TTR Amyloid: Cardiac Symptoms and Issues

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Introduction

Heart's electrical system:

Heart Problems with ATTR:

• Cardiomyopathy
• Heart Failure
• Arrhythmia
  – Heart rate is too slow
  – Heart rate is too fast
  – Atrial fibrillation

Cardiomyopathy

• Greek derivation:
  – Kardia → heart
  – Mys → muscle
  – Pathos → suffering
• WHO: “diseases of the myocardium associated with ventricular dysfunction”

Amyloid Cardiomyopathy

• Heart becomes too thick due to amyloid
• Typically affects all portions of the heart, but the ventricles (bottom chambers) are the most important.
• Strength of the heart (ejection fraction) can be normal, high, or low.
• The heart gets very stiff.
### TTR Amyloid Cardiomyopathy
- Cardiac involvement varies substantially among different TTR mutations.
- Val122Ile – prominent cardiac disease, typically recognized age 60 and later.
- Val30Met – cardiac problems tend to be less severe than neuropathy, but electrical heart problems (“heart block”) often occur despite transplant.

### Other problems that make the heart too thick:
- Hypertrophic cardiomyopathy (HCM)
  - IHSS (idiopathic hypertrophic subaortic stenosis)
  - HOCM (hypertrophic obstructive cardiomyopathy)
  - ASH (asymmetric septal hypertrophy)
- Hypertension
- Aortic stenosis

### Heart Failure
- The heart is not able to pump blood adequately to meet the demands from the rest of the body.
- Exercise / At rest
- It’s a “clinical diagnosis,” meaning that it is determined by a blood test or echocardiogram.

### Heart Failure Symptoms
- Shortness of breath (SOB)
- Fatigue
- Swelling (abdomen, ankles)
- Unable to lie down due to SOB
- Awakening during the night due to SOB
- Wheezing
- Coughing
- Lack of appetite

### Arrhythmia
- Heart goes too slowly (bradycardia).
  - Defined as less than 60 beats/minute, but not typically treated unless there are symptoms.
- Heart goes too quickly (tachycardia).
  - Defined as greater than 100 beats/minute.
  - Lots of different types (SVT, VT, sinus tach)
  - Usually treated
- Heart is out of rhythm (atrial fibrillation)
  - Top chambers (atria) have disorganized electrical activity.

### Atrial fibrillation:
- Very common (>5% of people >age 65)
- Frequent in cardiac amyloid and in all forms of heart failure.
- Complications:
  - Worse heart failure
  - Heart goes too fast or too slowly
  - Blood clots in the atria, which can then cause a stroke or clotted blood vessels.
Symptoms of arrhythmia

- “Syncope” (fainting, passing out)
- Palpitations
- Lightheadedness
- Shortness of breath
- Fatigue

Tests to find amyloid in the heart

- Discord between EKG:
  - Not amyloid
  - Amyloid
- And echocardiogram: 2 cm wall thickness for both

Tests to find amyloid in the heart

- Discord between EKG and echo
- Cardiac MRI may suggest it
- Heart biopsy, which is far less painful than a biopsy of a nerve.

Risks of heart biopsy

- Infection (rare)
- Damage to a blood vessel (rare)
- Electrical problems:
  - Electrical delay in the heart (bundle branch block; rare)
  - Extra heart beats (common)
- Hole in the heart (~1:1000)

Useful blood tests for heart disease in TTR amyloid:

- Troponin – a protein that comes from the heart. Normally it is not detected in the blood. In amyloid, low levels are very common. This can look like a heart attack.
- BNP or ProBNP – another protein from the heart, usually with very low level in blood. Heart failure (among other things) can increase this level.

Treatments: Medications

Commonly used for HF:

- Beta blockers
- ACE-inhibitors
- Angiotensin receptor blockers
- Digoxin
- Diuretics

Cardiac Amyloid:

- Mechanisms for those medications to help are mostly not applicable in amyloid.
- Digoxin may be particularly harmful for people with amyloid.
- Diuretics are usually very helpful for symptoms.
Atrial fibrillation - treatment

- Medications to help maintain normal rhythm
- Cardioversion (electrical shock to restore normal rhythm)
- Prevent heart from going too fast
- Blood thinners to help prevent strokes
  - Coumadin
  - Aspirin
  - Newer agents (Pradaxa, soon Apixaban)

Treatment of arrhythmias

- Pacemakers can be very helpful for slow heart rates or severe electrical heart block.
- Defibrillators:
  - Pacemaker-like devices that shock the heart if it goes too fast;
  - Likelihood of firing
  - Pros and cons
  - Personal decision

Natural remedies

- Both soy and curry have been shown (in massive amounts) to inhibit amyloid deposition, leading several people to ask me whether they should use these as treatment.

Other therapies...

Cardiac transplantation

- About 1,600 performed yearly in the USA
- Number on waiting lists is far greater
- Eligibility depends on many factors; amyloid generally excludes consideration unless liver transplant is also done.
- Imunosuppression, rejection, infections, and blockage of blood vessels are long term problems after transplant.
Left Ventricular Assist Device

- Mechanical pump attached to the heart, assisting with circulation.

Newer devices:

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Survival with LVADs

Problems with LVADs

- Need for continuous external power
- Infections through skin opening to connect to power source
- Gastrointestinal bleeding
- Only supports the left ventricle, not the right. Larger Bi-Ventricular Assist Devices are not portable.
What's next?

Total artificial heart (ie, Abiocor)

Summary

• Heart problems commonly occur for people with TTR amyloid.
• The most effective treatment right now is to get rid of congestion (diuretics) and prevent the heart from going too fast or too slowly.
• Technological improvements in care for end-stage heart failure are making mechanical support more feasible.