Never Too Old: A Nonagenarian With Apical Hypertrophic Cardiomyopathy

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INTRODUCTION

Hypertrophic cardiomyopathy, an inherited heterogeneous cardiac condition with diverse phenotypic expression, is a common cause of sudden cardiac death in young adults. Apical hypertrophic cardiomyopathy (ApHCM), a phenotypic variant of hypertrophic cardiomyopathy, was first described in Japan in 1976 by Sakamoto *et al.*[1] as a cardiac condition characterized by apical hypertrophy, an ace-of-spades configuration of the left ventricular cavity in end diastole, and giant negative precordial T waves. In ApHCM, hypertrophy is localized to the left ventricular apex with or without midsegment or basal involvement and with or without apical aneurysm.[2] Apical hypertrophic cardiomyopathy is distributed worldwide, affecting more men than women. It is typically diagnosed in midlife.[3,4] However, it can be diagnosed late in life and can carry a normal life expectancy. We report a case of ApHCM in a patient diagnosed 5 years prior to this presentation at 88 years of age.

CASE PRESENTATION

The patient first presented to the emergency department with left-sided chest pain at 88 years of age. The pain radiated to the left arm. The electrocardiogram (ECG) at that time showed sinus bradycardia (44 beats per minute), tall QRS complexes, and inverted T waves in V3 to V6 (Figure 1A). Inverted T waves were slightly more prominent than in the previous ECG from 11 years earlier (Figure 1B). Serial cardiac troponins were negative. A myocardial perfusion scan showed no stress-induced ischemia. The echocardiogram demonstrated features of ApHCM, and the patient was referred to our Hypertrophic Cardiomyopathy Center.

On evaluation at the cardiomyopathy center, the patient complained of daily paroxysmal chest pain since hospital discharge. They denied shortness of breath, palpitations, edema, orthopnea, paroxysmal nocturnal dyspnea, dizziness, near syncope, and syncope. The physical examination revealed a sustained apical impulse, loud S1, normal S2, and grade 1/6 apical systolic murmur of mitral regurgitation. The echocardiogram (Figure 2, Videos 1-5) showed apical hypertrophy, apically displaced posteromedial papillary muscle, and elongated posterior mitral valve leaflet with mild prolapse and mild mitral regurgitation. The other echocardiographic characteristics are shown in Table 1. A coronary angiogram revealed normal coronaries.

On a follow-up visit 3.5 years later, the patient was asymptomatic. The repeat echocardiogram was unchanged. The 48-hour Holter monitor showed predominantly sinus rhythm, with an average heart rate of 62 (range, 44–125) beats per minute. There were 131 ventricular ectopic beats (0.07%) with no sustained or nonsustained ventricular tachycardia and 380 supraventricular ectopic beats (0.19%) with 9 episodes of short, nonsustained supraventricular tachycardia, the fastest of which was 141 beats per minute. No atrial fibrillation or pauses were seen.

The patient 4.5 years later underwent cardiovascular magnetic resonance imaging (CMR), which showed normal left ventricular systolic function with a left ventricular ejection fraction of 68% as well as severely increased wall thickness in the apical segments with a maximal wall thickness of 22 mm in the lateral apical wall. The papillary muscles were apically displaced, and the anterolateral papillary muscle appeared bifid (Figure 3A and B, Video 6). There was evidence of patchy late gadolinium enhancement (LGE) in the apical segments involving approximately 13% of the myocardial mass as assessed by the quantitative method of mean +6× SD reference region of interest (6×SD method), which is consistent with replacement fibrosis. Extracellular volume was elevated and was calculated at 30%, which is an additional indication of underlying interstitial fibrosis.

The patient's daughter had been diagnosed with ApHCM at 53 years of age at our Hypertrophic Cardiomyopathy Center. Genetic testing with the comprehensive 157 cardiomyopathy/arrhythmia gene panel (Invitae) showed the *SCN10A* gene variant of unknown significance. The patient's other 3 daughters have no known history of hypertrophic cardiomyopathy. The patient's sister is also a patient at our clinic and has a genotype-negative basal septal variant of hypertrophic cardiomyopathy. The patient's other siblings have not been screened for hypertrophic cardiomyopathy.

DISCUSSION

We describe a 93-year-old patient who was discovered to have ApHCM at 88 years of age. The patient had no significant symptoms before that, attesting to the known benign nature of ApHCM in most patients. They did not have associated apical aneurysm or any other significant risk factors for sudden cardiac death, which explains the longevity of this patient, who remains asymptomatic with no limitations in daily activities.

The diagnostic criteria for ApHCM have evolved, changing from a unique spade-like configuration and marked apical obliteration seen

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Conflicts of Interest: None.

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VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, apical 4-chamber view, demonstrates the regional, focal left ventricular hypertrophic pattern consistent with ApHCM.

Video 2: Two-dimensional TTE, apical 3-chamber view, demonstrates the ApHCM.

Video 3: Two-dimensional TTE with an ultrasound contrast enhancement, apical 4-chamber view, demonstrates the ApHCM with no apical pouch.

Video 4: Two-dimensional TTE with an ultrasound-enhancing agent, zoomed apical 4-chamber view, demonstrates the ApHCM with multiple scattered microbubbles perfusing the apical hypertrophic myocardium. This feature would be absent in an apical thrombus as might be seen in a patient with hypereosinophilic syndrome (which is in the differential diagnosis of these echo findings).

Video 5: Two-dimensional TTE, apical 3-chamber view without (*left*) and with (*right*) color flow Doppler demonstrates a slit-like cavity in the apical region. This finding essentially excludes the possibility of an apical thrombus as would be seen in hypereosinophilic syndrome and is consistent with the diagnosis of an ApHCM.

Video 6: Cardiac magnetic resonance steady-state free precession cine sequence, 4-chamber display, demonstrates apically displaced papillary muscles in addition to the ApHCM.

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on left ventriculography along with giant negative precordial T waves and high-voltage QRS complexes seen on ECG to reliance on an apical wall thickness ≥15 mm and a ratio of maximal apical wall to posterior wall thickness of ≥1.5 based on echocardiography or CMR.[3] As the apex is the thinnest part of the left ventricle, a lower threshold (13–15 mm) has been suggested when clinical features and imaging characteristics also support the diagnosis.[2] Our patient had an apical wall thickness of 22 mm, with no midventricular involvement or presence of apical aneurysm. Global longitudinal strain was reduced to −16.5% on strain analysis. Furthermore, the ECG abnormalities fluctuate in patients with ApHCM. The reversal of the sequence of depolarization due to the severe localized apical hypertrophy has been proposed as a possible cause of giant negative T waves. Koga *et al.*[5] showed that T-wave inversions and R-wave amplitude initially increase, reach a peak, and then progressively decrease in patients with ApHCM. They noted the loss of giant negative T waves in 71% of their patients after ≥10 years of follow-up.[5] These changes could signify the development of an underlying cardiomyopathic process in these patients. Thus, the giant negative T waves likely present an opportunity to diagnose these patients earlier during the natural course of this disease. Furthermore, the less prominent T waves earlier in the course of the disease, as was the case in our patient, suggest that many cases of ApHCM may be missed if practitioners solely rely on ECG for the diagnosis. Finally, CMR is valuable, especially when echocardiographic images are suboptimal, in determining the site and extent of hypertrophy and the presence of an apical aneurysm. Most importantly, CMR is the only modality that provides noninvasive insight into the myocardium and the extent of LGE that is consistent with replacement fibrosis. Extensive LGE, defined by some studies as LGE ≥15%, is associated with increased risk of arrhythmia and sudden cardiac death.[6] By quantitative analysis with the 6×SD method, our patient had evidence of LGE of approximately 13% on CMR.

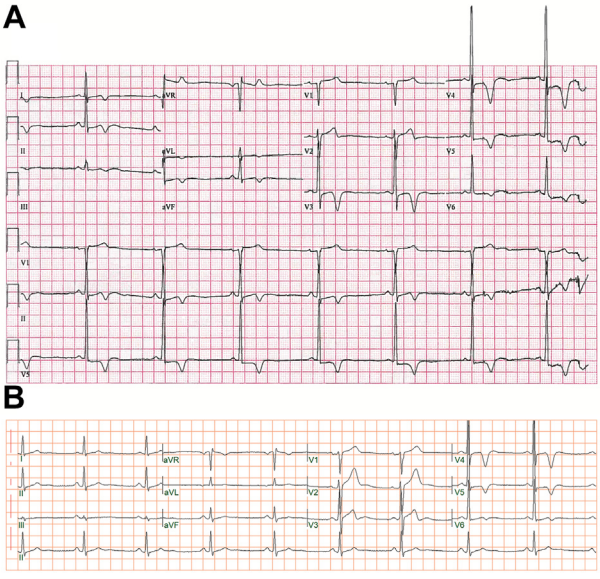

Figure 1 **(A)** The patient's ECG from 5 years before this evaluation shows evidence of left ventricular hypertrophy by Sokolow-Lyon criteria with the sum of the S wave in V1 and R wave in V5 equal to 36 mm. The negative T waves are seen in V3 to V6. **(B)** The patient's ECG from 11 years before this evaluation demonstrates T-wave inversions in V4 and V5.

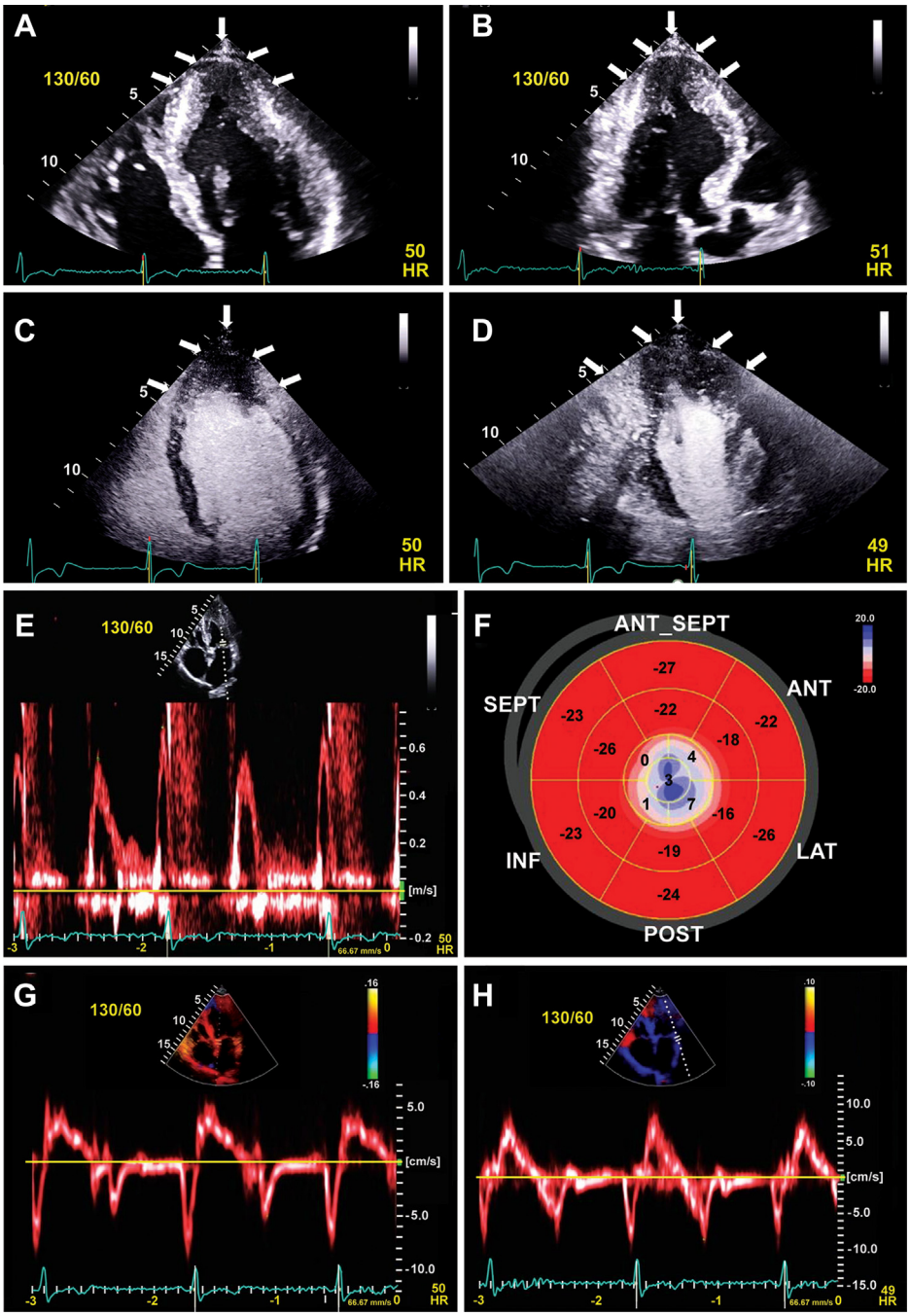

Figure 2 Two-dimensional transthoracic echocardiogram (TTE), apical 4-chamber **(A)** and apical long-axis **(B)** views, diastolic phase, demonstrate apical regional myocardial hypertrophy (*arrows*). After left ventricular opacification with an ultrasound-enhancing agent, the apical hypertrophy (*arrows*) is better visualized (**C**; diastolic phase) and demonstrates that no apical aneurysm is present in systole **(D)**. Pulsed-wave Doppler of the mitral inflow confirms grade 2 diastolic dysfunction pattern **(E)**. Global longitudinal strain bull's-eye map demonstrates markedly reduced peak systolic strain (−3%) of the apical segments **(F)**. Tissue Doppler display of the medial **(G)** and lateral **(H)** mitral annulus demonstrates reduced e′ velocity of 0.05 m/sec and 0.08 m/sec, respectively.

Additionally, through other techniques such as T1 mapping and extracellular volume calculation, CMR provides information on underlying interstitial fibrosis that may be more diffuse. In our patient, extracellular volume was elevated, which is likely multifactorial due to age, other comorbidities, and hypertrophic cardiomyopathy.

Octo- and nonagenarians with ApHCM are rare. An 84-year-old woman with ApHCM was reported by Stöllberger *et al.*[7] In that case, a 12-lead ECG showed inverted T waves in the lateral precordial leads, and an echocardiogram showed predominantly apical hypertrophy. Cardiac magnetic resonance imaging confirmed the diagnosis of

Table 1 Echocardiographic characteristics

Characteristics	Measurements
Apical thickness maximum, mm	20
Left ventricular end-diastolic diameter, mm	45
Ejection fraction, %	70
Global LS, %	−16.5
LS of the apical 5 segments, %	−3
LS of noninvolved myocardium 12 segments, %	−22
Diastolic dysfunction	Grade II
Left atrial volume index, mL/m^2	53
Pulmonary artery systolic pressure, mm Hg	30
Sinus of Valsalva, mm	40

LS, Longitudinal strain.

ApHCM and showed a small, left ventricular apical aneurysm. They had no evidence of life-threatening arrhythmias before they died at 93 years of age due to noncardiac causes despite the presence of an apical aneurysm. This suggests that many patients remain undiagnosed due to the benign course of ApHCM. Only 10% to 20% of patients with hypertrophic cardiomyopathy are diagnosed clinically,[8] and this number is likely lower in patients with ApHCM.

Støylen *et al.*[9] reported the case of a 92-year-old woman with ApHCM who presented with syncope and dyspnea and was found to have nonobstructive hypertrophic cardiomyopathy with postsystolic shortening leading to delayed emptying of the apex. Doppler flow showed delayed emptying of the apical chamber extending into the early filling phase.

In a study of a patient cohort at Mayo Clinic, Rochester, Minnesota, a patient with ApHCM is reported who died at 92.[10] Further details about this patient were not provided.

The differential diagnosis of ApHCM should always be considered in elderly patients. Metastatic tumors to the heart, particularly metastatic melanoma with cardiac metastasis to the apex, can sometimes masquerade as apical hypertrophy.[11] The presence of T-wave inversions in the old ECG in 2007 and the positive family history of ApHCM in the patient's daughter supported the diagnosis of ApHCM in this case.

CONCLUSION

ApHCM may present in very elderly patients and may have a benign course.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

FUNDING STATEMENT

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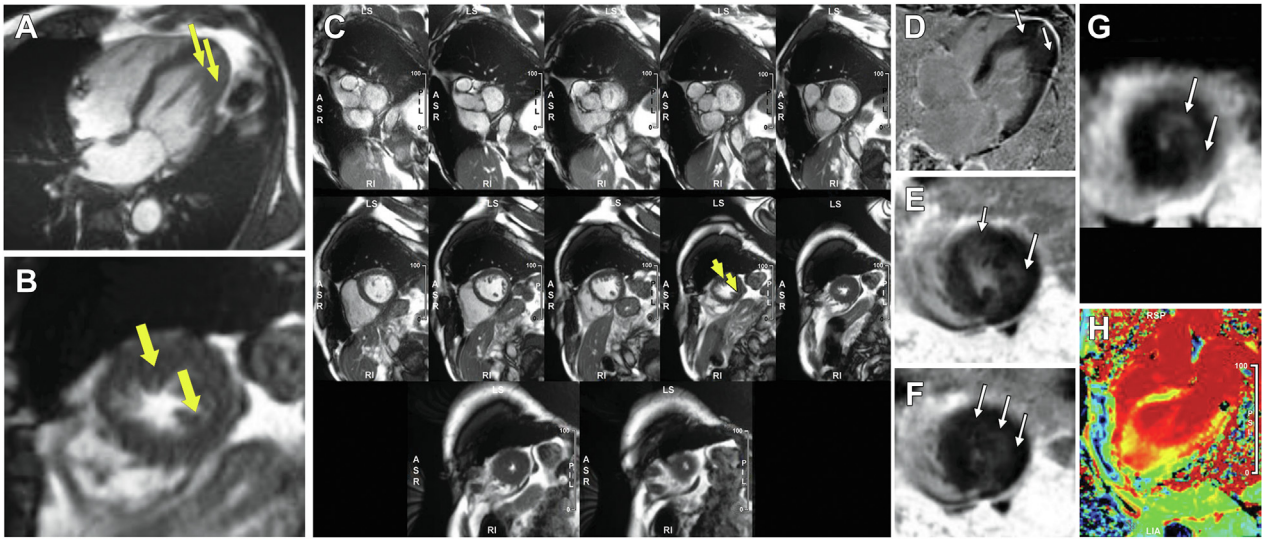

Figure 3 Cardiac magnetic resonance imaging, steady-state free precession sequence, 4-chamber **(A)**, apical short-axis **(B)**, and comprehensive short-axis stack **(C)** views, diastolic phase, demonstrates regional apical hypertrophy (22 mm) with apically displaced papillary muscles (*yellow arrows*). Three-dimensional reverse TI dark blood LGE method, 4-chamber **(D)** and short-axis **(E-G)** views, diastolic phase, demonstrates the apical hypertrophy with patchy LGE involving 13% of the myocardial mass (6×SD method) consistent with replacement fibrosis (*white arrows*). A parametric extracellular volume map, 3-chamber display **(H)** demonstrates elevated extracellular volume of ∼30% of the myocardium (*yellow area*) consistent with underlying interstitial fibrosis.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.case.2023.01.009.

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