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Case Report

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Left Ventricular Outflow Tract Obstruction (LVOTO) Causing Syncope in Hypertrophic Cardiomyopathy (HCM): A Case Report

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ABSTRACT

Background: Hypertrophic cardiomyopathy (HCM) is one of the most common inherited cardiovascular diseases. HCM can sometimes result in dynamic obstruction of the left ventricular outflow (LVOT) tract that can subsequently compromise adequate cardiac output. The symptoms of left ventricular outflow tract obstruction (LVOTO) can range from mild symptoms of impaired cardiac output to sudden cardiac death (SCD) in extreme cases.

Case Description: A 68-year-old female with comorbidities including obesity, obstructive sleep apnea (OSA), and hyperlipidemia but no prior diagnosis of HCM or known family history of HCM, presented after a witnessed syncope and subsequent head injury, who had an extensive evaluation of the etiology of her syncope. Transthoracic echocardiogram (TTE) revealed presence of HCM with evidence of dynamic LVOTO. The patient underwent a transesophageal echocardiogram (TEE) which showed hypertrophy of LVOT in the septal area causing moderate increase in LVOT mean gradient. The patient was started on medical management with diltiazem that was not tolerated because of bradycardia. The patient had a stable clinical course without any hemodynamic events and was discharged home with outpatient Cardiology follow-up. The patient was also advised to get a referral for a cardiac magnetic resonance (CMR) for further evaluation of HCM and the potential for dynamic LVOTO.

Conclusions: HCM can cause dynamic LVOTO that can lead to symptoms including fatigue, chest pain, presyncope, and syncope. Extreme cases of LVOTO can lead to SCD. Medical management is imperative in HCM with symptoms of LVOTO. In extreme cases risk stratification for implantable cardioverter defibrillator (ICD) implantation is indicated to prevent SCD.

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Key Findings

- Clinicians evaluating unexplained syncope need to consider HCM as one of the differential diagnosis.
- HCM can clinically present as syncope from underlying LVOTO.

What is known and what is new?

- HCM is the most prevalent inherited cardiovascular disease (1:200 to 1:500 in the general population).
- Risk stratification needs to be done in symptomatic HCM patients for ICD implantation for primary prevention.

What is the implication, and what should change now?

- HCM patients with evidence of LVOTO requires therapy.
- Beta blockade or calcium channel blocker is the first line therapy for patients with HCM and evidence of LVOTO.
- Symptomatic patients with risk factors need to be referred for ICD implantation.
- Patients with severe LVOTO need to be referred for definitive management with surgical myectomy (open surgical approach) Vs alcohol septal ablation (percutaneous approach) as appropriate.

Introduction

Hypertrophic cardiomyopathy (HCM) is a hereditary disorder that causes left ventricular hypertrophy and a non-dilated left ventricle with an ejection fraction that is preserved or increased [1]. Mutations in the cardiac sarcomeres are accountable for 40% of HCM cases globally, while the etiology of 60% of the cases of HCM is unclear [2]. HCM can often result in diastolic dysfunction of the left ventricle. HCM can even cause sudden cardiac death (SCD) specifically in young adults and adolescents. Major risk factors associated with SCD in patients with HCM include syncope, family history of SCD, non-sustained ventricular tachycardia, and severe left ventricular hypertrophy [1]. HCM is the most prevalent inherited cardiovascular disease with an alarming incidence of around 1:200 to 1:500 in the general population [3]. Left ventricular outflow tract obstruction (LVOTO) can occur as a sequela of HCM. LVOTO can ensue in 25-30% of patients with HCM at rest, but up to 70% of the HCM patients with provocative physiologic maneuvers including exercise or Valsalva maneuver [4]. LVOTO with provocation or even at rest is present in a considerable proportion of patients with HCM and LVOTO is usually caused by systolic anterior motion (SAM) of the mitral valve (MV). LVOTO is considered pathologic if the resting peak LVOT gradient measures ≥30 mm Hg or if the provoked LVOT gradient is ≥50 mm Hg [5].

2D echocardiography/transthoracic echocardiogram (TTE) is the preferred imaging modality to for diagnosing HCM.

Cardiovascular magnetic resonance (CMR) can be used to get additional information or as an alternative to TTE for patients in whom echocardiogram findings are inconclusive. A diagnosis of HCM is made if the TTE shows a left ventricular end diastolic wall thickness/left ventricular end diastolic diameter (LVEDD) of ≥15 mm of any portion of the left ventricle in the absence of other pathologies that can cause ventricular hypertrophy. A LVEDD of 13-14 mm is diagnostic of HCM if present along with positive family history or a positive genetic test for pathogenic sarcomere gene [5]. Although hypertrophy can ensue in any segment in the left ventricle, it occurs most commonly in the interventricular septum (IVS) [6].

Literature shows that a large proportion of the patients with HCM are clinically unrecognized and the number of patients diagnosed with HCM is significantly less than the estimated incidence of HCM in the general population [7]. This means that a large proportion of patients with HCM are undiagnosed throughout their life until they present with symptoms related to HCM or from a clinical scenario triggered by HCM. The objective of this case report is to gain an insight into the important characteristics of HCM and the pearls to remember in the management of patients with HCM who are symptomatic. This article also highlights the clinical significance of risk stratification in symptomatic HCM to aid preventing any SCD associated with HCM.

Case Presentation

A 68-year-old woman with medical comorbidities including obesity, obstructive sleep apnea (OSA), hyperlipidemia, and a remote history of first lumbar vertebral fracture from a previous fall, who presented to the Emergency Department (ED) after she had a witnessed fall from approximately 6 feet above the ground level from a presumed syncope. As per the witness, the patient fell backwards from the stairs (approximately 6-8 steps) to the driveway hitting the back of her head. There were no reported tonic-clonic movements, urinary incontinence, or tongue bite. However, the witness said that the patient's eyes were rolled up while she was briefly unresponsive but regained consciousness up on calling her name. The patient denied any chest pain or shortness of breath. She denied feeling dizzy before the fall. She has no known history of any seizure disorder. Computerized tomography (CT) of the brain showed a right occipital skull fracture, left frontal subarachnoid hemorrhage (SAH), bilateral frontal contusions, and a right frontal subdural hematoma (SDH). CT of the abdomen and pelvis showed age indeterminate fractures of lumbar 1 (L1) and sacral 3 (S3) vertebrae. The patient was admitted to the Intensive Care Unit (ICU) for further care.

A TTE was done that showed a left ventricular ejection fraction of 65% and no wall motion abnormalities. There was evidence of grade 1 diastolic dysfunction. There was dynamic LVOT obstruction with a peak gradient of 26 mm Hg at rest (no provoked LVOT gradient was done on this study). The mean aortic valve (AV) gradient was 48 mm Hg. The LVEDD on this study was 12 mm and interventricular septum (IVS) diastolic thickness was 13 mm. There was mild to moderate mitral regurgitation. A Cardiology consult was obtained for further evaluation of these findings and concerns for LVOTO that might have contributed to the patient's syncope and the resultant fall. A repeat TTE was ordered by Cardiology that was done 48 hours after the first TTE. The follow-up TTE revealed a peak LVOT gradient of 14 mm Hg with a mean AV gradient of 35 mm Hg. The study also revealed moderate eccentric and anteriorly directed MV regurgitation. No LVEDD was reported on this study. There was also evidence of a thick septum causing moderate subaortic valve stenosis. However, there was no changes in AV and LVOT gradients with Valsalva maneuver. Although this TTE reported no changes in LVOT gradient with Valsalva maneuver, it is arguable that if Valsalva maneuver can reproduce the same amount of exertion as climbing a flight of stairs (prior to the syncopal episode). No LVEDD and IVS diameter were reported on this study. The patient subsequently underwent a transesophageal echocardiogram (TEE) that showed hypertrophy of LVOT in the septal area causing moderate increase in LVOT mean gradient of 18 mm Hg. However, the AV appeared to be opening well without any significant stenosis. The IVS diastolic thickness was 14 mm (normal = 6 to 9 mm).

Beta blockers are the first line agents recommended in patients with HCM and evidence of LVOTO. In cases where beta blockers are contraindicated non-dihydropyridine calcium channel blockers have been found to be beneficial in symptomatic HCM. Disopyramide, an old antiarrhythmic drug often in combination with beta blockers has also been found to be effective in patients with symptomatic HCM [8]. Beta blockers could not be used in this patient who had sinus bradycardia at baseline. Following the TEE, Cardiology concluded that the patient's LVOTO was moderate and the patient would benefit from diltiazem for calcium channel blockade. Nevertheless, the patient could not tolerate diltiazem because of significant bradycardia (up to 45/min). Cardiology recommended outpatient CMR and follow-up for definitive management of the patient's HCM and subsequent LVOTO.

Meanwhile, the patient was evaluated by Neurosurgery for her intracranial bleeds. Her blood pressure was maintained <140 mm Hg and it was ensured that the patient remained off any antiplatelets or any chemical venous thromboembolism (VTE) prophylaxis including subcutaneous heparin or low molecular weight heparin during her hospital stay. She was evaluated using repeat imaging studies of her brain and the repeat imaging studies showed no progression of the intracranial lesions evident on the initial brain CT. The patient had no evidence of any focal neurological deficits. Neurosurgery recommended follow-up in 1 to 2 weeks following discharge from the hospital. The patient underwent a carotid Doppler study and this was negative for any hemodynamically significant stenosis. The patient did not have any evidence of lethal arrhythmias during her stay in the ICU. Neither did she have any evidence of orthostasis. There was no suspicion for any toxidromes contributing her clinical presentation. As such, no drug screen was done on this patient. The patient was discharged home in stable condition after 72-hour stay in the ICU. The patient had a repeat TTE as part of her follow-up in two weeks after her hospitalization and this showed a LVEDD of 15 mm. The patient also had a loop recorder placed during this follow-up to rule out any arrhythmias that might be contributing to her symptomatology. Loop recording did not reveal any arrhythmias that can contribute to syncope although the recordings showed episodes of bradycardia up to 48/min while the patient was asleep. At the time of writing the case report, the patient has not done a CMR yet.

Discussion

This patient has no documented diagnosis of HCM. The patient denied any known family history of HCM or SCD. Although the patient's LVEDD on the TTE done during her hospitalization did not technically meet the diagnostic criteria for HCM based on the TTE (LVEDD 13 mm), the patient had evidence of dynamic LVOTO on this study and repeat studies also did show LVOTO. However, the LVOT gradient was 26 mm Hg at rest (LVOT gradient of ≥30 is diagnostic for LVOTO). Of note, no LVEDD was reported in the repeat TTE but TEE showed a LVEDD of 14

mm. Surprisingly TTE done during outpatient follow-up showed an LVEDD of 15 mm that establishes a diagnosis of HCM in this patient. Although the patient declined any family history of SCD, it is unclear if the patient has family history of HCM that the patient is unaware of. No genetic testing could be done in the patient at the given inpatient setting to identify any genetic predisposition of the patient for developing HCM. Nevertheless, the patient had other suggestible evidence of HCM including presence of LVOTO, increased IVS thickness, and evidence of diastolic dysfunction. Based on the clinical presentation and reports from the witness, it is unclear that if the patient had a syncope secondary to LVOTO from underlying physical exertion (the patient was climbing stairs when the reported event happened) or if the patient had any non-perfusing rhythm from a transient episode of arrhythmia induced by the underlying HCM. It is also possible that the patient might had an isolated dynamic LVOT obstruction that is unrelated to her HCM.

The patient's initial TTE showed evidence of dynamic obstruction of the LVOT (LVOT gradient of 26 mm Hg at rest). Dynamic outflow obstruction often occurs in HCM secondary to SAM of the MV anterior leaflet and mitral-septal contact with resultant impingement of the MV leaflet on a hypertrophied IVS (Figure 1). The LVOTO is dynamic that results from a pressure gradient causing the anterior MV leaflet to be displaced anteriorly with resultant outflow tract obstruction. The magnitude of obstruction is dependent on the loading conditions and contractility at the time. Left ventricular diastolic dysfunction is frequently seen in HCM with resultant impaired filling of the left ventricle that can further make the obstruction worse. Since coronary perfusion happens during diastole, the increased left ventricular stiffness along with the outflow tract obstruction can result in myocardial ischemia. This can culminate in lethal ventricular arrhythmias and subsequent SCD. This usually ensues during times of increased myocardial demand such as during strenuous exercise. However, in extreme cases of HCM and accompanying LVOTO, this can even happen while the patient is at rest [6]. Although SAM can be relevant in HCM, isolated cases of LVOTO can occur in other clinical scenarios such as isolated LVOTO cases in non-HCM patients even in the absence of hypertrophied IVS [10].

Risk Stratification

Presence of 1 or more conventional risk factors in HCM is regarded as an indication for ICD implantation for primary prevention of SCD. Unexplained recent syncope is a risk factor that recommends ICD implantation in patients with HCM [3]. Therefore, ICD implantation might have been considered for this patient. However, clinical decisions on ICD implantation in patients with HCM is often challenging especially when there is a lack of evidence to confidently determine a risk level. In such cases clinical judgement and medical reasoning augmented by fully informed and transpicuous discussion with the patient along with weighing the risk/benefit ratio of ICD implantation need to be considered before arriving at a decision on implantation [3]. Although there was a recent unexplained syncope in this patient who presented following a fall, multiple imaging studies of the heart did not reveal significant LVOTO that prompted interventions like ICD implantation or referral for definitive management of the underlying LVOTO [3]. Therefore, more inputs from further imaging studies including CMR and possibly late gadolinium enhancement (LGE) was needed in this patient before making a clinical decision on ICD implantation. Other risk factors that indicate ICD implantation in HCM include extreme left ventricular hypertrophy, a family history of SCD, end-stage HCM, left ventricular apical aneurysm, evidence of fibrosis on LGE, and episodes of non-sustained ventricular tachycardia (NSVT) [3]. The patient did not have any other risk factors that indicated prompt ICD implantation based on the available data.

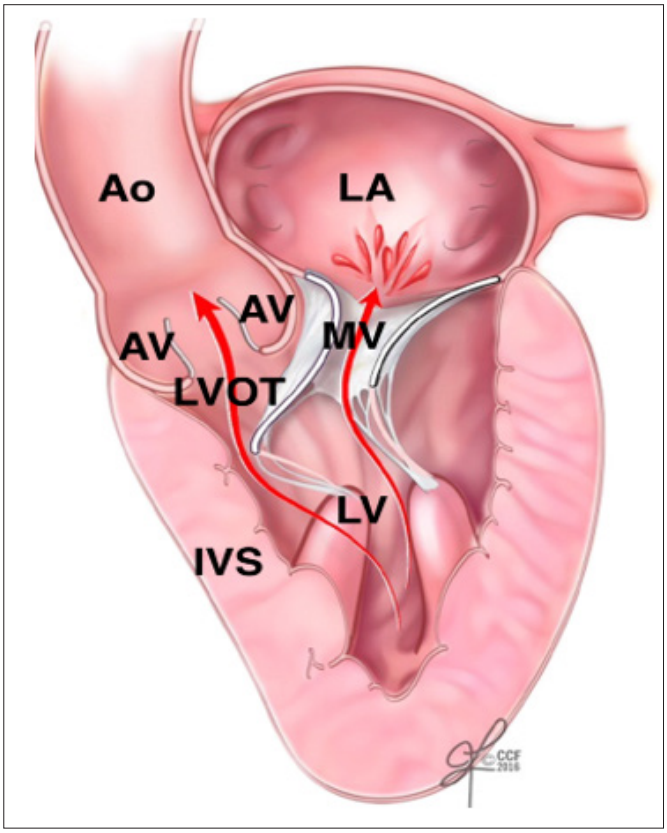

Figure 1: SAM of Mitral Valve. Systolic anterior motion of the anterior mitral valve that is very close to the interventricular septum causing narrowing of the left ventricular outflow tract. The figure also shows the associated mitral regurgitation [11].

AO = Aorta, **LVOT** = Left Ventricular Outflow Tract, **AV** = Aortic Valve, **MV** = Mitral Valve, **LA** = Left Atrium, **LV** = Left Ventricle, **IVS** = Interventricular Septum

Conclusion

This case report is a very good example for clinicians evaluating unexplained syncope. Despite its high incidence in the general population, a large proportion of patients with HCM remain undiagnosed. Early recognition along with adequate monitoring and management are key in the care of HCM. Poorly monitored or improperly managed HCM can result in increasing oxygen consumption, left ventricular remodeling, secondary MV regurgitation, heart failure and even SCD [3]. Betablockers and non-dihydropyridine calcium channel blockers are the first line agents used in the management of symptomatic HCM. Symptomatic HCM that does not respond to first-line therapy often requires escalation of therapy including novel cardiac myosin

inhibitors (mavacamten), and even septal reduction therapy (SRT) [5]. While evaluating patients with unexplained syncope, HCM with possible dynamic LVOTO should be considered as one the differentials until this is ruled out. In patients with known HCM with evidence of dynamic LVOTO, exercising risk stratification and using ICDs can prevent SCD. SRT can be performed either surgically via a sternotomy or percutaneously. Surgical myectomy is the definitive treatment in patients with HCM refractory to medical management as it can correct LVOTO and associated symptoms. Surgical myectomy is a very effective and relatively low risk surgery especially in experienced centers [3]. Alcohol septal ablation (ASA), a percutaneous approach can also be employed for definitive management of obstructive symptoms associated with HCM. Current guidelines support ASA as a class 1 indication for obstructive symptoms with effectiveness similar to surgical myectomy especially when no concomitant significant valve or coronary surgical indication is present [9].

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Footnote
Conflicts of Interest: The author does not have any conflicts of interest to declare.

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