimensional echocardiographic study. J Am Coll Cardiol **2**: 437–444, 1983

38) Wigle ED, Sasson Z, Henderson MA, Ruddy TD, Fulop J, Rakowski H, Williams WG: Hypertrophic cardiomyopathy: The importance of the site and the extent of hypertrophy. A review. Prog Cardiovasc Dis **28**: 1–83, 1985

39) Spirito P, Maron BJ, Bonow RO, Epstein SE: Severe functional limitation in patients with hypertrophic cardiomyopathy and only mild localized left ventricular hypertrophy. J Am Coll Cardiol **8**: 537–544, 1986