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Hypertrophic Cardiomyopathy

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Hypertrophic Cardiomyopathy (HCM) is a genetic disorder which causes clinically unexplained cardiac hypertrophy. This is not due to some hemodynamic problem i.e. Aortic stenosis or Hypertension. It leads to symptoms, dynamic left ventricular obstruction (obstructive HCM) and some life threatening arrhythmias[1]. HCM is inherited as an autosomal dominant disease and at present 11 genes coding for various cardiac sarcomeric proteins are associated with HCM[2]. HCM is most common genetic cardiovascular disease and occurs in approximately 1 in every 500 adults[3]. Almost 50% cases have family history of disease and others occur sporadically. Usually HCM is asymptomatic initially and is picked up on abnormal electrocardiogram, heart murmur or screening echocardiography.

CLINICAL PRESENTATION

Symptoms due to HCM are angina, syncope and dyspnea.

Angina is seen usually in absence of epicardial coronary disease and is caused by compression of small arteries due to myocardial hypertrophy, abnormal diastolic filling pressures, oxygen supply demand mismatch and abnormal coronary flow reserve[4].

Syncope is seen in around 20% of HCM patients. It is mostly due to left ventricular (LV) outflow obstruction and activation of LV baroreceptors which leads to reflex vasodilatation and atrial and ventricular arrhythmias.

Dyspnea is usually caused by a combination of LV outflow tract obstruction, mitral regurgitation and LV diastolic dysfunction.

In elderly patients hypertension is common and echo reveals sigmoid septal configuration[5]. There may be concomitant cardiac diseases e.g. calcific aortic stenosis, coronary heart disease and mitral annular calcification.

Natural history of HCM is variable. But the main concern is **sudden cardiac death (SCD)**. Although overestimated in the past the contemporary studies report overall sudden cardiac death rates of 0.5-1% per year[6,7]. Sudden cardiac death (SCD) may be first manifestation of hypertrophic cardiomyopathy. It is most frequent in young adults less than 30 years of age but is rare in infants and young children[6,8]. Various factors that increase the risk of SCD are history of cardiac arrest, family history of SCD, severe LVH, documented non-sustained ventricular tachycardia, LV outflow tract obstruction and abnormal blood pressure response to exercise[6,8].

Prevalence of **atrial fibrillation(AF)** is high in HCM and is seen in about 22% cases with annual incidence of 3%[9]. This is four times as compared to same in general population. Systemic embolism occurs in 6% of patients.

Heart failure is seen to develop in 5% of patients with HCM. There is cardiac dilatation with ejection fraction <50%. With development of heart failure LV dilates and LV outflow tract obstruction may decrease[10].

Infective endocarditis is seen in 4-5% of patients with HCM. Lesions usually seen on interventricular septum and mitral valve[11].

DIAGNOSTIC TESTING

Various diagnostic tests used for HCM are electrocardiography, chest X-Ray, Echocardiogram, Cardiac magnetic resonance imaging, Nuclear imaging and cardiac catheterization.

Electrocardiogram (ECG) may be normal but ECG changes are seen in >90% cases[6]. Various ECG findings are left ventricular hypertrophy, repolarisation (ST-T) changes, abnormal Q waves[12].

X-Ray chest shows mild to moderate cardiac enlargement with LV contour rounded. There is usually left atrial enlargement.

Echocardiography (Echo): Increased LV wall thickness measured by imaging technique is the basis for diagnosis of HCM. Hypertrophy may be diffuse, localized, asymmetrical, apical, hour glass type and so on. This is the basis of classifying HCM as **obstructive, non obstructive or apical** HCM.

LV wall thickness of ≥15mm at end diastole in one or more segments in adults and wall thickness more than two standard deviations greater than the predicted mean in children in absence of any hemodynamic cause are sufficient to diagnose HCM. In case of 1rst degree relatives of diagnosed case of HCM LV wall thickness ≥13mm in one or more LV myocardial segments is diagnosed as HCM. Hypertrophy most commonly involves interventricular septum causing asymmetrical septal hypertrophy (ASH) (Fig. 1 and 2) although it can occur in any segment or even in right ventricle[13]. It is important to screen all segments of LV and avoid inclusion of right ventricular structures i.e. moderator band or crista supraventricularis in measurements of wall thickness.

It is important to correlate the ECG and increased LV wall thickness on ECHO. Low voltage ECG with increased LV wall thickness is suggestive of infiltrative diseases like amyloidosis. (1). Increased LV wall thickness in absence of hemodynamic explanation is also seen in athletes. Athletic heart is usually associated with dilated LV and LV wall thickness ≥13-15mm[14]. LV outflow tract obstruction (LVOTO) is other ECHO finding in HCM. We should also rule out any other cause of LVOTO. Dynamic LVOTO is associated with systolic anterior motion of anterior mitral leaflet (SAM of AML) as is seen in our patient. (Fig 1). Less commonly we may see SAM of posterior mitral leaflet. LVOTO is defined as instantaneous peak Doppler outflow gradient of ≥30mmHg. Gradient may be noted at rest or on provocative maneuvers i.e. standing, exercise or Valsalva maneuver. Some patients have also associated mitral regurgitation. Doppler color flow imaging can be used to determine the presence and severity of mitral regurgitation[15]. One should also assess for primary abnormality of mitral valve apparatus. Diastolic dysfunction is also assessed by measuring left atrial dimensions, pulmonary venous flow, transmitral flow and tissue Doppler imaging[16]. Assessment of left ventricular ejection fraction may overestimate LV systolic function. Tissue Doppler imaging and mitral annular motion is useful to assess LV systolic function[16].

Trans-esophageal echo may help in assessment of mitral valve and rule our discrete subvalvular stenosis. It is also used in peri- and intraoperative monitoring of septal myectomy.

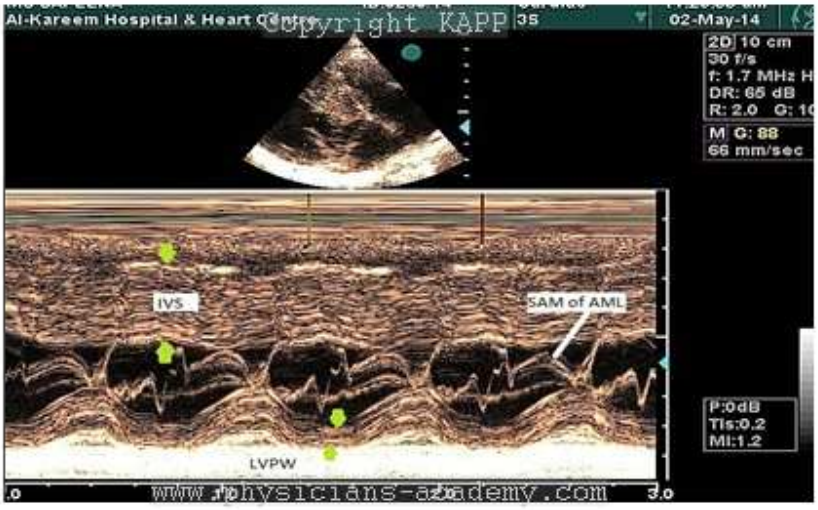

Fig 1. M-mode echo showing asymmetrical septal hypertrophy (ASH) and systolic anterior motion of AML (SAM of AML)

Fig.2. 2D Echo. Parasternal Long axis view showing thick Interventricular septum with relatively thin posterior LV wall and dilated LA

Cardiac Magnetic Resonance Imaging (CMRI): CMRI provides high resolution imaging of the myocardium and accurately determines the site and extent of hypertrophy[16]. Apical and anterolateral hypertrophy or right ventricular hypertrophy are well picked up by CMRI. It is also helpful to assess mitral valve apparatus.

Nuclear Imaging: Single photon emission computed tomography (SPECT) and Positron Emission Tomography (PET) scanning will help to assess reversible and fixed defects in absence of any epicardial coronary artery disease.

Cardiac Catheterisation: Although not necessary but cardiac catheterization may be used if there is discrepancy between Echo and clinical presentation. Also we can rule out associated epicardial coronary artery disease on angiography. LVOTO can also be assessed by cardiac catheterization.

TREATMENT

Medical Therapy. Various precautions are to be taken in general in HCM with LVOTO. Avoid dehydration, avoid excessive alcohol consumption, maintain healthy weight. Avoid vasodilators (Venous and arterial vasodilators). AF is poorly tolerated and may need immediate cardioversion.

Medical therapy used in form of B-blockers, Nondihydropyridine calcium channel blockers (Verapamil and Diltiazem). These drugs decrease heart rate and have negative ionotropic effect. Sometimes Disopyramide is helpful because of its negative ionotropic effect which decreases LVOTO[1,6].

Septal Reduction Therapy. Symptomatic patients with LVOTO with gradient ≥50 mmHg not responding to medical therapy will need septal reduction therapy.

Surgical septal myectomy is the gold standard therapy in HCM with obstruction and non-response to medical therapy[1]. Procedure consists of transaortic resection of muscle from interventricular septum (Marrow procedure).

Alcohol septal ablation is also used to induce necrosis of septal muscle by injecting alcohol in septal branch of left anterior descending artery. Healing and remodeling leads to reduction of LVOT obstruction[1]. Current guidelines recommend a thorough anatomical and functional evaluation of septum, mitral valve and subvalvular apparatus to guide the septal reduction therapy[1].

Dual chamber pacing is also used to treat LV outflow tract obstruction. Pacing results in alteration of LV depolarization which decreases septal contraction and protrusion into outflow tract and thus decreases LVOTO[6,17].

Treatment of nonobstructive HCM is again B-blockers or calcium channel blockers. If there is dilatation of LV with signs of failure then guideline directed treatment of heart failure is used.

For **prevention of sudden cardiac death** implantable cardioverter defibrillator is most effective. although amiodarone has shown some benefit in some cases of non-sustained ventricular tachycardia[18].

Anticoagulation should be used in HCM patients with atrial fibrillation. Vitamin K antagonists have shown reduction in incidence of strokes.

Pregnant females with HCM are treated on same pattern as we treat other patients with HCM. Epidural anesthesia should be used cautiously as it may cause peripheral vasodilatation and drop in preload and afterload.

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