Amyloid Heart Disease: Diagnosis & Treatment

Sitaramesh Emani, MD
Advanced Heart Failure & Cardiac Transplant

Relevant Disclosures

- St. Jude Medical (Thoratec)
  - Consultant
  - Grant Funding

- Gilead
  - Grand Funding

- Boston Scientific
  - Advisory Board

- CareDx
  - Advisory Board

- I will discuss investigational agents
Amyloid Review

- Defined by the deposition of abnormal fibrils
  - Misfolding of proteins causing insolubility
    - Abnormal β-sheet cross formation
  - Abnormality a common final finding – various underlying causes
  - Deposition into organ tissue leads to dysfunction

- Pathognomonic feature is apple green birefringence on Congo Red staining

Wechalekar AD, et al., Lancet 2016;387:2641-54

Amyloid Review

- Light-chain amyloid (AL)
  - Related to plasma cell dyscrasias (MGUS, myeloma)
- Hereditary amyloid
  - Often liver based
- Transthyretin
  - Familial ATTR or wild-type ATTR
- Reactive amyloid (AA or SAA)
  - Secondary to chronic inflammatory conditions
- Senile amyloidosis (SSA)
Amyloid Review

- Many organs can be affected
- Cardiac involvement associated with increased morbidity and mortality
- High prevalence of cardiac involvement, especially with certain types
  - AL
  - ATTRwt

Clinical Findings

- Can affect many/multiple organs
- Cardiac involvement most associated with M&M
- Non-cardiac involvement
  - Kidneys
  - Neuropathy
  - GI system
Clinical Cardiac Findings

- Development of restrictive cardiomyopathy
- Right-heart failure symptoms
- Low cardiac output
- Hypotension

When to suspect amyloid

- "Classic Findings"
  - Macroglossia
  - Periorbital purpura
  - Low-voltage EKG
  - Speckled pattern on echocardiogram
  - Unanticipated/unexpected LV thickening

- In presence of other problems
  - Renal disease (especially proteinuria)
  - Hematologic disease (MGUS, myeloma)
  - Unexplained neuropathy with heart failure symptoms
Role of Cardiac Imaging

- Echo findings:
  - LV thickening
  - Increased echogenicity of myocardium (“sparkling”)
  - Preserved EF
  - Pericardial effusion
  - Diastolic abnormalities/restrictive pattern

- Findings not specific to amyloid
Cardiac MRI

- Key component of evaluation
- Major feature: diffuse, sub-endocardial LGE
- 4 chamber thickening

Biopsies

- “Tissue is the issue”
- Pathological specimen needed to evaluate subtype
  - Mass spectroscopy
- Any potentially involved organ is fair game
  - Fat pad – poor negative predictive value but easy to get
  - Rectal biopsy
  - Endomyocardial biopsy
- Biopsies are not 100% sensitive
Treatment of Cardiac Amyloid

- Standard GDMT
  - No/poor evidence to support use
  - Difficult to tolerate for most (hypotension)

- Supportive/symptomatic therapies
  - Diuretics (sometimes need combination therapy)
  - But also pre-load dependent

- Device Therapy
  - Increased risk of SCD/ventricular arrhythmias
  - However, primary prevention ICD survival benefit unclear
  - Bradycardia risk with evidence of conduction disease

Stanford Protocol for ICD

Treatment of Amyloid

• Current strategies
  – RNA inhibitors
  – Fibril formation stabilizers & inhibitors
  – Immunotherapeutic targeting of fibrils

• Therapy in conjunction with hematology

• Dependent on type of amyloid

Therapies for Amyloid

• AL type
  – Chemotherapy aimed at plasma cells
  – Doxycycline – reduces light chain fibril formation

• ATTR
  – Liver transplant if discovered early
  – Combined heart-liver if a candidate
    • Unfortunately, disease often discovered late in process
  – Diflunisal (NSAID) – binds and stabilizes fibrils
  – Tafamidis – protein stabilizer (in clinical trials)
  – RNA inhibitors – reduce production (in early trials)
References


Zhao L, Fang Q. Recent advances in the noninvasive strategies of cardiac amyloidosis. Heart Fail Rev 2016.

Thank you
Silaramesh.emani@osumc.edu