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Predicting apical hypertrophic cardiomyopathy using T-wave inversion: Three case reports

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Abstract

BACKGROUND

Apical hypertrophic cardiomyopathy (AHCM) is a subtype of hypertrophic cardiomyopathy. Due to its location, the thickening of the left ventricular apex can be missed on echocardiography. Giant negative T waves (GNTs) in left-sided chest leads are the hallmark electrocardiogram (ECG) change of AHCM.

CASE SUMMARY

The first patient was a 68-year-old woman complaining of recurrent chest tightness persisting for more than 3 years. The second was a 59-year-old man complaining of spasmodic chest tightness persisting for more than 2 years. The third was a 55-year-old woman complaining of recurrent chest pain persisting for 4 mo. In all three cases, GNTs were observed several years prior to apical cardiac hypertrophy after other causes of T-wave inversion were ruled out.

CONCLUSION

Electrophysiological abnormalities of AHCM appear earlier than structural abnormalities, confirming the early predictive value of ECG for AHCM.

Key Words: Electrocardiogram; Negative T waves; Hypertrophic cardiomyopathy; Apical hypertrophic cardiomyopathy; Echocardiography; Case report

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Core Tip: Apical hypertrophic cardiomyopathy (AHCM) is a subtype of hypertrophic cardiomyopathy that is thought to be associated with sudden death. Owing to its atypical clinical symptoms and insidious progression, early diagnosis is difficult. We followed up three patients who eventually progressed to AHCM over a period of several years. Giant negative T waves in the left-sided chest leads of these three patients occurred earlier than thickening of the left ventricular apex as detected *via* echocardiography. Therefore, we suggest that electrophysiological abnormalities in AHCM appear earlier than structural abnormalities and that electrocardiogram may have early predictive value for AHCM.

INTRODUCTION

Apical hypertrophic cardiomyopathy (AHCM) is an uncommon type of hypertrophic cardiomyopathy (HCM) characterized by thickening of the left ventricular apex. The prevalence rate of AHCM is higher in Asia than those in Europe and America[1]. In China, AHCM accounts for 16% of all cases of HCM[2]. It lacks specificity in clinical symptoms with about 50% of patients not having obvious symptoms[3]. The concept of AHCM was first proposed in 1976 by Sakamoto *et al*[4], who summarized its features as giant negative T waves (GNTs) in leads V3-V4 on electrocardiogram (ECG) and a spade-like configuration of the left ventricular cavity at end-diastole on left ventriculography. Because the lesion site of AHCM is the left ventricular apex, its diagnosis may be overlooked on echocardiography. Therefore, patients considered likely to progress to AHCM can initially be screened by ECG. In addition, if patients with AHCM tendencies are identified early, early medical intervention can be initiated to delay disease progression. This could reduce the hospitalization rate and risk of sudden death in patients with AHCM. Before the diagnosis of AHCM, some patients exhibit T-wave changes similar to AHCM on their ECG, but echocardiography at the

time shows no left ventricular apical myocardial thickening. Only several years later is AHCM diagnosed by echocardiography. Despite not reaching the diagnostic criteria of AHCM, cardiac hypertrophy in such patients appears in the left ventricular apical myocardium. Here, we report three cases of patients presenting with T-wave changes several years prior to apical cardiac hypertrophy being detected on echocardiography.

CASE PRESENTATION

Chief complaints

Case 1: A 68-year-old woman complained of recurrent chest tightness persisting for more than 3 years.

Case 2: A 59-year-old man complained of spasmodic chest tightness that had persisted for over two years and was aggravated two days prior to his hospital visit.

Case 3: A 55-year-old woman complained of recurrent chest pain persisting for more than 4 mo.

History of present illness

Case 1: For the previous 3 years, the patient had experienced recurrent episodes of chest tightness, each lasting no more than 10 min. Her chest tightness was often induced by exercise and could be relieved by rest. She experienced no marked radiating discomfort in the shoulder or back.

Case 2: The patient had developed spasmodic chest tightness more than 2 years before the current visit. The episodes of chest tightness had no obvious trigger, occurred once or twice a week, lasted 3-5 min each, and resolved spontaneously. In the previous 2 days, the frequency of chest tightness attacks had increased to three to five times per day, prompting the patient's hospital visit.

Case 3: The patient had recurrent episodes of chest pain for nearly 4 mo. Her chest pain was often induced by exercise or emotional excitement, lasted about 5 min per episode, and was relieved after rest. She did not experience marked radiating pain in the shoulder or back when she had chest pain.

History of past illness

Case 1: She had a medical history of rheumatoid arthritis and had been admitted repeatedly for chest tightness or arthralgia from 2016 to 2020.

Case 2: The patient had a medical history of type 2 diabetes and an abnormal lipid profile.

Case 3: The patient had a medical history of systemic lupus erythematosus.

Personal and family history

Case 1: The patient had no related personal or family history.

Case 2: The patient had a history of smoking of more than 30 years and no family history of related diseases.

Case 3: The patient had no relevant personal or family history.

Physical examination

Case 1: Physical examination of the patient's heart, lungs, and abdomen was unremarkable. Her first interphalangeal joint and wrist joint were swollen and painful.

Case 2: Physical examination results were unremarkable.

Case 3: Physical examination of the heart, lungs, and abdomen was unremarkable. The patient had butterfly-shaped erythema on the face, swelling and pain of the knee joints and elbows, and scattered ring erythema on the legs.

Laboratory examinations

Case 1: Laboratory test results were unremarkable.

Case 2: Laboratory test results were unremarkable.

Case 3: Laboratory test results were unremarkable.

Imaging examinations

Case 1: After echocardiography was performed four times over the years, she was finally diagnosed with AHCM in 2020. In 2016, the patient's ECG showed negative or biphasic T waves in leads V4 to V6, which evolved dynamically. ECG changes were seen significantly earlier than hypertrophy in the left ventricular apex and the diagnosis of AHCM (Figure 1). In addition, the patient had undergone coronary angiography in 2016, and the results showed no coronary artery stenosis.

Case 2: The patient underwent echocardiography twice in 2016 and 2020. In 2016, the patient underwent cardiac MR examination, and no obvious abnormalities were found Echocardiography in 2020 showed cardiac hypertrophy in the left ventricular apex. However, the ECG of the patient in 2016 showed GNTs in leads V3-V6 (Figure 2). The patient had undergone coronary angiography in 2016, and the results showed no coronary artery stenosis.

Case 3: The patient underwent echocardiography three times between 2016 and 2020. Echocardiography in 2020 showed cardiac hypertrophy at the left ventricular apex. The ECG of the patient in 2016 showed GNTs in leads V3-V6 (Figure 3). The patient

underwent coronary angiography in 2019, and the results showed no coronary artery stenosis.

FINAL DIAGNOSIS

Based on the examination findings, the final diagnosis was AHCM in all three cases.

TREATMENT

The underlying diseases and comorbidities of the three patients were treated with symptomatic treatment.

In case 1, sublingual nitroglycerin was given to relieve the patient's paroxysmal chest tightness and chest pain. Methotrexate and leflunomide were taken continuously and regularly, and oral glucocorticoids were used intermittently for the patient's rheumatoid arthritis. Celecoxib was also administered to relieve joint pain.

In case 2, sublingual nitroglycerin was given to relieve paroxysmal chest tightness, oral metformin and acarbose were given to treat type 2 diabetes mellitus, oral atorvastatin was given to treat dyslipidemia, and aspirin was given to inhibit platelet aggregation.

In case 3, sublingual nitroglycerin was given for relief of paroxysmal chest pain. Cyclophosphamide, taken regularly and continuously, and oral glucocorticoids were used for systemic lupus erythematosus.

OUTCOME AND FOLLOW-UP

The patient in case 1 died from malignant arrhythmia in 2020. The remaining patients are still being monitored.

DISCUSSION

The three patients reported herein had extensive T-wave changes in left-sided chest leads (V3-V6) and GNTs on average 2.3 years before the diagnosis of AHCM. These diagnoses were made after excluding myocardial ischemia due to coronary artery

disease by coronary angiography. No cerebrovascular accidents had occurred, nor did the patients have Takotsubo syndrome or other possible conditions that might lead to the observed ECG changes. The T-wave changes of these patients did not disappear and showed a trend of continuous evolution even after hypertrophy in the left ventricular apex was found by echocardiography and AHCM was diagnosed. Unexplained T-wave inversion in left-sided chest leads is not uncommon, but the final diagnosis of AHCM by echocardiography after long-term follow-up is rare.

AHCM is considered an autosomal dominant disease with familial clustering. It is more prevalent in men (74.4%)[5]. From the perspective of pathophysiology, left ventricular apical hypertrophy impacts left ventricular diastolic function. This reduces left ventricular filling volume, resulting in lower cardiac output and progressive heart failure. Apical myocardial fibrosis reduces the relaxation and compliance of ventricular muscles, resulting in increased left ventricular filling pressures potentially leading to left atrial enlargement, atrial fibrillation, and an increased risk of stroke. Hypertrophic apical myocardium could lead to myocardial ischemia unrelated to coronary arteries owing to papillary muscle microvascular dysplasia and low blood flow reserve. This could then develop into myocardial infarction or apical ventricular aneurysm, thereby increasing the chances of malignant arrhythmias and sudden death[6,7]. In short, AHCM is a latent threat to patients' lives. Early prediction and early intervention could profoundly delay its progression and prevent complications.

The diagnosis of AHCM is based on echocardiography and myocardial magnetic resonance imaging. Currently, the most accepted diagnostic criteria are a maximum apical thickness ≥ 15 mm, maximum apical thickness/left ventricular posterior wall thickness ≥ 15 mm, and exclusion of other causes of cardiac hypertrophy[6]. Some experts argue that the imaging diagnostic criterion of maximum apical thickness ≥ 15 mm could be lowered to ≥ 13 mm when a patient with a thin myocardium at the apex has typical ECG changes, a family history of HCM, or genetic testing results indicating AHCM[8].

ECG also has value in the diagnosis of AHCM. Sakamoto *et al*[4] emphasized the value of GNTs in the diagnosis of AHCM, which has been affirmed in the European Society of Cardiology HCM Diagnosis and Treatment Guidelines[9]. Studies have shown that approximately 90% of patients with AHCM have T-wave inversion, and the incidence of GNTs is approximately 11%-47%[3].

We found that the ECG showed obvious GNT changes several years before the imaging findings of hypertrophy in the left ventricular apex, which implies the greater sensitivity of ECG for apical hypertrophy compared to imaging. Thus, it follows that for AHCM, cardiac electrophysiological abnormalities are seen earlier than structural abnormalities. In the three patients reported herein, significant T-wave inversion in left-sided chest leads was observed at an average of 2.3 years before the appearance of hypertrophy in the left ventricular apex on echocardiography. The average duration of ECG changes is affected by the frequency of echocardiography and ECG during follow-up. Although the small sample in our report inevitably subjects our results to bias, it suggests the predictive value of ECG on cardiac hypertrophy in the left ventricular apex. It can also prove the importance of long-term follow-up in patients with T-wave inversion in left-sided chest leads.

In addition, the clinical symptoms of the three patients appeared later than the changes found on echocardiography, and only when cardiac hypertrophy evolved to a certain degree did the symptoms become apparent. Simultaneously, because ECG is more sensitive in the prediction of apical cardiac hypertrophy, its auxiliary diagnostic value for early asymptomatic patients with AHCM should not be ignored.

In the future, more patients with extensive T-wave inversion in left-sided chest leads need to be evaluated in case-control studies with higher levels of evidence in order to enable evidence-based medicine for such patients. At the same time, early genetic testing combined with T-wave changes in ECG should provide a more accurate clinical diagnosis.

CONCLUSION

Extensive T-wave inversion in leads V3-V6 occurred significantly earlier than left ventricular apical cardiac hypertrophy detected by echocardiography. Therefore, after excluding other conditions that may cause extensive T-wave inversion in left-sided chest leads, extensive T-wave inversion in leads V3-V6 may have early predictive value for AHCM. For patients with extensive T-wave inversion in left-sided chest leads, no left ventricular apical cardiac hypertrophy on echocardiography, and exclusion of other causes such as ischemia, the possibility of AHCM should be considered. This may improve clinical decision-making.

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Figure Legends

Figure 1 Evolution of left ventricular apical thickness and T-wave amplitude in chest leads of electrocardiogram in case 1. A: B:

Figure 2 Evolution of left ventricular apical thickness and T-wave amplitude in chest leads of electrocardiogram in case 2. A: B:

Figure 3 Evolution of left ventricular apical thickness and T-wave amplitude in chest leads of electrocardiogram in case 3. A: B:

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