



Novel Insights into the Natural History of Apical Hypertrophic Cardiomyopathy during Long-Term Follow-Up

Edward G. Abinader MD FRCPI, Dawod Sharif MD, Arie Shefer MD and Johanan Naschitz MD

Heart Institute, Bnai Zion Medical Center, and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Key words: cardiomyopathy, apical, aneurysm, ventricular tachycardia

Abstract

Background: Long-term follow-up in apical hypertrophic cardiomyopathy is rare.

Objective: To study the natural history of the disease.

Methods: We followed 11 patients, 5 women and 6 men, for 5–20 years.

Results: At presentation all 11 patients had typical features of apical hypertrophic cardiomyopathy, with dyspnea in 3 and chest pains in 8, of whom 5 were typical of angina and 3 had myocardial infarction. R-wave voltage and T-wave negativity progressively decreased in magnitude at serial electrocardiograms in four patients. Perfusion defects were detected on thallium myocardial scintigraphy in three, increased apical uptake in two, and normal in one patient. Apical aneurysm with normal coronary arteries developed in a patient who had sustained ventricular tachycardia. All of the 10 catheterized patients had normal coronaries except for one with significant left anterior descending artery stenosis and another with a minor lesion. Symptomatic sustained ventricular tachycardia was found in two patients, one of whom required the implantation of an internal cardioverter defibrillator.

Conclusions: Apical hypertrophic cardiomyopathy may develop morphologic and electrocardiographic changes with life-threatening arrhythmias necessitating close follow-up and treatment.

IMAJ 2002;4:166–169

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It took more than 100 years from the original pathologic observations on hypertrophic cardiomyopathy [1] to describe the separate subtype of apical hypertrophic cardiomyopathy with giant negative T-waves [2]. Because the first description of apical hypertrophic cardiomyopathy referred predominantly to Japanese males [2,3] it was initially thought to be confined to Japan. However, several publications have described the disease in other countries [4–6] where it constitutes only 1–2% of cases of hypertrophic cardiomyopathy. The rate in Japan is about 25% [7]. Both the initial scarce reports and current practice often relate to apical hypertrophic cardiomyopathy as being a relatively benign condition [7]. In view of the paucity of reports in the English-language medical literature it is relevant to report long-term follow-up, including changing features and complications during the natural course of the disease.

Patients and Methods

The study group consisted of 11 patients, 6 men and 5 women, in whom long-term follow-up of 5–20 years was achieved. All patients underwent serial clinical interviews, physical examinations, 12-lead electrocardiograms, complete two-dimensional echocardiograms, treadmill exercise tests and, when clinically indicated, ambulatory ECG recordings, myocardial perfusion stress tests and coronary angiography with left ventriculography. Apical hypertrophic cardiomyopathy was diagnosed by the presence of giant negative T-waves greater than 10 mm associated with increased R voltage in the left precordial leads, characteristic left ventricular apical hypertrophy on the long axis, and four-chamber views of the two-dimensional echocardiogram and concentric apical hypertrophy with typical spade-like configuration in the right anterior oblique ventriculogram at end-diastole. Patients not fulfilling all these criteria specific to the Japanese form of apical hypertrophic cardiomyopathy [8] and those with ventricular septal hypertrophy localized to the apical region [9] were excluded from the study.

Results

According to the inclusion criteria and the definition of apical hypertrophic cardiomyopathy, we found the following at the initial evaluation: severe symmetric hypertrophy of the left ventricular apex, spade-like appearance on echocardiography and/or left ventriculography, without pressure gradients, in addition to tall R-waves and giant T-wave negativity on the ECG.

Clinical presentation and outcome

At initial evaluation the patients' mean age was 56.6 ± 5 (range 45–67 years); one had mild hypertension and one was a smoker. Eight patients presented with chest pains, five of whom had angina pectoris; one had recurrent myocardial infarction, one had an old anterior MI, and one had non-Q anterior wall MI associated with sustained ventricular tachycardia [Table 1]. Three patients had dyspnea, three had palpitations, one had dizziness and another had syncope. The follow-up period extended from 5 to 20 years. In all nine patients with up to 10 years follow-up, the clinical course was stable and uneventful. In two patients followed for 17 and 20 years

ECG = electrocardiography

MI = myocardial infarction

Table I. Patient characteristics and outcome

Patient no.	Age (yr), gender	History	Follow-up (yr)	Outcome	ECG at follow-up	Echo at follow-up	Thallium scan at follow-up	Coronary angiography
MS	52, male	Chest pains	10	Same	Same	Same	Not done	Normal
HH	45, female	Chest pains, palpitations, dyspnea	20	Ventricular tachycardia, atrial fibrillation	R↓, T↓	Apical aneurysm	Not done	Normal
HB	59, female	Angina pectoris, MI	6	Same	Same	Same	Not done	Percutaneous coronary intervention LAD
SM	67, female	Dizziness, palpitations	10	Same	Same	Same	Normal	Normal
YS	58, male	Angina pectoris, MI syncope	17	Ventricular tachycardia, atrial fibrillation	Same	Same	Not done	Normal
RF	67, female	Angina pectoris	6	Same	Same	Same	Apex +	Not done
DA	54, male	Dyspnea	6	Same	Same	Same	Inf-, Apex +	Normal
NS	59, female	Angina pectoris, dyspnea	5	Same	Same	Same	Not done	IVD
AM	56, male	Angina pectoris, MI	5	Same	R+, T↓	Same	Apex –	Normal
RT	60, male	Palpitations	6	Same	R↓, T↓	Mild mitral regurgitation	Not done	Normal
EY	45, male	Chest pains	5	Same	R↓, T↓	Mild mitral regurgitation	Not done	Normal

Apex + = increased uptake, Apex– = decreased uptake, INF- = inferior defect, R↓ = decrease in R-wave amplitude, R+ = tall R-wave, T↓ = decrease in T-wave negativity.

respectively, sustained ventricular tachycardia and paroxysmal atrial fibrillation developed [Table 1].

ECG follow-up

In seven patients the electrocardiogram did not change. In one patient the R-wave remained tall while T-wave negativity decreased. In three other patients R-wave amplitude and the negativity of precordial T-waves decreased progressively [Table 1]. In a typical female patient who was followed for 20 years, R-wave voltage decreased in magnitude from 3.5 mv in 1980 to 1.3 mv in 1990 and to 0.5 mv in 1998, while T-wave negativity diminished from 13 mm in 1980 to 10 mm in 1990 and to 5 mm in 1998 [Figure 1]. This patient complained of palpitations and had increased ventricular ectopic activity and unsustained ventricular tachycardia on ambulatory Holter recordings. She recently presented with sustained ventricular tachycardia responsive to amiodarone. In addition, this patient developed paroxysmal atrial fibrillation, which resolved during amiodarone loading. During electrophysiologic study monomorphic ventricular tachycardia was induced. An automatic internal cardiac defibrillator was implanted and proved useful in defibrillating symptomatic paroxysms of ventricular tachycardia at later follow-up. Another patient was found unconscious and diaphoretic at his home, associated with monomorphic ventricular tachycardia. Following electric cardioversion, sinus rhythm was established with first-degree atrioventricular block, and later atrial fibrillation ensued and was treated successfully with amiodarone.

Echocardiography

The pattern of diastolic left ventricular cavity spade-like appearance with severe symmetric apical hypertrophy was maintained in all except one patient who developed apical aneurysm at extended follow-up more than 15 years after presentation. Left ventricular systolic gradients of 25 mmHg developed only in this patient 2 years before the detection of the apical aneurysm.

Myocardial perfusion imaging

Thallium stress tests performed in four patients were normal in one, showed increased apical uptake in one, apical perfusion defect in one, and increased apical uptake with inferior perfusion defect in one [Table 1].

Cardiac catheterization

Coronary angiography performed in 10 patients was normal in 8, of whom 2 had a history of myocardial infarction. One patient showed 40% narrowing in the mid-left anterior descending coronary artery and another patient had 90% mid-LAD stenosis with thrombus that was successfully dilated and stented. In a female patient with 20 years follow-up, coronary angiography was normal, however left ventriculography revealed large apical aneurysm with clot formation replacing the site of apical hypertrophy, without clinical evidence of myocardial infarction [Figure 2]. This patient (HH, Table 1) developed ventricular tachycardia and atrial fibrillation. In another

LAD = left anterior descending coronary artery

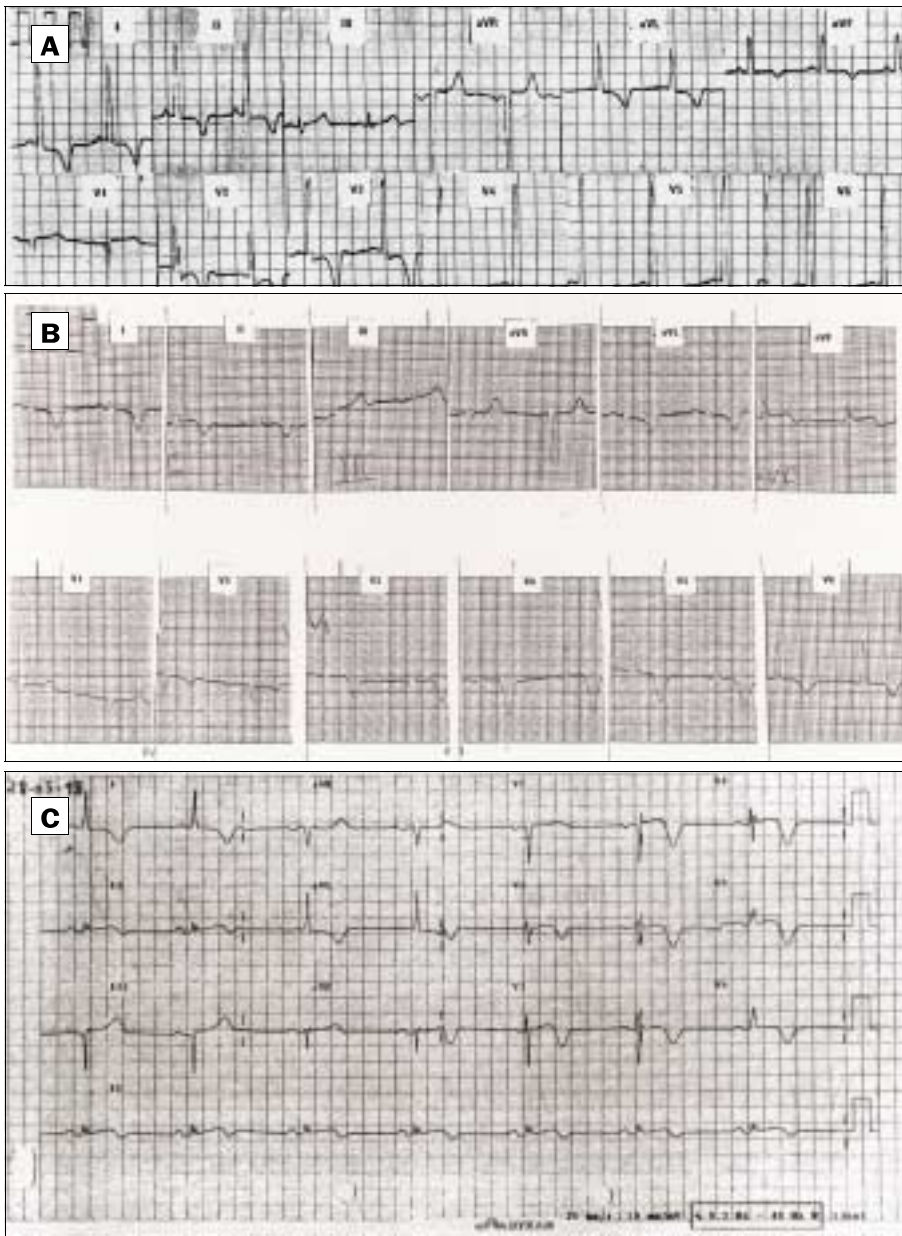


Figure 1. Twelve-lead ECG recorded in 1980 showing tall R-waves and giant negative T-waves [A] followed by decrease in R-wave voltage in 1990 [B] and later marked decrease in T-wave negativity in 1998 [C].

patient the malignant presentation with the ventricular tachycardia appeared without left ventricular aneurysm, with marked symmetric apical hypertrophy, high precordial R-waves of 3.7 mv and deep precordial negative T-waves of 13 mm. Coronary angiography in this patient revealed 90% mid-LAD stenosis with thrombus. A non-Q anterior myocardial infarction was diagnosed and the patient underwent a successful angioplasty and stenting.

Discussion

The present study demonstrates that with the increase in the duration of follow-up in patients with apical hypertrophic cardiomyopathy, this previously considered benign entity may undergo

significant clinical, ECG and morphologic evolution. Patients were selected carefully to fulfill the diagnostic criteria of the Japanese form of apical hypertrophic cardiomyopathy [2-4,10,11] in order to avoid the inclusion of a non-homogenous group of patients with distally located septal hypertrophy without giant negative T-waves and without the typical left ventricular spade-like configuration at end-diastole [8,9]. Although the majority of patients had chest pains – five with typical angina and three with myocardial infarction – significant coronary artery disease was found only in one case at coronary angiography. The resting changes in repolarization compound the ECG interpretation of the exercise tests and may be misdiagnosed as coronary artery disease. Moreover, exercise Thallium studies were confusing as they showed perfusion defects as well as increased uptake in the presence of normal coronary angiogram. This variable spectrum of Thallium uptake decreases the applicability of this test in the diagnosis of coronary artery disease in this entity.

During long-term follow-up the classical ECG at presentation with tall R-waves and giant negative T-waves were gradually modified in some patients [Figure 1], leading to decreases in R-wave amplitude and T-wave negativity [12]. Thus the typical ECG picture seen in this disease may vary or disappear according to the phase at which the ECG is recorded, possibly leading to underdiagnosis of this entity in its later stages.

Apical left ventricular remodeling and aneurysm formation with clot developed without clinical, ECG or enzymatic evidence of myocardial infarction in a

female patient with normal coronary angiogram. This may be related to small vessel disease and reduced coronary flow reserve [13]. Myocardial hypertrophy may increase oxygen demand in the presence of reduced myocardial capillary density, leading to progressive apoptosis and necrosis with insidious left ventricular wall thinning and silent aneurysm formation [Figure 2]. Moreover, apical clots may lead to peripheral embolization. Ventricular arrhythmias during follow-up in the form of ventricular ectopy, unsustained and sustained ventricular tachycardia were encountered in two patients, one of whom presented with aborted sudden cardiac death. In both these patients paroxysmal atrial fibrillation ensued and in one an internal cardioverter defibrillator was

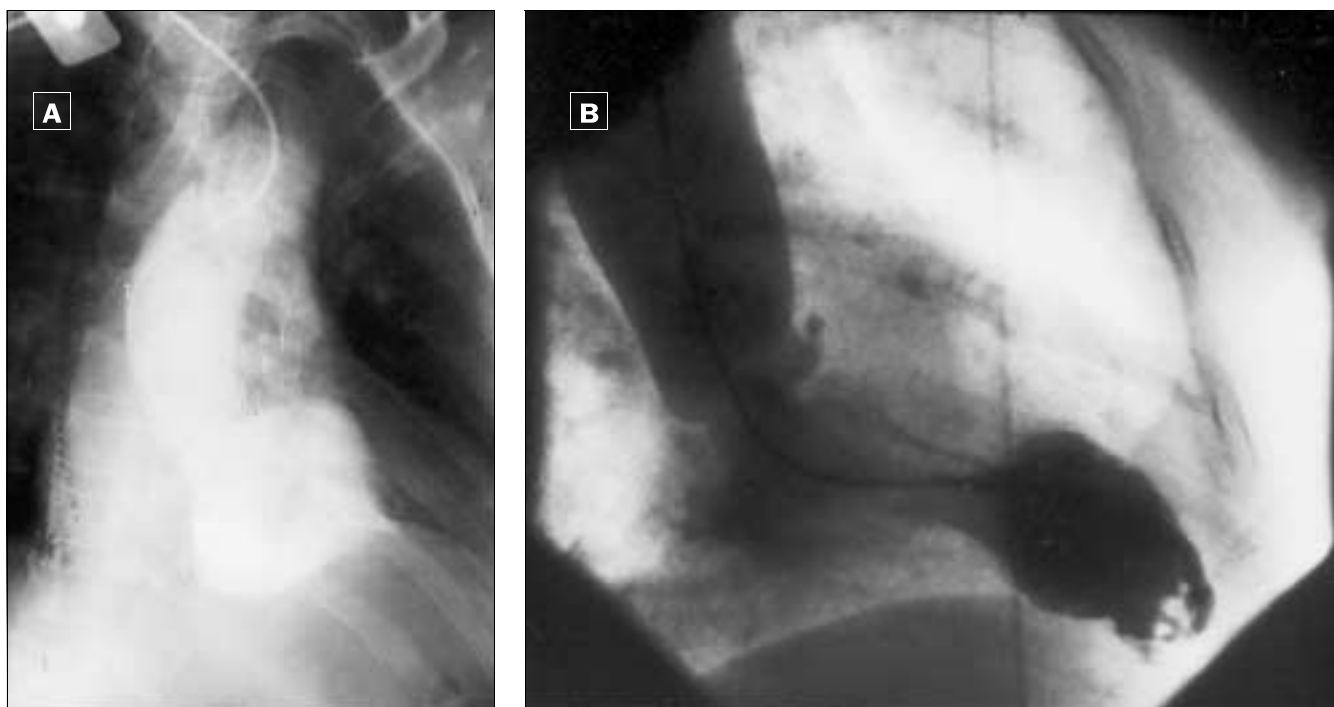


Figure 2. Left ventriculogram in the right anterior oblique view performed in 1980 **[A]** showing the typical spade-like appearance at end-diastole, and at follow-up cineangiography in 1998 **[B]** the hypertrophic apex was replaced by an apical aneurysm with thrombus.

implanted. Aneurysmectomy is another valid option, depending on the findings at electrophysiologic studies. Symptomatic sustained ventricular tachycardia may manifest in the absence of left ventricular aneurysm and relatively early in the course of the disease before the decrease in R-wave amplitude and T-wave negativity, however this patient also had significant coronary disease.

Thus, contrary to prevailing concepts, the course of apical hypertrophic cardiomyopathy is not entirely benign and may undergo significant clinical, electrocardiographic, arrhythmogenic and morphologic evolution, which may appear during long-term follow-up with more complications manifesting in the elderly.

Limitations

The major limitation of the study lies in the relatively small number of patients who were followed, however this is a rare disease in the western world and as such the reports are scarce. Another issue relates to the need for an extended period of follow-up beyond 10 years in each patient in order to monitor the clinical, morphologic and ECG changes that may appear very late in the natural history of the disease.

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Correspondence: Dr. E.G. Abinader, Cardiology Section, Bnai Zion Medical Center, P.O. Box 4940, Haifa 31048, Israel.

Phone: (972-4) 835-9744

Fax: (972-4) 837-2991

email: abinader@netvision.net.il