Infiltrative and Restrictive Cardiomyopathy: Recognition by Echo

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Restrictive Cardiomyopathy

- Least common of the cardiomyopathies
- The cardiac chambers cannot stretch normally = stiff/noncompliant
- Filling is restricted
- Normal LV and RV size,
- Atrial enlargement – reflects increased ventricular filling pressures/atrial pressure

Pathophysiology of Restrictive Cardiomyopathy

- Rigid myocardium
- Ventricular filling
- Decreased stroke volume
- Jugular vein distention
- Hepatomegaly and ascites
- Peripheral edema
- Weakness
- Fatigue
90% x small EDV = small SV

Rise in PCWP
Flat stroke volume response to exercise
### Familial types of cardiomyopathy

<table>
<thead>
<tr>
<th>HCM</th>
<th>ECM</th>
<th>ARVC</th>
<th>RCM</th>
<th>Unclassified</th>
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</thead>
<tbody>
<tr>
<td>1. Obstructive hypertrophic cardiomyopathy (diabetic heart disease)</td>
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<td>2. Restrictive cardiomyopathy (drug-induced)</td>
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<td>3. Arrhythmogenic (surgical)</td>
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<td>4. Other</td>
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### Non-familial types of cardiomyopathy

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<td>1. Hypertrophic cardiomyopathy</td>
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<td>2. Diastolic cardiomyopathy</td>
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<td>3. Ischemic</td>
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<td>4. Idiopathic dilated cardiomyopathy</td>
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Case 1: The Admiral
Diagnosis?

- Amyloidosis
- Sarcoidosis
- HCM
- Other
### Diagnosis?

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### The Systemic Amyloidoses

- **Primary (AL) or light chain disease**
  - Plasma cell dyscrasia
  - Immunoglobulin light chains
  - 12 month survival without treatment
  - 6 month survival with cardiac disease
- **Familial (AF)**
  - Mutations in transthyretin (TTR)
  - Ile 122 of particular interest

### The Systemic Amyloidoses

- **Senile systemic amyloid (SSA)**
  - TTR-based non-genetic (i.e., TTR normal)
  - Cardiac predilection
  - Male gender, onset after age 60
- **Secondary amyloidosis (AA)**
  - Chronic inflammatory states
Amyloid Cardiomyopathy

- Very poor prognosis (6 mo survival)
- Restrictive cardiomyopathy with profound abnormalities of diastolic function
  - Systolic dysfunction late manifestation
- Classic teaching
  - Biventricular thickening in a small ventricle
  - Valvular thickening
  - Atrial enlargement
  - Pericardial effusion/evidence of elevated filling pressures

Amyloid Cardiomyopathy

- Patients do NOT respond to normal medication for CHF
  - ACE inhibitors, beta-blockers, dig
- There is a treatment for AL amyloid
  - Autologous bone marrow transplant
- Patient selection critical
  - Assessment of cardiac involvement

Continuum of Amyloid

- Advanced disease is too late
- Initial changes are abnormalities of diastolic function
- As wall thickness progresses restrictive physiology ensues
- Systolic dysfunction late stage
Case 2: The Attorney

HPI

- 58 year old male who presented with dizziness and presyncopal symptoms with possible fall and left leg pain, numbness and swelling in both lower extremities.
- Patient reported that at 1:30 am, he had gotten out of bed, felt dizzy and went down to the floor due to weakness. He denied LOC but noted that he was on the floor for approx. 30 minutes before he got himself back to bed. He noticed that there was urine on the floor.
- He called his HCP who arrived at his home at 4am and sent him to the ED.
- The patient denied chest discomfort, SOB or palpitations.
- The patient also reported LBP radiating from his left buttock down through the back of his LLE for 3 weeks while he was in Florida. He had driven back to Worcester at 7pm the night of admission and continued to have left leg pain, numbness and swelling in both lower extremities.
Past Medical History

- Paroxysmal a-fib with hx of RVR 11/16/2005
- NSTEMI, demand 11/16/2005, peak troponin of 11.5. 1 prior other demand NSTEMI.
- Normal left and right heart cath 11/18/2005
- Stage IV CKD
- Streptococcal Group G beta hemolytic bacteremia 6/16/2009
- LLE cellulitis 6/16/2009
- Asthma, mild
- Gout
- Severe frostbite of hands
- Severe neuropathy
- Gout
- Anemia
- Secondary hyperparathyroidism
What is the etiology of the patient’s hypertrophic cardiomyopathy?

- Stage 4 CKD
- Peripheral neuropathy with loss of temperature and pin prick.
- Prior 10/29/09 note mentioned the below skin lesions on abdomen and upper legs:

![Image of skin lesion]

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Clinical Problems That Should Raise Suspicion of Fabry Disease

| Table 1: Clinical Problems That Should Raise Suspicion of Fabry Disease*

| Fabry Disease Cardiac Manifestations |

- Left ventricular hypertrophy
- Hypertrophic cardiomyopathy, generally symmetric.
- Conduction defects: Short PR interval, QT prolongation often with RBBB, tachyarrhythmias, SCD.
- Aortic root dilatation
- Aortic and mitral valve insufficiency
- Ischemic disease, either due to endothelial dysfunction, microvasculature dysfunction or secondary to severe LV hypertrophy.

Echo Findings

- A thickened hyperechogenic layer, which represents intracellular glycolipid deposition in the endocardium and the subendocardial myocardium.
- A hypoechogenic layer that parallels the hyperechogenic layer all along the ventricular contour, which represents either the mildly affected midwall myocardium or possibly a shadowing artifact due to the intracellular lipid-rich layer.
LVH Screening

- Those who also have a binary appearance of the LV endocardial border.
- Among patients who have hypertrophic cardiomyopathy, particularly if symmetric, those with either no family history of HCM or a family history consistent with X-linked disease.
- Measurement of plasma alpha-galactosidase A.

Histopathologic changes in a small cutaneous blood vessel showing vacuolation of endothelial and smooth-muscle cells (periodic acid–Schiff stain).

Long Term effects of Enzyme Replacement Therapy on Fabry Cardiomyopathy: Evidence for a Better Outcome With Early Treatment

- 32 patients over 3 years receiving ERT
- Matched with 20 age-matched healthy controls
- Underwent MRI, echocardiography, color doppler myocardial imaging studies and bicycle stress tests at baseline and every year.
- Patients assigned to 3 groups depending on amount of fibrosis
- Patients with fibrosis in one LV segment were in mild fibrosis group
- 14 patients had hypertension, all were almost normotensive  
Fabry, LVH and HCM

- 3% (7/230) of middle aged men with LVH had Fabry’s disease (10% of unexplained)  
- In patients with Fabry disease
  - 50% no LVH
  - 37% concentric LVH
  - 10% asymmetric LVH
  - 3% eccentric LVH  
- 4% of patients (6/153) with HCM had Fabry’s Disease  
  Sachdev B. et al Circulation. 2002;105:1407-1411

Diagnosis

- Blood test to measure the level of α-galactosidase A activity  
  - this may be misleading in female carriers due to the random nature of X-inactivation
- Genetic Testing  
  - chromosomal analysis of the GLA gene  
  - many mutations (>300)  
  - gold standard
- Kidney biopsy  
  - for proteinuria

MRI of 3 typical Fabry patients at baseline

- Patient “No Fibrosis”  
- Patient “Middle Fibrosis”  
- Patient “Severe Fibrosis”
Case 3: The Industrial Chemist

28 y/o M with PMHx of HTN p/w chest pain for last 4 days.
- Chest pain constant, dull, worse with inspiration.
- Denies SOB, orthopnea, PND, palpitations, presyncope, n/v.
- No URI sx$s, but son has active URI.

EKG on arrival

NB: EKG completely normal 6 months ago
Echocardiography

Echo

Normal LV systolic size, thickened walls c/w HCM or infiltrative CMP. LVEF 50%.
Small pericardial effusion.
RV hypertrophic mildly dilated with mildly reduced systolic function.
Normal biatrial size. Grade 1 diastolic dysfunction.
Mild to moderate TR.
ECHO
thick walls—15-17 mm
normal LV size
high relative wall thickness
high LV mass index

Troponin trend

CORONARY CIRCULATION:
There was no angiographic evidence for coronary artery disease.
LVEDP 27.

ECHO
LVIDd 49 mm
FS 25%
BSA = 1.8 m²
CO = \pi \times (1.05 \text{ cm})^2 \times 12.1 \text{ cm} \times 84
CI = \frac{3.4}{1.8} = 1.9 \text{ L/min/m}^2

LABS trend:

**BMP Trend**

**Troponin and BNP trend**
Right Heart Cath

- RA: 19 mm Hg
- PA: mean 33 mm Hg
- PCWP: 24 mm Hg
- C.O by TD: 2.92 L/mt
- C.I: 1.58 L/mt
- RA sat: 46%
- PA sat: 41%

- Post IABP insertion: plus Milrinone 0.38 + Levophed 0.02
- PA sat: 57.6%

Biopsy Guidelines:

Cooper et al, Circulation. 2007;116:2216-2233;

Diagnosis:

FINAL PATHOLOGIC DIAGNOSIS: EMBRYOPHAGIA (RIGHT VENTRICLE), BISESS: MULTIPLE MICROVASCULAR MYOCARDITIS

Note: There is extensive inflammatory infiltrate with associated myocyte injury.

The inflammatory infiltrate is primarily composed of lymphocytes, macrophages and eosinophils. This myocarditis is best classified as acute necrotizing eosinophilic myocarditis (ANE). Giant cells are not observed. ANE is sometimes initiated by a hypersensitivity reaction. Giant cell myocarditis can not be definitively excluded, but is not favored.
Hospital course: OSH

- Started on high dose steroids, ABG on arrival 7.10/66/450. IABP removed, continued on ECMO. Repeat echo showed EF 15%. Wide complex bradycardia with rate in 20s. Placed on hypothermic protocol.
- 12/28 – started on CVVH
- 1/2 - ECMO Decanulated.

Take home points: ANEM

- Myocardial wall thickening is due to edema and Not LVH, as shown by decreased wall thickness on repeat ECHO.
- Pericardial effusions more common.
- Initiate immunosuppression early if suspicion is high and infection is not suspected. Usual doses of Hydrocortisone 100 q8h for days and then taper to prednisone PO.
- Any amount of supportive treatment may be needed.
- Myocardium can recover in DAYS on steroids.
- Response is re-assessed with repeat biopsy
- Goal is to find the lowest possible doses to suppress eosinophilic activity.
- 6 monthly ECHO as end organ damage is independent of eosinophilia.

ANEM Pathophys - 3 stages

1) Acute Necrotic Stage (2-3 weeks):
   infiltration and extracellular deposition of eosinophils and consequently IL-5 mediated injury.

2) Thrombotic Stage: layered thrombus along damaged endocardium due to activation of tissue factor by eosinophils, cerebral thromboemboli common

3) Fibrotic Stage: Myocardial fibrosis
ANEM

- **Epidemiology:** Occurs in previously healthy individuals, ~ 0.1% of all myocarditis cases
- **Diagnosis:** biopsy
- **Prognosis:**
  - Usually fatal, early mortality 38%
  - Diagnosis usually confirmed on autopsy
- **Treatment:**
  - Early diagnosis and treatment with corticosteroids is crucial for survival.
  - If suspicion is high for ANEM, initiation of therapy should not be delayed for biopsy results

Restrictive Cardiomyopathies

- Amyloidosis
- Loeffler’s
- Fabry’s disease