Case Report

# Cerebrovascular Disease as the Initial Manifestation of Apical Hypertrophic Cardiomyopathy

***Doença Cerebrovascular como Manifestação Inicial de Cardiomiopatia Hipertrófica Apical***

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## Introduction

Apical hypertrophic cardiomyopathy (AHCM) is a condition that primarily involves the apex of the left ventricle. Two of its main characteristics are a non-obstructive physiology and apical hypertrophy of the left ventricle with giant negative T waves. AHCM is uncommon, and its prevalence is notably affected by ethnicity. The diagnosis is challenging to make and requires multimodal imaging techniques.[1,6] Here we describe two cases of AHCM with cerebrovascular disease as the presenting condition: Patient 1 had atrial fibrillation (AF), while Patient 2 showed evidence of aortic plaques as the possible embolic source. Nonetheless, Patient 2 also presented an akinetic apex. Hence, it was impossible to rule out the previous migration of an apical thrombus as the cause of the ischemic stroke. The main clinical lesson learned from our cases is that stroke in patients with AHCM is a multifactorial complication potentially caused by AF, aortic plaques, and intracavitary thrombus. Therefore, although AHCM is uncommon, it should be considered when determining the cause of cerebrovascular embolic events.

## Case presentation

### Patient 1

A 51-year-old woman with suspected multiple sclerosis presented with numerous sudden-onset and -cessation tachycardic events. During these events, she suffered from low cardiac output symptoms and occasional transient cerebral ischemia signs. She had a history of hyperthyroidism, uncontrolled arterial hypertension, and small vessel cerebrovascular disease. Computed tomography (CT) revealed multiple embolic cerebral infarcts. Electrocardiography (ECG) showed sinus rhythm with left-ventricular hypertrophy criteria and giant negative T waves (Figure 1). Transthoracic echocardiography (TTE) revealed a normal-sized left ventricle (LV) with a 24-mm apical hypertrophy (Figure 2). Other findings included conserved global and segmental mobility at rest, an LV ejection fraction (LVEF) of 67%, E/A ratio of 0.73 (impaired relaxation), and normal systolic pulmonary artery pressure (SPAP; 33 mmHg). In contrast, a 7-day Holter monitoring study revealed evidence of AF. Thus, anticoagulation with apixaban was initiated. The patient also received metoprolol, amlodipine/valsartan, atorvastatin, and amitriptyline.

### Patient 2

A 75-year-old woman presented to the emergency room with somnolence, dysarthria, and ataxic movements. She had a history of essential arterial hypertension, which was diagnosed 3 years ago, in medical control. On CT, a hypodense zone in the left cerebellum was found, which was associated with an embolic origin. The ECG showed sinus rhythm with criteria for left-ventricular hypertrophy and giant negative T waves in the precordial leads. Transthoracic and transesophageal echocardiography (TEE) revealed a normal-sized LV with a 16-mm apical hypertrophy and an akinetic apex. Additional findings were an E/A ratio of 0.6 (impaired relaxation), LVEF of 65%, normal SPAP (32 mmHg), dilated left atrium, and mitral and aortic valve sclerosis paired with mild mitral and tricuspid insufficiency. Additionally, a grade 5 complex atheromatous plaque was noted in the ascending aorta at the sinotubular junction (Figure 3A). Moreover, there was evidence of diffuse atheromatosis in the aortic arch and the descending segment with diffuse intimal thickening and both simple and complex plaques (Figure 3B). Hence, the patient was treated with apixaban along with irbesartan/hydrochlorothiazide, atorvastatin, and fluoxetine. Table 1 compares the clinical and therapeutic parameters of the two cases.

## Discussion

AHCM, also known as Yamaguchi syndrome, is an uncommon disease that was first described by Sakamoto *et al*. in 1976.[2] It accounts for 3% and 13–25% of hypertrophic cardiomyopathy cases in the United States and Japan, respectively.[3]

Clinically, AHCM has a nonspecific manifestation with no pathognomonic complaints. Accordingly, its diagnosis is often delayed by around 4.7 years.[4] However, some common clinical findings at presentation include atypical chest pain, dyspnea, exercise intolerance, palpitations, AF, and syncope or presyncope.[1] Patients may also have hypertension (30%) and family members with hypertrophic cardiomyopathy

## Keywords

Cerebrovascular Disease; Echocardiography; Embolism; Hypertrophic Cardiomyopathy.

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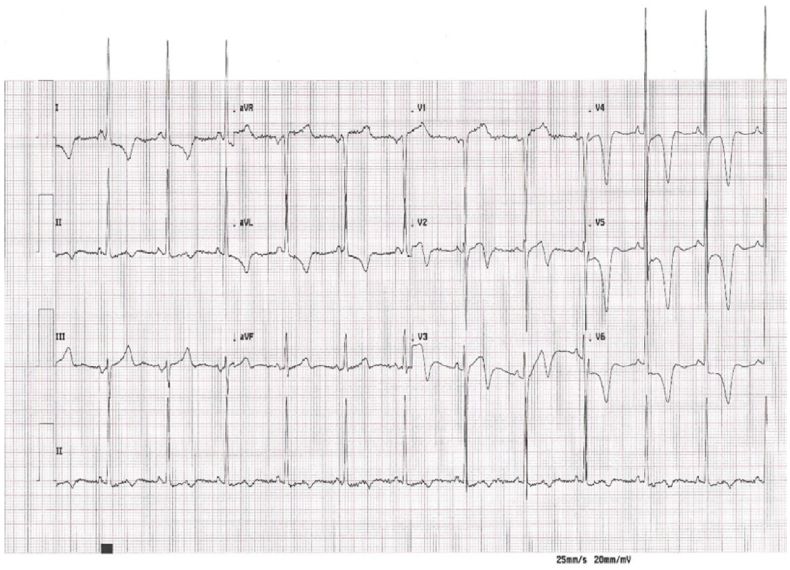


**Figure 1 –** *Electrocardiogram of Patient 1 showing evidence of left ventricle hypertrophy and giant negative T waves.*

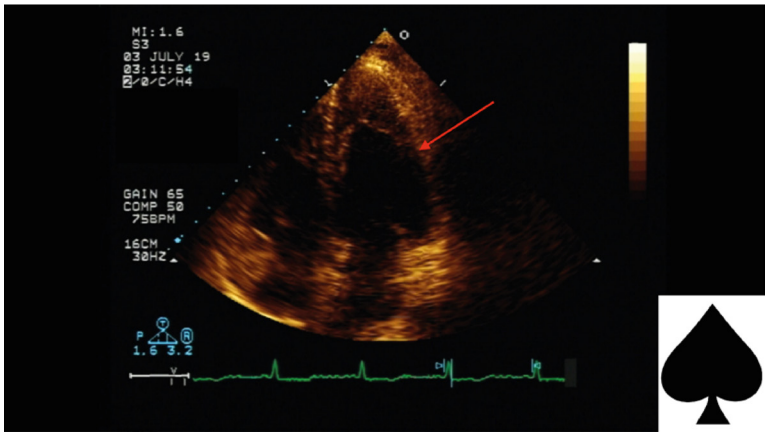


**Figure 2 –** *Transthoracic echocardiogram (apical 4-chamber view) of Patient 1 showing left-ventricular apical hypertrophy with the characteristic "ace of spades" shape.*

or a history of sudden cardiac death (26%).[1,8] Additionally, around 30% of patients with AHCM will present one or more morbid events such as AF, myocardial infarction, congestive heart failure, transient ischemic attack, stroke, ventricular tachycardia, and ventricular fibrillation.[4]

The reported prevalence of AF in AHCM is 12–31%.[4,5] Furthermore, cerebral embolic events were found to affect 6.7–18.8% of the patients, with left atrium size (hazard ratio, 1.2) and AF (hazard ratio, 5.5) as the main risk factors.[4,5] Both of our patients presented a cerebrovascular condition as a complication of AHCM, but only Patient 1 had evidence of AF, whereas Patient 2 presented with aortic plaques. However, Patient 2 also had an akinetic apex on TEE evaluation, which could represent a potential embolic source. This leads us to remark that, in patients with a history of stroke, hypertrophic cardiomyopathy (as well as other structural pathologies), along with AF and arterial plaques, should be considered potential sources of embolic events.

For the diagnosis of AHCM, a multimodality imaging approach is often used. This commonly starts with an ECG and includes echocardiography and cardiovascular magnetic resonance (CMR). In our case, the key signs that led us to the diagnosis of AHCM were the giant negative T waves and the left-ventricular apical hypertrophy with the classical "ace of

**Table 1. Key patient characteristics.**

| Parameter / Study | Case 1 | Case 2 |
|---|---|---|
| | **General** | |
| Age [years] | 51 | 75 |
| Gender | Female | Female |
| Pre-existing medical conditions/comorbidities | - Paroxysmal tachycardia events with low cardiac output symptoms and transient cerebral ischemia signs<br>- Uncontrolled essential systemic hypertension<br>- Hyperthyroidism<br>- Small vessel cerebrovascular disease<br>- No evidence of diabetes mellitus or dyslipidemia | - Controlled essential systemic hypertension<br>- Hip replacement surgery<br>- Patient showed no evidence of diabetes mellitus or dyslipidemia |
| Atrial fibrillation evidence | Yes | No |
| | **Studies/Laboratory tests** | |
| ECG | - Sinus rhythm<br>- Negative giant T waves in precordial leads<br>- 7-day Holter monitoring revealed atrial fibrillation | - Sinus rhythm<br>- Negative giant T waves in precordial leads |
| Computed Tomography | - Multiple cerebral infarctions with high suspicion of embolic origin | - Hypodense zone in left cerebellum with suspicion of embolic origin |
| Echocardiogram | - TTE<br>1. Normal sized left ventricle with apical hypertrophy of 24 mm<br>2. LVEF = 67%<br>3. E/A = 0.73<br>4. SPAP = 33 mmHg | - TEE<br>1. Normal sized left ventricle with apical hypertrophy of 16 mm<br>2. Akinetic LV apex<br>3. LVEF = 65%<br>4. E/A = 0.6<br>5. SPAP = 32 mmHg<br>6. Complex atheromatous plaque in the ascending aorta (Grade 5)<br>7. Diffuse atheromatosis in the horizontal portion and descending aorta<br>8. Dilated left atrium<br>9. Mitral and aortic valve sclerosis<br>10. Mild mitral and tricuspid insufficiency |
| | **Treatment** | |
| Anticoagulation | - Apixaban | - Apixaban |
| Antiplatelet therapy | No | No |
| Antihypertensive | - Amlodipine/Valsartan<br>- Metoprolol | - Irbesartan/Hydrochlorothiazide |
| Statins | - Atorvastatin | - Atorvastatin |
| Other treatments | - Amitriptyline | - Fluoxetine |

*BNP: B-type natriuretic peptide; ECG: electrocardiogram; LV: Left Ventricle; SPAP: Systolic Pulmonary Artery Pressure; TEE: Transesophageal Echocardiography; TTE: Transthoracic Echocardiography.*

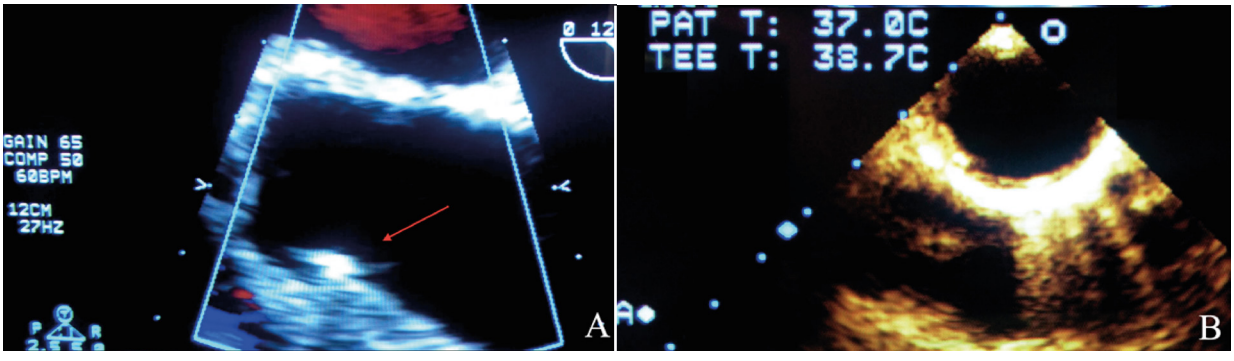


**Figure 3 –** *A ) Transesophageal Doppler echocardiogram of Patient 2 showing a grade 5 complex atheromatous plaque in the ascending aorta at the sinotubular junction. The plaque has a heterogeneous appearance with a predominant calcific component, irregular borders, and debris. B) Transesophageal echocardiogram of Patient 2 showing diffuse atheromatosis in the descending aorta. There is evidence of diffuse intimal thickening and plaques that are simple (less than 5-mm protrusion) and complex (more than 5-mm protrusion).*

spades" shape observed on the echocardiogram (Figure 2). However, it is important to remember that giant negative T waves are not specific to AHCM since a considerable number of conditions such as Wellens' syndrome, cocaine ischemia, non-Q wave myocardial infarction, myocarditis, Takotsubo cardiomyopathy, massive pulmonary embolism, and subarachnoid hemorrhage could also cause them.[6]

In the diagnosis of AHCM made via echocardiography, the apex should be measured below the insertion of the papillary muscle, and it must be thicker than 15 mm (with a basal-to-apex wall thickness ratio of 1.3 or greater).[1,6] It is also important to measure the gradient between the apex and the left ventricular cavity since it increases the risk for thromboembolism, ventricular arrhythmias, and perfusion abnormalities.[1] Moreover, the global ejection fraction is commonly preserved, but signs of diastolic dysfunction are often observed, as seen in both of our cases.

TEE is helpful for detecting intracavitary thrombus and guiding cardiac surgery.[1] Unfortunately, false-negative results are possible in an echocardiography examination. Hence, CMR may be used. Relevant clinical findings of AHCM with CMR include the left-ventricular "ace of spades" silhouette and apical wall width greater than 15 mm, with a basal-to-apex wall thickness ratio exceeding 1.5.[1]

Valuable treatment options are available for patients with AHCM. In cases with a preserved ejection fraction, β-blockers or calcium channel blockers are recommended in maximal tolerated doses.[1,6] Patients with AHCM often present diastolic dysfunction and thus benefit from diastole prolongation.[1] Furthermore, surgical treatments such as apical myectomy are available.[1] Finally, there is no strong consensus about the prognosis of AHCM since it is considered a relatively benign disease, but a few cases are complicated by atypical angina, heart failure with a preserved ejection fraction, AF, apical aneurysm, thrombus, and cardioembolic stroke.[6] Table 2 presents the most important guidelines released by the American and European Cardiology Societies.

## Conclusions

As previously discussed, AHCM is a relatively uncommon disease that is occasionally complicated by stroke. Both cases presented here demonstrated cerebrovascular embolic events as the leading manifestation of AHCM. It is interesting to note that one patient presented with AF, while the other had aortic plaques and an akinetic LV apex. We believe that these conditions are associated with AHCM with the cause of stroke. In contrast, Patient 1 had both AF and hyperthyroidism, a known cause of AF.[10] Thus, it is uncertain whether AF resulted from the hyperthyroidism or from the relationship between AHCM and diastolic dysfunction, leading to increased LV filling pressure, dilation of the left atrium, and an increased risk of AF.[2] Finally, as stated in the guidelines, since the echocardiography findings were conclusive of AHCM, we decided not to order a CMR scan. Figure 4 illustrates the mechanism of cerebrovascular embolic events as well as the diagnostic methods we used.

## Author contributions

Research design: González-Rayas JM, Rayas-Gómez AL, Rico-Rosas A, Landa-Alvarado PD, León-Vargas IMP, González-Yáñez JM; Data collection: González-Rayas JM, Rayas-Gómez AL, Rico-Rosas A, Landa-Alvarado PD; Data analysis and interpretation: Rayas-Gómez AL, Landa-Alvarado PD, León-Vargas IMP, Ramos-Verdugo JM, González-Yáñez JM; Writing the manuscript: Rayas-Gómez AL, Rayas-Gómez AL, Rico-Rosas A, González-Yáñez JM; Critical review of the manuscript for important intellectual content: Rayas-Gómez AL, Landa-Alvarado PD, León-Vargas IMP, Ramos-Verdugo JM, González-Yáñez JM.

## Conflict of interest

The authors have declared that they have no conflict of interest.

**Table 2 - Current guideline recommendations regarding apical hypertrophic cardiomyopathy.**

| ACC/AHA (2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy)[7] | | |
|---|---|---|
| **Recommendation** | **COR** | **LOE** |
| "CMR imaging is reasonable in patients with HCM to define apical hypertrophy and/or aneurysm if echocardiography is inconclusive." | IIa | B |
| "TTE combined with the injection of an intravenous contrast agent is reasonable if the diagnosis of apical HCM or apical infarction or severity of hypertrophy is in doubt, particularly when other imaging modalities such as CMR are not readily available, not diagnostic, or are contraindicated." | IIa | C |
| **ESC (2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy)[9]** | | |
| **Recommendation** | **COR** | **LOE** |
| "CMR with LGE imaging should be considered in patients with suspected apical hypertrophy or aneurysm." | IIa | C |
| "In patients with sub-optimal images or with suspected LV apical hypertrophy or aneurysm, TTE with LV cavity opacification—using intravenous contrast agents—should be considered as an alternative to CMR imaging." | IIa | C |

*ACC: American College of Cardiology; AHA: American Heart Association; CMR: Cardiovascular Magnetic Resonance; COR: Class of Recommendation; ESC: European Society of Cardiology; HCM: Hypertrophic Cardiomyopathy; LGE: Late Gadolinium Enhancement; LOE: Level of Evidence; TTE: Transthoracic Echocardiogram.*

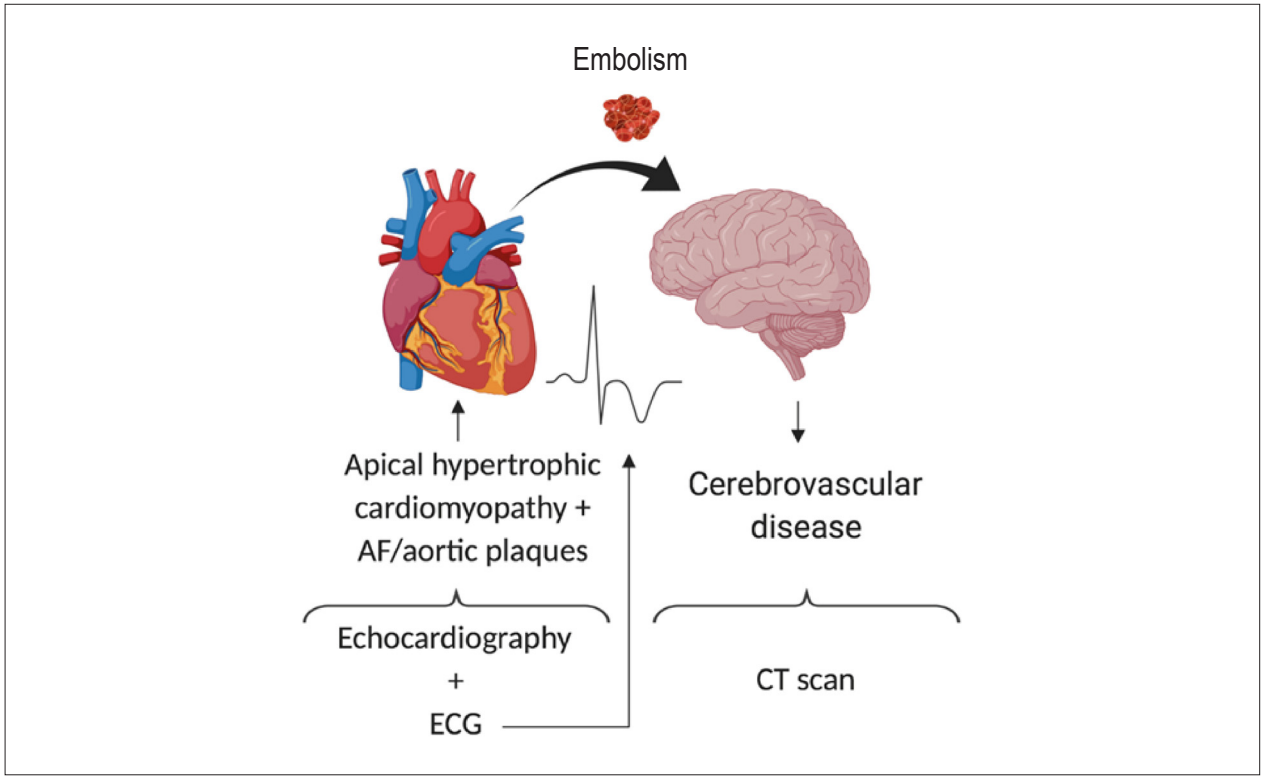


**Figure 4 –** *Central figure depicting the relationship between apical hypertrophic cardiomyopathy and cerebrovascular disease in our cases. The diagnostic modalities we used as well as the characteristic appearance of apical hypertrophic cardiomyopathy on the electrocardiogram are described. Created with Biorender.com. AF, atrial fibrillation; CT, computed tomography; ECG, electrocardiography.*

## References

1. Paluszkiewicz J, Krasinska B, Milting H, Gummert J, Pyda M. Apical hypertrophic cardiomyopathy: diagnosis, medical and surgical treatment. KITP. 2018; 15: 246–53.
2. Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y, Hayashi T, et al. Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasono-cardiotomographic study. Jpn Heart J. 1976; 17: 611–29.
3. Kitaoka H, Doi Y, Casey SA, Hitomi N, Furuno T, Maron BJ. Comparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States. Am J Cardiol. 2003; 92: 1183–1186.
4. Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, et al. Long-term outcome in patients with apical hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002; 39: 638–645.
5. Chung T, Yiannikas J, Freedman SB, Kritharides L. Unusual Features of Apical Hypertrophic Cardiomyopathy. Am J Cardiol. 2010; 105: 879–883.
6. Leaphart D, Waring A, Suranyi P, Fernandes V. Call a Spade a Spade: Missed Diagnosis of Apical Hypertrophic Cardiomyopathy. Am J Med Sci. 2019; 358: 299-303.
7. Bernard J. Gersh, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, et al. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy. Circulaton. 2011; 124: e783-831.
8. Martínez Baca-López F, Lilia Rayas-Gómez A, Ramírez-Arias E, Marisol Alonso Bravo R, Yáñez-Gutiérrez L, Bernal-Ruiz E, et al. Clinical and Echocardiographic Aspects of Mid-Ventricular Hypertrophic Cardiomyopathy. Echocardiography. 2005; 22: 517–524.
9. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. Eur Heart J. 2014; 35: 2733–2779.
10. Reddy V, Taha W, Kundumadam S, Khan M. Atrial fibrillation and hyperthyroidism: A literature review. Indian Heart Journal. 2017; 69: 545–550.