Myocardial Diseases

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objectives

- classify myocardial diseases into three major phenotypes
- describe their clinical presentation during the initial encounter
- delineate the diagnostic process and the role of different tests
- interpret these results in the context of pathophysiology
- employ the stages of heart failure to delineate therapeutic steps

advanced heart failure

patient-physician encounter

Doc, can you help me with my advanced heart failure?

patient

team

history/exam/tests?

patho(physio)logy/etiology?

prognosis/therapy?

economics?

time

age, sex & heart failure

cardiomyopathy phenotypes

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy

systems biology strategy

- level distinction
- relationships within levels
- relationships between levels
- iterative strategy

epidemiology

- cancer
- AHF medical
- months after diagnosis

macroscopic pathology

- hypertrophic cardiomyopathy
- normal
- dilated cardiomyopathy

Cardiomyopathy phenotypes

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy

NYPH
Hammer Health Sciences Building
transgenic animals

Cardiac Compartment-specific Overexpression of a Modified Retinoic Acid Receptor Produces Dilated Cardiomyopathy and Congestive Heart Failure in Transgenic Mice

specific cardiomyopathies

- Ischemic
- Valvular
- Hypertensive
- Inflammatory (Idiopathic, Autoimmune, Infectious)
- Metabolic (Endocrine, Amyloid)
- General system Disease (Connective Tissue Disorders)
- Muscular Dystrophies
- Neuromuscular Disorders
- Sensitivity and Toxic Reactions
- Peripartum

ischemic dilated cardiomyopathy

initial presentation

- 55 y male
- married, 2 kids
- large anterolat wall AMI
- 10/31/04 Impella pump
- 11/03/04 HeartMate 1 MCSD
- evaluation for heart transplant
- 2/17/05 heart transplant

follow-up

- Stable post-transplant course
- Back to work and normal life

teaching points

- Benefits of hi-tech medicine

GE #4734815 *1950 m

dilated cardiomyopathy

- history
  - fatigue, lightheadedness, exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea
- physical exam
  - cardiomegaly, low blood pressure, tachycardia, diffuse atrial impetus, SS, systolic mitral murmur, pulmonic gallop, diastolic co persistence, jugular venous distention, hepatosplenomegaly, axilla, peripheral edema
- diagnostic tests
  - chest radiograph
  - ECG
  - echocardiography
  - cardiac catheterization
  - biopsy
**Xray inflammatory myocarditis**

**Teaching points**
- Reversible cardiomyopathy

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**Xray giant cell myocarditis**

**Teaching points**
- Rapidly progressive cardiomyopathy

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**Initial presentation**
- 26 y male
- Married, previously healthy
- Flu-like syndrome x 3 weeks
- Biventricular failure
- Evaluation for MCSD and heart transplant

**Follow-up**
- Stable recovery
- Close follow-up

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**Initial presentation**
- 33 y male
- Single, cyclist
- Autoimmune disposition
- Biventricular failure
- Evaluation for MCSD and heart transplant

**Follow-up**
- MCSD 2/02
- Stroke
- Heart transplant 4/02
- LAD-occlusion 5/004
- Giant cell recurrence 7/05
- Retransplantation 10/05
- Stable recovery

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**endomyocardial biopsy**

**macroscopic pathology**

- Normal
- Dilated cardiomyopathy

**idiopathic dilated cardiomyopathy**

- Masson trichrome stain
- Extensive interstitial fibrosis (blue) with myocytes in red and epicardial fat/pericardium to the left

**idiopathic dilated cardiomyopathy**

- Hematoxylin & eosin stain:
  - Myocyte hypertrophy (very enlarged and irregular nuclei)

**myocarditis**

- Inflammatory infiltrate in the myocardium associated with myocyte damage
myocarditis

inflammatory infiltrate in the myocardium associated with myocyte damage

giant cell myocarditis

multinucleated giant cells

chagas disease

Trypanosoma cruzi
Amastigotes

Columbia University College of Physicians & Surgeons

dilated cardiomyopathy

- pathology
  - enlargement of all four chambers, mild hypertrophy, interstitial fibrosis
- pathophysiology
  - Frank-Starling mechanism, neurohormonal activation, myocardial remodeling
- etiology
  - genetic, infectious, inflammatory, toxic, metabolic, neuromuscular

AHF pathophysiology & therapy

- adrenergic system
  - renin-angiotensin system
- natriuretic system
  - cytokine system
- growth hormone
  + organ failure -
  + cachexia -
  + congestion -
  + hypoperfusion -
  + afterload -
  + preload -
  + contractility -
  + heart rate -
  + remodeling -
  + ischemia -
  + arrhythmia -
heart failure & remodeling

- preload:
  - stroke volume
    - normal
    - moderate HF
    - severe HF

- afterload:
  - stroke volume
    - normal
    - moderate HF
    - severe HF

- contractility:
  - stroke volume
    - normal
    - moderate HF
    - severe HF

- cardiac cycle:
  - pressure
    - LV pressure
    - RV pressure
    - ECG

- transcriptome>proteome>phenotype

- gene
  - cell
  - organ
  - organism
  - asymptomatic
  - symptomatic
  - wall stress
  - fibrosis
  - reentry
  - automaticity
  - triggered activity
**dilated cardiomyopathy**

- **prognosis**
  - 1-year survival 10-90%, 5-year survival 50%
  - Improved with active therapy

- **therapy**
  - underlying cause, relief of congestion, augmentation of cardiac output, prevention of arrhythmias and thromboemboli

**Framingham Study - mortality**

- No ALVD (EF >50%), no HF history
- MHE ALVD (EF 40% to 50%)
- Mod.-Severe ALVD (EF <40%)
- Systolic HF (EF <50%)

![Framingham Study - mortality graph](image)


**CHF stages and steps of treatment**

- **Stage A** High risk with no symptoms
- **Stage B** Structural heart disease, no symptoms
- **Stage C** Heart failure, prior or current symptoms
- **Stage D** REF in severe symptoms, requiring special intervention

- Systolic only
- Systolic & diastolic

- VAD, TX, Isotropes, nesiritide
- Mitrail or CARG surgery
- Short-term isotrope, neosinilide
- Aldosterone antagonists
- CRT, ICD if applicable
- ACE inhibitors and beta-blockers in all patients
- Aldosterone antagonists

**quality vs quantity**

- **quantitative**
  - quantity

- **qualitative**
  - quality

- ideal life

**giant cell myocarditis**

**initial presentation**
- fever
- RUL, RR, rapid heart, 2 LDE, DMO 5L
- CK-MB, ECG, C3, C4, ANA, anti-nuclear antibodies, anti-jo1, Kappa, Lambda
- Giant cell myocarditis: biopsy or echocardiograph
- Immunocompromised treatment
- HIV/AIDS heart transplant evaluation
- HIV/AIDS heart transplant evaluation

**follow-up**
- Nodular or nodular transplanted cause
- EKG/CT/CI/SA/ECG + PPM
- PT/INR/PTTH/PTTH + INR/PTTH
- DVT/MI/PTTH (dual base)
- VAD/MD
- CRT/ ICD (atypical PPM)
- Thrombus/AVC/ABT (transonic PPM)

**teaching points**
- high degree of suspicion for GCM

**initial presentation follow-up**
- 49 y female
- ICU nurse, married, 2 kids, BMI 22
- 8/21/01 HAV, typhoid vaccination
- Giant cell myocarditis> BV HF & arrhythmias
- immunosuppressive treatment
- 9/5/2001 heart transplant evaluation
- 10/1/01 heart transplant
- stable early post-transplant course
- 7/26/02 AV-block II > PPM
- 12/22/02 NSVT > defibrillator
- 5/5/06: ISHLT 3A/2R (Steroid Pulse)
- 12/16/06 LVEF: 65%
- MMF: 750 BID, CSA 150 BID, Pred 2QD
- Pravachol, Norvasc, Lasix
- "The Grateful Heart"
- Myocarditis Foundation

**MC #4533193 *1951 f**

- high degree of suspicion for GCM
cardiomyopathy phenotypes

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy

hypertrophic cardiomyopathy phenotypes

- autosomal dominant trait
  - 2/3 of patients have family history
  - more than 200 mutations in 10 genes encoding contractile sarcomeric proteins
  - two genes for non-sarcomeric proteins and mitochondrial genome

HCM mutation frequencies

- 44 y female
- heart murmur since childhood
- married, 4 kids
- 3/6/06 mitral valve repair & myectomy
- 3/8/06 mitral valve replacement
- complicated postoperative course

- HOCM surgically challenging

Teaching points

- initial presentation
- follow-up
- surgical/mortality outcomes

- initial presentation
- diagnostic testing
- management

- follow-up
- symptoms
- imaging
- medications

- teaching points
- non-sarcomeric, mitochondrial proteins

- initial presentation
- symptoms
- diagnostic testing
- treatment

- follow-up
- symptoms
- imaging
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- teaching points
- non-sarcomeric, mitochondrial proteins

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- teaching points
- non-sarcomeric, mitochondrial proteins
**hypertrophic cardiomyopathy**

- **history**
  - sudden death during vigorous exercise
  - angina, dyspnea

- **physical exam**
  - S4, systolic murmur (LVOT obstruction – increased by Valsalva, MR)

- **diagnostic tests**
  - X-ray
  - ECG (LAH, LVH)
  - Echocardiogram (asymmetric hypertrophy)
  - Cardiac catheterization (LVOT gradient)
  - Genetic testing

- **teaching points**

**cardiomyopathy phenotypes**

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy
**amyloidosis cardiomyopathy**

**PRIMARY:** amyloid light chain (AL)
- lambda: kappa = 2:1

**SECONDARY:** serum amyloid A (AA)

**SENILE CARDIAC:** (SCA); transthyretin

**FAMILIAL:** autosomal dominant with mutations in transthyretin, gelsolin, apolipoprotein A-I, lysozyme, or fibrinogen genes.

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**iron storage disorders**

- Iron overload – Hemosiderosis – following multiple blood transfusions.
- Hereditary Hemochromatosis
  - Autosomal recessive
  - *HFE* gene on chromosome 6
  - Increased intestinal absorption of dietary iron

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**restrictive cardiomyopathy**

**initial presentation**
- 51 y male
- banker, 2 kids
- rapidly progressive heart failure
- heart transplant evaluation
- heart transplantation 2003
- autologous stem cell transplantation (CAMP9)

**follow-up**
- successful post-heart/stemcell transplant course
- initial presentation follow-up
- amyloid-related cardiomyopathy DD
  - challenging
  - teaching points

**teaching points**
- restrictive cardiomyopathy
- fatigue, exercise tolerance ↓
- physical exam
  - rales, neck veins ↑
  - ascites, peripheral edema, KUSMAUL SIGN
- diagnostic tests
  - Xray: normal sized heart, congestion
  - ECG: ST/T-changes, a-fib, AB-block, BBB
  - echocardiography
  - endomyocardial biopsy

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**restrictive cardiomyopathy**

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hypertrophic cardiomyopathy normal
dilated cardiomyopathy

macroscopic pathology

concentric hypertrophy

microscopic pathology HCM

myocyte disarray

microscopic pathology amyloid

Amyloid encircling a myocyte (original magnification, x1890)

Amyloid: 7-10 nm fibrils haphazardly arranged

Congo Red stain of amyloid deposits in the heart

Congo Red stain under polarized light: Amyloid deposits are birefringent.

Microscopic pathology amyloid

Macroscopic pathology amyloid

Microscopic pathology amyloid

Microscopic pathology amyloid
Endomyocardial Biopsy: Iron storage disease in the heart

Iron deposits in myocytes and interstitial macrophages
Prussian Blue stain: Iron is blue

Iron storage disease

Columbia Presbyterian 1872

Hypertrophic Cardiomyopathy

Pathology
Asymmetric septal hypertrophy, myocardial fibers in disarray, compensatory hypertrophy and fibroblast proliferation

Pathophysiology
Compliance and relaxation reduced, dynamic LV outflow tract obstruction, abnormal motion of the anterior mitral leaflet

Etiology
Sarcomere complex mutations (b-myosin heavy chain, cardiac trop T, myosin-binding protein C), resultant diastolic dysfunction

Restrictive Cardiomyopathy

Pathology
Abnormally rigid ventricles (not necessarily hypertrophied), endocardial fibrosis or scarring or myocardial infiltration

Pathophysiology
Upward shift of passive ventricular filling curve > elevated pulmonary and systemic venous pressures
Reduced cavity size > stroke volume/cardiac output

Etiology
Infiltrative: amyloidosis, sarcoidosis
Storage disease: hemochromatosis, glycogen storage disease
Endocardial fibrosis
Hypereosinophilic syndrome
Metastatic tumors
Radiation therapy
Noninfiltrative: scleroderma, idiopathic

Compliance

Filling pressure

Normal (diastolic filling)
Hypertrophy

Filling volume
LV outflow tract obstruction

- Hypertrophic cardiomyopathy
  - Prognosis:
    - Sudden death: 4-6% per year (children), 2-4% (adults)
  - Therapy:
    - Avoid strenuous exercise
    - Beta-blockers (myocardial oxygen demand, LVOT gradient ↓)
    - Calcium channel antagonists
    - Amiodarone (a-fib)
    - Antibiotics prophylaxis
    - Septal ablation with ethanol injection

- Restrictive cardiomyopathy
  - Prognosis:
    - Very poor prognosis
  - Therapy:
    - Salt restriction
    - Diuretics (cautious use)
    - Maintenance of SR
    - Intra-arterial thrombus: anticoagulation

- Amyloidosis management

Entrance
summary cardiomyopathies

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Braunwald E. Heart Disease (4th Ed). Saunders, Philadelpia

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top 10 controversies

- classification or staging
- risk stratification
- choice of BB/ACEI
- role of added ARB
- risks of aldo-antagonists
- role of infusion therapy
- indication for ICD
- indication for CRT
- timing of MCSD
- selection for Hx

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deng lab

http://cardiactransplantresearch.cumc.columbia.edu