Clinical history

- 73 yo man with chest pain
- Systemic hypertension and WG
- Stress EKG N
- Stress echocardiogram:
  - Concentric hypertrophy
  - Hypokinesis of LV-Inf
- Cardiac catheterization: no CAD
Complications:

- Usually minor

Cardiac perforation with tamponade:

- 4/1,300: no surgery, no deaths
- 4 (0.7%) possible and 3 (0.5%) definite: 2 (0.4%) death
Processing

- 4-6 pieces
- Clinical information
- Anthracycline cardiotoxicity:
  - All for electron microscopy
- Cardiac transplant rejection:
  - All for light microscopy
  - 3 H&E levels
Processing

- Diagnostic:
  - 4 pieces for LM:
    - 2 H&E levels
    - 1 amyloid stain (sulfated alcian blue)
    - 1 iron stain
  - 1 piece for EM optional
  - 1 piece frozen optional
  - Myocarditis: 10 H&E levels
Immunohistochemical study:

Protein P + 
Transthyretin +
SAA -
Light chains -
B2- microglobulin -

Transthyretin
Diagnosis

CARDIAC AMYLOIDOSIS, SENILE TYPE
Amyloidosis

- Heterogeneous group of disorders
- Deposition of amyloid:
  - 95% protein in abnormal fibrillar form:
    - Histology and EM uniform
    - Chemically variable
  - 5% serum amyloid P protein and sulfated glycosaminoglycans
## Amyloidosis

<table>
<thead>
<tr>
<th>Major proteins</th>
<th>Clinical syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AL (light chains)</strong></td>
<td>Primary amyloidosis</td>
</tr>
<tr>
<td>AL</td>
<td>Local nodular amyloidosis</td>
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<tr>
<td>AA</td>
<td>Reactive amyloidosis</td>
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<tr>
<td><strong>Transthyretin (N)</strong></td>
<td>Senile systemic amyloidosis</td>
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<tr>
<td>Transthyretin (M)</td>
<td>Hereditary amyloidosis</td>
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<tr>
<td><strong>Beta 2 microglobulin</strong></td>
<td>Hemodialysis-associated amyloidosis</td>
</tr>
<tr>
<td>A beta</td>
<td>Senile amyloidosis of brain</td>
</tr>
</tbody>
</table>
Cardiac amyloidosis

• 4 major forms of clinical significance:
  – Primary 75%  $\lambda / \kappa$ light chains
  – Senile 20%  Transthyretin (N)
  – Familial <5%  Transthyretin (M)
  – Secondary <5%  Amyloid A protein

• 1 form of unknown clinical significance:
  – Isolated atrial  80-90%  AANF
Analysis of EMB

Mayo Clinic 1997-2002 n=455

- Hypertrophy: 69%
- Amyloidosis: 16%
- Myocarditis: 7%
- Other: 8%
- Neoplasm: 0.4%
Cardiac amyloidosis

- Immunohistochemical study:
  - Protein P
  - Kappa/ Lambda
  - Protein A
  - Transthyretin
  - Beta-2-microglobulin
  - Albumin
Primary amyloidosis
Clinical manifestation

- 40-60 years old
- Protean, systemic and cardiac
- RCM:
  - CHF right-sided
  - Low QRS on EKG
  - Echo with sensitivity of 87%:
    - Ventricular wall thickening, small ventricular cavity, enlarged atria and atrial pressures
    - Granular sparkling
Primary amyloidosis
Clinical manifestation

• Arrhythmia with conduction system
• Ischemic heart disease with:
  – Normal coronary angiogram
  – Obstruction of intramyocardial vessels
• Valvular heart disease
Primary amyloidosis

- Plasma cell dyscrasia:
  - 5-15% myeloma
  - Monoclonal gammopathy:
    - Serum and/or urine
    - 10% “non-secretor”
  - With or without tumor mass

- Light chain: Lambda

- Poor prognosis:
  - Median 12-15 mos
  - Cardiac death 50%
Senile systemic amyloidosis

- > 80 years old
- Usually asymptomatic
- Mainly cardiac symptoms
- Similar to primary
- Transthyretin
- Prognosis:
  - Median 5 years
  - Cardiac death
Familial amyloidotic cardiomyopathy

- > 60 years
- Limited to heart
- Transthyretin
- Black population:
  - 3.9% with mutant gene
  - Point mutation transthyretin gene
Indications of EMB

- **Primary amyloidosis:**
  - Extra-cardiac biopsies + 55%
  - Echocardiogram c/w 68%
  - Indicates poor survival

- **Distinguish senile from primary:**
  - “Non-secretors” 10%
  - Co-existence of both
  - Different prognosis and treatment
Differential diagnosis of RCM

- **Myocardial:**
  - Non-infiltrative:
    - Idiopathic
    - Familial
  - Infiltrative:
    - Amyloidosis
    - Sarcoidosis
  - Storage disease:
    - Hemochromatosis
    - Fabry

- **Endomyocardial:**
  - Fibrosis
  - Hypereosinophilic syndrome
  - Metastatic cancer
  - Carcinoid heart disease
  - Anthracycline toxicity

- S/O constrictive pericarditis
Histologic differential diagnosis

Fibrosis

Amyloid
Histologic differential diagnosis

Fibrosis

Amyloid
Histologic differential diagnosis
Histologic differential diagnosis

Fibrosis

Amyloid
Take home messages

- Protean disease
- Several cardiac forms
- SAB and immunohistochemical study