ECHO IN MYOCARDIAL DISEASES

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HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY
HISTORICAL PERSPECTIVE

- HCM was initially described by Teare in 1958
  - Found massive hypertrophy of ventricular septum in small cohort of young patients who died suddenly
- Braunwald was the first to diagnose HCM clinically in the 1960s
- Many names for the disease
  - Idiopathic hypertrophic subaortic stenosis (IHSS)
  - Muscle subaortic stenosis
  - Hypertrophic obstructive cardiomyopathy (HOCM)

BACKGROUND

- Prevalence of HCM: 1:500 to 1:1000 individuals
  - This occurrence is higher than previously thought, suggesting a large number of affected but undiagnosed people
- Men and African-Americans affected by almost 2:1 ratio over women and Caucasians
- Global disease with most cases reported from USA, Canada, Western Europe, Israel, & Asia
The pathophysiology of HCM involves 4 interrelated processes:

- Left ventricular outflow obstruction
- Diastolic dysfunction
- Myocardial ischemia.
- Mitral regurgitation.
SYSTOLIC ANTERIOR MOTION -SAM

• Subaortic outflow obstruction is caused by systolic anterior motion (SAM) of the mitral valve - leaflets toward the ventricular septum
• SAM is generated by Venturi effect (A drag effect )

LV OUTFLOW OBSTRUCTION IN HCM

❖ Physiological consequences of Obstruction:
❖ Elevated intraventricular pressures.
❖ Prolongation of ventricular relaxation.
❖ Increased myocardial wall stress .
❖ Increased oxygen demand.
❖ Decrease in forward cardiac output.
Hypertrophic Cardiomyopathy

Asymmetric septal hypertrophy without obstruction

Asymmetric septal hypertrophy (ASH)

Mitral valve in normal position

Cavity reduced in size

Hypertrophic Cardiomyopathy

Asymmetric septal hypertrophy with obstruction

Blood leaks back through mitral valve = mitral regurgitation

Mitral valve presses against septum causing obstruction to blood flow

ASH

Systolic anterior motion of the mitral valve (SAM)
PATHOPHYSIOLOGY OF HCM

- **Diastolic Dysfunction:**
  - Contributing factor in 80% of patients.
  - Impaired relaxation.
    - High systolic contraction load.
    - Ventricular contraction relaxation not uniform.
  - Accounts for symptoms of exertional dyspnea.
    - Abnormal diastolic filling increased pulmonary venous pressure.
PATHOPHYSIOLOGY OF HCM

Myocardial Ischemia:
- Often occurs without atherosclerotic coronary artery disease.
- Postulated mechanisms:
  - Abnormally small and partially obliterated intramural coronary arteried as a result of hypertrophy.
  - Inadequate number of capillaries for the degree of LV mass.

Mitral Regurgitation:
- Results from the systolic anterior motion of the mitral valve.
- Severity of MR directly propotional to LV outflow obstruction
- Results in symptoms of dyspnea, orthopnea in HCM patients
MICROSCOPY

- The microscopy of HOCM demonstrates:
- Myocyte hypertrophy.
- Myocardial fibre disarray.
- Interstitial and perivascular fibrosis.
- Intimal and medial hypertrophy in intramural arteries.
- These changes lead to LV diastolic dysfunction by impairing relaxation and reducing compliance and scarring of the myocardium.
GENETIC BASIS OF HCM

- Autosomal dominant trait
- Mutation usually in B-myosin heavy chain, myosin binding protein C and cardiac tropnin T.
- > 450 mutation in 13 cardiac sarcomere & myofilament-related genes identified.
GENETICS OF HCM

<table>
<thead>
<tr>
<th>Table 1: Causative Genes in Hypertrophic Cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Encoded Protein</strong></td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>β-Myosin heavy chain</td>
</tr>
<tr>
<td>Myosin-binding protein C</td>
</tr>
<tr>
<td>Troponin T</td>
</tr>
<tr>
<td>Troponin I</td>
</tr>
<tr>
<td>α-Tropomyosin</td>
</tr>
<tr>
<td>Regulatory Myosin light chain</td>
</tr>
<tr>
<td>Essential Myosin light chain</td>
</tr>
<tr>
<td>Actin</td>
</tr>
<tr>
<td>Titin</td>
</tr>
<tr>
<td>Muscle LIM protein</td>
</tr>
<tr>
<td>Telethonin</td>
</tr>
<tr>
<td>Myxin-2</td>
</tr>
<tr>
<td>Vinculin</td>
</tr>
</tbody>
</table>

CLINICAL PRESENTATION

- **Dyspnea on exertion (90%), orthopnea pnd.**
- **Angina (70-80%).**
- **Syncope (20%), presyncope (50%).**
- **Outflow obstruction worsens with increased contractility during exertional activities.**
- **Sudden cardiac death.**
- **HMC is the most common cause of SCD in young people, including athletes.**
PHYSICAL EXAMINATION

- **Carotid Pulse:**
  Bifid – short upstroke & prolonged systolic ejection.

- **Jugular venous pulse**
  Prominent a wave – decreased ventricular compliance.

- **apical Impulse:**
  Double or triple.

- **Heart Sounds**
  S4 usually present due to hypertrophy

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PHYSICAL EXAMINATION

- **Murmur:**
  * Medium – pitch crescendo – decrescendo systolic murmur along LSB without radiation.

- **Dynamic maneuvers:**
  * Murmur intensity increases with decreased preload (i.e. Valsalva).
  * Murmur intensity decreases with increased preload (i.e. squatting, hand grip)
DYNAMIC MURMUR OF HOCM

- Smaller LV volume brings septum closer to anterior MV leaflets: more obstruction and louder murmur.

- Larger LV volume separates upper septum from anterior MV leaflets, less obstruction and softer murmur.

HOW TO ALTER LV VOLUME

- **Increase LV volume:**
  * Squatting
  * Isometric Handgrip
  * Beta Blockers
  * Phenylephrine
  * Passive leg lifting
  * Slow heart rate
  * IV volume infusion

- **Decrease LV volume:**
  * Stand (after squatting)
  * Valsalva maneuver
  * Amyl nitrate
  * Nitroglycerin
  * Increase heart rate
  * Volume depletion
  * Isoproterenol
  * Exercise
PHYSICAL EXAMINATION IN HCM

DIAGNOSTIC EVALUATION

- Electrocardiogram.
- Echocardiogram.
- Catheterization.
ELECTROCARDIOGRAM IN HCM

ECHOCARDIOGRAPHY IN HCM
TRANSESOPHAGEAL ECHO

Coronary Angiography demonstrates septal bulge on LV cavity.

Hyperdynamic systolic function results in almost complete obliteration of the LV cavity.
CARDIAC MAGNETIC RESONANCE

- CMR demonstrates myocardial scarring, which differentiates HCM from other LV hypertrophies.
- CMR is indicated when ECHO views are limited due to unusual distribution of hypertrophy, or to detect milder magnitudes of hypertrophy.
- CMR with gadolinium enhancement imaging will detect myocardial scarring in about two thirds of HOCM patients.

DILATED CARDIOMYOPATHY
INTRODUCTION

IDIOPATHIC DILATED CARDIOMYOPATHY

EPIDEMIOLOGY

- ANNUAL INCIDENCE: 5-8/100,000
- PREVALENCE: 36/100,000

INCREASED RISK ASSOCIATED WITH:
  * MALE GENDER.
  * BLACK RACE.
  * HYPERTENSION.
  * CHRONIC BETA-AGONIST USE.
CAUSES

- **ISCHEMIC**: 50% atherosclerosis, Kawasaki disease, anomalous origin of left coronary artery.
- **IDIOPATHIC**: 45%.
- **HEREDITARY**: 25-35% autosomal dominant, autosomal recessive, X-linked, mitochondrial.
- **ACUTE AND CHRONIC MYOCARDITIS**: coxsackievirus, HIV, adenovirus.
- **AUTOIMMUNE DISEASES**.
- **CHRONIC TACHYCARDIA**.

- Drugs: alcohol, sympathomimetics, anthracyclines.
- End-stage hypertrophic cardiomyopathy.
- Endocrine: growth hormone deficiency, hyperthyroidism, hypothyroidism, hypocalcemia, diabetes mellitus, pheochromocytoma.
- Inborn error of metabolism.
- Muscular dystrophies.
- Nutritional deficiency: selenium, carnitine, thiamine.
- Peripartum.
- Structural heart disease.
- Systemic hypertension.
- Toxins: cobalt, lead.
PATHOLOGY

- **Cardiac dilatation**
  - ? Adaptive – due to increased loading conditions.
  - idiopathic DCM – maladaptive.

- **Myocellular hypertrophy and cell death**
  - cardiac hypertrophy - adaptive response (increase in collagen content preserves myocardial performance).
  - cumulative loss of myofibrils and cardiac myocytes: apoptosis, cellular necrosis & decrease in the wall thickness.

- **Extracellular matrix remodeling**
  - Cardiac fibroblast proliferate.
  - Mechanically stable cross linked collagen is degraded by metalloproteinases.
  - Excess of poorly cross-linked collagen is deposited into interstitium.
  - Increased myocardial mass, interstitial fibrosis, ventricular dilatation.
IDIOPATHIC DILATED CARDIOMYOPATHY
PATHOLOGIC FINDINGS

GENETICS

Sarcomere

Sarcolemma

Cytoskeleton

Nucleus
MOLECULAR DEFECTS IN DILATED CARDIOMYOPATHY

GENES:
- Lamin A/C
- σ-sarcoglycan
- Dystrophin
- Desmin
- Vinculin
- Titin
- Troponin-T
- α–tropomyosin
- β – myosin heavy chain
- Actin
- Mitochondrial DNA mutation
<table>
<thead>
<tr>
<th>Gene†</th>
<th>Protein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMNA</td>
<td>Lamin A/C</td>
<td>Structure/stability of inner nuclear membrane; gene expression</td>
</tr>
<tr>
<td>MYH6</td>
<td>Alpha-myosin heavy chain</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>MYH7</td>
<td>Beta-myosin heavy chain</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>MYPN</td>
<td>Myopalladin</td>
<td>Sarcomeric protein; Z-disc</td>
</tr>
<tr>
<td>TNNT2</td>
<td>Cardiac troponin T</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>SCN5A</td>
<td>Sodium channel</td>
<td>Controls sodium ion flux</td>
</tr>
<tr>
<td>MYBPC3</td>
<td>Myosin-binding protein C</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>RBM20</td>
<td>RNA-binding protein 20</td>
<td>RNA-binding protein of spliceosome</td>
</tr>
<tr>
<td>TMPO</td>
<td>Thymopoietin</td>
<td>Also LAP2, a lamin-associated nuclear protein</td>
</tr>
<tr>
<td>LAMA4</td>
<td>Laminin alpha 4</td>
<td>Extracellular matrix protein</td>
</tr>
<tr>
<td>VCL</td>
<td>Metavinculin</td>
<td>Sarcomere structure; intercalated discs</td>
</tr>
<tr>
<td>LDB3</td>
<td>LIM domain-binding 3; cypher: Z-band</td>
<td>Cytoskeletal assembly; clustering of membrane proteins</td>
</tr>
<tr>
<td></td>
<td>alternatively spliced PDZ motif-containing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>protein</td>
<td></td>
</tr>
<tr>
<td>TCAP</td>
<td>Titin-cap; telethonin</td>
<td>Z-disc protein that associates with titin; sarcomere assembly</td>
</tr>
<tr>
<td>PSEN1/2</td>
<td>Presenilin 1/2</td>
<td>Transmembrane proteins; gamma secretase activity</td>
</tr>
<tr>
<td>ACTN2</td>
<td>Alpha-actinin 2</td>
<td>Sarcomere structure; anchor for myofibrillar actin</td>
</tr>
<tr>
<td>CRYAB</td>
<td>Alpha B crystallin</td>
<td>Cytoskeletal protein</td>
</tr>
<tr>
<td>TPM1</td>
<td>Alpha-tropomyosin</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>ABCC9</td>
<td>Sulfonylurea receptor 2A</td>
<td>Kir6.2 regulatory subunit; inwardly rectifying cardiac potassium ATP channel</td>
</tr>
<tr>
<td>ACTC</td>
<td>Cardiac actin</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>PDZLIM3</td>
<td>PDZ LIM domain protein 3</td>
<td>Cytoskeletal protein</td>
</tr>
<tr>
<td>ILK</td>
<td>Integrin-linked kinase</td>
<td>Intracellular serine-threonine kinase; interacts with integrins</td>
</tr>
<tr>
<td>TNNC1</td>
<td>Cardiac troponin C</td>
<td>Sarcomeric protein; muscle contraction</td>
</tr>
<tr>
<td>TNNI3</td>
<td>Cardiac troponin I</td>
<td>Sarcomeric protein; muscle contraction; also seen as recessive</td>
</tr>
<tr>
<td>PLN</td>
<td>Phospholamban</td>
<td>Sarcoplasmic reticulum calcium regulator; inhibits sarco/endoplasmic reticulum calcium-ATPase pump</td>
</tr>
<tr>
<td>DES</td>
<td>Desmin</td>
<td>DAGC; transduces contractile forces</td>
</tr>
<tr>
<td>SGCD</td>
<td>Delta-sarcoglycan</td>
<td>DAGC; transduces contractile forces</td>
</tr>
<tr>
<td>CSRP3</td>
<td>Cysteine- and glycine-rich protein 3;</td>
<td>Sarcomere stretch sensor/Z-discs</td>
</tr>
<tr>
<td></td>
<td>muscle LIM protein</td>
<td></td>
</tr>
<tr>
<td>TTN</td>
<td>Titin</td>
<td>Sarcomere structure/extendible scaffold for other proteins</td>
</tr>
<tr>
<td>EYA4</td>
<td>Eyes absent 4</td>
<td>Transcriptional coactivator</td>
</tr>
<tr>
<td>ANKRD1</td>
<td>Ankyrin repeat domain-containing protein 1</td>
<td>Cardiac ankyrin repeat protein; localized to myopalladin/titin complex</td>
</tr>
<tr>
<td>DMD1</td>
<td>Dystrophin</td>
<td>DAGC; transduces contractile force</td>
</tr>
<tr>
<td>TAZ/G4.5</td>
<td>Tafazzin</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
FAMILIAL DILATED CARDIOMYOPATHY
COMMON ASSOCIATED ABNORMALITIES

- Conduction system disease.
- Skeletal muscle myopathy or muscular dystrophy.
- Autosomal dominant inheritance pattern is most common.
- Recessive, X-linked, mitochondrial.
- Extracardiac manifestations:
  - Sensorineural hearing loss
  - Neutropenia

DIAGNOSIS

- ECG.
- CXR.
- 2D_ECHO.
HISTOPATHOLOGY OF ACUTE LYMPHOCYTIC MYOCARDITIS

DILATED CARDIOMYOPATHY
ELECTROCARDIOGRAPHIC FINDINGS

- Disease Etiology: pathologic Q_waves
- Ischemic cardiomyopathy: 10/12 (83%)
- Idiopathic cardiomyopathy: 2/21 (10%)
SEGMENTAL WALL MOTION ABNORMALITIES IN DILATED CARDIOMYOPATHY

- Regional wall motion abnormalities observed in at least 50% of patients with non-ischemic causes of dilated cardiomyopathy.
- Most frequent wall motion abnormalities: anterior wall and apex.
- Posterior and lateral walls most likely to be preserved.
- Type of abnormality:
  - Hypokinesis (83%)
  - Akinesis (11%)
  - Dyskinesis (6%)
- Heterogeneity in regional oxidative metabolism using C_{11} acetate clearance has been demonstrated in DCM.

MRI

- Black blood images: enlarged cardiac chambers and thin myocardial walls.
- Cine images: show LV hypokinesia, increased volumes (end diastolic volumes that constitute a dilated CMP > 140 mL for the LV and >150 mL for the RV.
- Phase–contrast sequences: impaired diastolic function. Transvalvular flow may be characterized by a restrictive pattern.
- Late gadolinium enhancement.

Non Ischemic Cardiomyopathy
### ISCHEMIC DCM

#### Table: Comparison of Idiopathic Dilated Cardiomyopathy (DCM) vs Ischemic Dilated Cardiomyopathy (IDCM)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Idiopathic Dilated Cardiomyopathy (DCM)</th>
<th>Ischemic Dilated Cardiomyopathy (IDCM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Past History of CAD</strong></td>
<td>Should be absent</td>
<td>Present in most</td>
</tr>
<tr>
<td><strong>Antecedent fever, systemic illness</strong></td>
<td>May be present</td>
<td>Not relevant</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Angina uncommon</td>
<td>Angina may be present</td>
</tr>
<tr>
<td><strong>ECG</strong></td>
<td>Generally not useful; Q waves are more common in IDCM.</td>
<td>Diffuse q waves not confining to an arterial territory may suggest idiopathic DCM. Please remember q waves are not synonymous with infarct. It can occur with scars, fibrosis, extreme atrial enlargement (Cavity potential)</td>
</tr>
<tr>
<td><strong>X-ray chest</strong></td>
<td>Global Cardiomegaly</td>
<td>More of LV configuration</td>
</tr>
<tr>
<td><strong>ECHO</strong></td>
<td>4-chamber dilatation</td>
<td>LV, LA dilatation predominant</td>
</tr>
<tr>
<td><strong>Wall motion defect</strong></td>
<td>Uniform Global Hypokinesia</td>
<td>Global hypokinesia with regional variation</td>
</tr>
<tr>
<td><strong>Myocardial scars</strong></td>
<td>Less common (More of thinning)</td>
<td>Significant scars, Random and patchy. (Makes CKT difficult)</td>
</tr>
<tr>
<td><strong>Mitral regurgitation</strong></td>
<td>Usually present (Central jet)</td>
<td>Often present (Occasional jet common due to differential papillary muscle involvement)</td>
</tr>
<tr>
<td><strong>Diastolic dysfunction</strong></td>
<td>Often restrictive</td>
<td>Grade 1 or 2 (Rarely restrictive)</td>
</tr>
<tr>
<td><strong>RV dysfunction (RVO)</strong></td>
<td>High incidence (True myopathies do not differentiate RV and LV)</td>
<td>Less common (RVO is due to spiral muscle sharing between RV and LV)</td>
</tr>
</tbody>
</table>

*www.dreamslides.co.in*
DIFFERENTIATION OF ISCHEMIC FROM NON-ISCHEMIC DCM

<table>
<thead>
<tr>
<th></th>
<th>Idiopathic dilated cardiomyopathy (DCM)</th>
<th>Ischemic dilated cardiomyopathy (DCM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary angiogram</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usually normal. Minor lesions may be present.</td>
<td>Extensive lesions common</td>
<td></td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response to medical therapy better.</td>
<td>Medical management + A revascularisation procedure must be done whenever possible.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Diastolic dysfunction more difficult to tackle).</td>
<td></td>
</tr>
<tr>
<td><strong>Response to CRT</strong> (Cardiac resynchronisation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable</td>
<td>Less favorable</td>
<td></td>
</tr>
<tr>
<td>(Dysynchrony is uniform. And predictable. Hence easy to tame it by wires)</td>
<td>(Dysynchrony is random and chaotic. Scar interference an issue)</td>
<td></td>
</tr>
<tr>
<td><strong>Natural history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highly variable</td>
<td>Usually predictable</td>
<td></td>
</tr>
<tr>
<td>Complete recovery to rapid downhill possible</td>
<td>Progressive</td>
<td></td>
</tr>
<tr>
<td>Mean prognosis better</td>
<td>(Response to resynchronisation not uniform)</td>
<td></td>
</tr>
<tr>
<td><strong>Risk of Sudden cardiac death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No major difference. VTs more common with scarred IDC. Severity of LV dysfunction primary determinant.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Survival</strong> (Mayo clinic data 2000 with care)</td>
<td>77%</td>
<td>55%</td>
</tr>
</tbody>
</table>

*Diagnosis of idiopathic DCM depends upon the efforts we make to arrive at a specific diagnosis. Almost all idiopathic DCM in a peripheral hospital can become a specific cardiomyopathy in a teaching hospital. Hence the primary aim in every patient with DCM is to identify reversible cause (Connective tissue disorder, Alcohol, toxins, etc.). **Coronary angiogram is probably indicated in every patient with DCM** to rule out potential ischemic etiology. (Gated SPECT is a good option in patients at low risk of CAD).

**Presence of diabetes, HTN, and chronic kidney disease modifies the behavior of myocardium to a great extent. In fact, there can be an important overlap between DCM/IDCM if the above conditions are associated. Many times differentiation between these two entities is purely an academic pursuit, as management, strategies, and outcome are more similar than different.*

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**Myocardial Scar Photography by MRI**

**Ischemic DCM**
- Regional Sub-Endocardial
- Transmural

**Non Ischemic DCM**
- Mid Myocardial Focal
- Epi-Cardial
- Diffuse Sub-Endocardial

*Idiopathic DCM
Myocarditis
HOCM
Amyloidosis
Fabry’s
Chagas*
RESTRICTIVE CARDIOMYOPATHY

Disorder characterized by primary decrease in ventricular compliance resulting in impaired ventricular filling during diastole.
The myocardium is partially infiltrated by noncontractile tissue or extracellular material.

This infiltration of the myocardium impaired ability of the heart to dilate.
ETIOLOGY

- **Infiltrative causes**: Amyloid, sarcoid.

- **Noninfiltrative causes**: Idiopathic, scleroderma.

- **Other causes**: Hemochromatosis, diffuse interstitial fibrosis, sarcoidosis, post radiation fibrosis, metastatic tumors, inborn errors of metabolism.

*Horizontal cross-section of the heart. The heart is hypertrophic and the light colored masses observed in the ventricular wall are amyloid deposits.*
MORPHOLOGY

• **Ventricles**: normal/ slightly enlarged cavities – not dilated
• **Myocardium**: firm and noncompliant.
• **Atria**: biaxial dilation.
• **Microscopy**: interstitial fibrosis.

CLINICAL FEATURES

- Usually causes diastolic dysfunction.
- *Patients have signs and symptoms of CHF with prominent right sided features*.
ENDOMYOCARDIAL FIBROSIS

- Fibrosis of ventricular endocardium and subendocardium.
- Extends from apex upward often involving tricuspid and mitral valves.
- Children and young adults.
- Africa & other tropical regions.
ENDOMYOCARDIAL FIBROSIS

- Fibrous tissue markedly diminishes the volume and compliance of affected chambers
- Induces a restrictive functional defect.
- Ventricular mural thrombi & fibrous tissue results from its organization.
- Etiology unknown