A novel case of Yamaguchi syndrome in the Saudi population

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ABSTRACT

Background: Apical hypertrophic cardiomyopathy (ApHCM) known as Yamaguchi syndrome, is an uncommon variant of hypertrophic cardiomyopathy, with higher incidence reported in the Asian populations. The clinical presentation of ApHCM is vague and thus can mimic other conditions, which can lead to a delayed or missed diagnosis. Only a few reports have described the incidence of Yamaguchi syndrome in other populations other than Asians.

Case Presentation: A 46-year-old male, heavy smoker, with unremarkable past medical history was presented to the emergency department with severe central chest pain that radiates to the left side, exacerbated by exertion, and relieved by rest not associated with shortness of breath or palpitation. In addition, the patient reported two similar episodes that occurred the past 4 days. However, physical examination was unremarkable. Initially the patient was labeled as high-risk acute coronary syndrome (unstable angina vs. non-ST segment myocardial infarction). Cardiac markers including troponin I and Creatine kinase-MB were within normal range. Electrocardiograph revealed deep T wave inversion in the inferior limb leads and pericardial leads suggestive of right coronary and left anterior descending artery or left main coronary lesion. The patient underwent for urgent cardiac catheterization which revealed normal coronary arteries. Transthoracic echocardiograph showed isolated apical hypertrophy with preserved left ventricle function, suggestive of ApHCM. The patient was advised on smoking cessation and discharged on beta blocker.

Conclusion: There is an imminent need to establish further research investigating the prevalence of Yamaguchi syndrome among the Saudi population.

Keywords: Yamaguchi syndrome, apical hypertrophic cardiomyopathy, ApHCM, case report, Saudi Arabia.

Introduction

Yamaguchi syndrome, also known as apical hypertrophic cardiomyopathy (ApHCM), is a rare form of nonobstructive hypertrophic cardiomyopathy (HCM) that affects the apical region of the left ventricle (LV) [1]. ApHCM was first described by H Yamaguchi in Japan in 1979 [1].

The prevalence is higher among the Asian population compared to the non-Asian population affecting up to 25% and 1%-10%, respectively [2]. Due to the similarities in the clinical presentation and initial electrocardiograph findings, ApHCM can mimic other disorders including acute coronary syndrome (ACS), fabry disease, and athlete heart [3].

Patients with ApHCM can present with a variety of clinical manifestations including chest pain, dyspnea, palpitation, syncope, and heart failure [4]. The disease course is considered to be benign with management being directed toward symptomatic medical treatment [5]. However, some patients might develop life-threatening complications namely ventricular tachycardia (VT) and sudden cardiac death (SCD); therefore, close follow-up and risk stratification are warranted[3].
A case of Yamaguchi syndrome was reported in a 46-year-old Saudi male who presented with chest pain and bizarre ECG findings.

Case Presentation

A 46-year-old male, heavy smoker, with an unremarkable past medical history, presented to the emergency department with severe central chest pain that radiates to the left side, exacerbated by exertion, and relieved by rest not associated with shortness of breath or palpitation. In addition, the patient reported two similar episodes that occurred in the past 4 days. Physical examination was unremarkable.

Initially, the patient was labeled as high-risk ACS (unstable angina vs. non-ST segment myocardial infarction). Cardiac markers including troponin I and Creatine kinase-MB were within normal range. ECG revealed deep T wave inversion in the inferior limb leads and pericardial leads suggestive of right coronary and left anterior descending artery or left main coronary lesion (Figure 1).

The patient underwent urgent cardiac catheterization which revealed normal coronary arteries. Transthoracic echocardiogram (TTE) showed isolated apical hypertrophy with preserved LV function, suggestive of ApHCM.

Furthermore, cardiac magnetic resonance imaging (CMR) detected ApHCM with no fibrosis or scar (Figure 2).

These findings confirmed the diagnosis of Yamaguchi syndrome. In addition, to investigate the risk of SCD and the need for implantable cardiac defibrillator (ICD) insertion, the patient had both electrophysiology (EP) study, which revealed no inducible VT, and 24-hour Holter which did not detect any arrhythmias.

The patient was advised on smoking cessation and discharged on beta blocker. In addition, screening was recommended for the family with ECG, echocardiography, CMR, and EP. On the follow-up visit, ECG was completely normalized, and the patient denies any episodes of chest pain since (Figure 3).

Discussion

Dr. Yamaguchi and his colleagues first reported ApHCM in 1979. The study included 1,002 consecutive patients who underwent left heart catheterization, and among whom, 30 patients showed a distinctive “ace of spades” shape of the LV, which has become a hallmark related to this condition [1].

Further research has revealed a higher occurrence of ApHCM in Asian populations than in American populations. One study conducted by Kitaoka et al. [6] revealed a prevalence of 15% in a randomly selected group of Japanese individuals, while only 3% in a similar group from Minneapolis. The study also found that the incidence of ApHCM was higher in men compared to women, regardless of whether they were Japanese or American [6].

Another study conducted in Germany analyzed data from more than five million patients and found that men had a higher prevalence of ApHCM than women across all age ranges. However, further research is needed to determine the exact prevalence and risk factors associated with ApHCM.

Figure 1. ECG revealed deep T wave inversion in the inferior limb leads and pericardial leads.
The study also revealed that the incidence of the condition increased with age and was more pronounced in men as they grew older [7].

The workup for ApHCM can include a variety of laboratory and imaging studies. Cardiac biomarkers, namely high-sensitivity cardiac troponin T have been shown to correlated with age, left atrium area, and maximum LV wall thickness in different morphological subtypes of HCM including ApHCM [8].

Moreover, another study showed that troponin I was significantly lower in ApHCM compared with classical HCM and correlated with the male gender, maximum LV wall thickness and LV dysfunction [9].

Voltage criteria on ECG including LV hypertrophy, T-wave inversion, and a characteristic giant negative T-waves of ≥ 1mV can be highly suggestive of ApHCM, however, it is not pathognomonic as it might be seen in other cardiac conditions [5]. Furthermore, Holter monitoring is used to detect atrial fibrillation (AF), asymptomatic, and symptomatic VT [5].

Echocardiography can show apical hypertrophy and identify some prognostic factors, e.g., the presence of diastolic dysfunction, aneurysm and mid-ventricular
obstruction and cavity obliteration (MVOCO) [10]. Nevertheless, early ApHCM phenotypes can be missed by echocardiography, therefore, other imaging modalities are required for patients with deep t-wave inversions and noncontributory echocardiography findings [11].

CMR has been shown to detect early phenotypes of ApHCM better than echocardiography [12]. In a recent study, CMR detected apical hypertrophy in 40% of patients who were missed by echocardiography [13]. Cardiac computerized tomography (CT) can be used as an alternative option when CMR is not recommended. Myocardial fibrosis can be detected using cardiac CT with iodine-based contrast revealing late enhancement findings [14].

Finally, angiography might reveal a distinctive ACE of the spade pattern of the LV cavity [15]. The diagnostic criteria for ApHCM based on echocardiography or CMR included the presence of LV hypertrophy predominating in the apex, with apical wall thickness ≥15 mm and a ratio of maximal apical to posterior wall thickness of ≥1.5 [5].

Management of ApHCM is mainly medical and aims to improve symptoms that might be precipitated by heart failure, tachyarrhythmias, and MVOCO and prevent the possibility of SCD [3]. B-blockers and nondihydropyridine calcium channel blockers are the first and second lines in ApHCM medical management, respectively. In addition, anticoagulants are considered in cases of AF [3]. In cases of monographic VT, the use of catheter ablation has been reported to be successful [3].

Currently, there are no published trials on the role of ICDs in ApHCM. ApHCM patients tend to score negatively for SCD in the current criteria of the European Society of Cardiology algorithm due to the sporadic pattern of the disease, consequently, these factors might have ultimately resulted in the underutilization of ICDs among ApHCM patients [3]. Finally, apical myomectomy has been reported to improve symptoms and increase end-diastolic dimensions [3]. Based on recent data, the annual cardiac death rate is approximated to be 0.5%-4%. In addition, higher cardiovascular morbidity was observed with patients who presented at a younger age at presentation (<41 years), complete end-systolic cavity obliteration at the level of the papillary muscles, paradoxical diastolic flow jet by echocardiography and apical asynergy [3].

This report highlighted a case of a medically free patient who presented with clinical features resembling ACS but with normal cardiac biomarkers. The ECG, however, was suggestive of left anterior descending artery or left main coronary lesion. The TTE and CMR findings were consistent with the diagnosis of Yamaguchi syndrome, and the patient was managed conservatively by advising smoking cessation and prescribing a B-blocker. On a follow-up visit, the patient’s clinical status has improved and the ECG was completely normalized.

**Conclusion**

Healthcare providers should keep Yamaguchi syndrome in mind as a potential differential diagnosis when assessing patients with presentation resembling angina.
Furthermore, epidemiological research is needed to investigate the frequency of ApHCM in Saudi Arabia. Finally, there is a necessity for focused therapeutic randomized control trials to investigate the role of ICDs in ApHCM patients and pursue alternative management options.

List of Abbreviations

| ACS | Acute coronary syndrome |
| ApHCM | Apical hypertrophic cardiomyopathy |
| AF | Atrial fibrillation |
| CMR | Cardiac magnetic resonance imaging |
| CT | Computerized tomography |
| ECG | Electrocardiograph |
| EP | Electrophysiology |
| ICD | Implantable cardiac defibrillator |
| LV | Left ventricle |
| MVOCO | Mid ventricular obstruction and cavity obliteration |
| SCD | Sudden cardiac death |
| TTE | Transthoracic echocardiograph |
| VT | Ventricular tachycardia |

Conflict of interests

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Consent for publication

Informed consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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