Transplantation for TTR Amyloidosis 2011

Steve Zeldenrust, MD, PhD
Mayo Clinic

Scottsdale, Arizona
Rochester, Minnesota
Jacksonville, Florida
Rationale

• Why liver transplant?
  • Removing source only known cure
  • Majority of circulating TTR made in liver
  • Not for asymptomatic gene carriers

• What about transplanting other organs?
Liver Transplant

• First liver transplant performed in Sweden 1990

• The FAP World Transplant Registry:
  • Updated 12/31/09
  • 1782 OLT performed worldwide
  • 120 transplants/year
  • Portugal, France and Sweden account for over two-thirds
Outcomes

• Low mortality rate (3%)

• Predictors of outcome:
  • mBMI
  • Disease duration (?)
  • Mutation (V30M vs non-V30M)
  • Autonomic neuropathy
V30M Outcomes

- Neuropathy stable or improved in up to 40%
- Nutrition improves in up to 80%
- Cardiac progresses in ~50%
- Kidney involvement unaffected
- Eye deposits progress
Non-V30M Outcomes

- Small numbers make prediction difficult (n=108)
- Neuropathy – autonomic most likely to improve, sensory variable
- GI improves in most
- Eye and brain can worsen due to local production of variant TTR
Non-V30M Outcomes

• Cardiac progresses in many

• Evidence that pace of deposition can increase after transplant

• Cardiac deposits develop in those with no heart involvement at dx.

• New deposits contain normal TTR made by transplanted liver
Heart Transplant in ATTR

• FAPWTR:
  • Liver + heart 19
  • Liver + previous heart 8
  • Liver + sequential heart 1
  • Liver + heart + kidney 1
Heart Transplant in ATTR

• Outcomes similar to other indications for heart transplant

• Some centers advocating combined heart/liver transplant in non-V30M

• Controversy over timing (combined vs. sequential)
Kidney Transplant in ATTR

- Kidney involvement in most at diagnosis
- Only symptomatic in ~10%
- FAPWTR: Liver + kidney 39
- Survival worse than liver alone, but related to low mBMI
What Does It All Mean?

- Known:
  - Survival improved with liver transplant in V30M
  - Most effective if early
  - Major benefit is nutrition
  - Combined liver + heart and liver + kidney feasible
What Does It All Mean?

- **Unknown:**
  - When is it futile?
  - Which mutations benefit?
  - If heart involved need combined heart + liver?
  - Is amyloid halted, slowed, reversed or accelerated?
Implications

• ATTR clear indication for liver transplant
• Early and accurate diagnosis critical
• Possibility of domino shortens wait time
• Need for multiple organs lengthens wait time
Future Directions

- Better follow-up needed to answer important questions (disease progression, etc.)
- Impact of new treatments (alternative to transplant vs. adjunct to transplant)