Transplantation for Amyloidosis: 18 Years Later

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Rationale

• Why liver transplant?

• What about transplanting other organs?
Liver Transplant

- First liver transplant performed in Sweden 1990

- The FAP World Transplant Registry:
  - Updated 6/30/09
  - 1523 OLT performed worldwide
  - 110 transplants/year
  - Portugal, France and Sweden account for nearly two-thirds
Outcomes

• Low mortality rate (4%)

• Predictors of good 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 worsen
Non-V30M Outcomes

• Small numbers make prediction difficult (n=100)

• 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 5
  - 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 43

• 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)
Other Types of Amyloidosis

• AFib:
  • Synthesized exclusively in the liver
  • Liver + kidney due to extensive kidney involvement
  • Excellent outcomes
Other Types of Amyloidosis

- AApoAI and AApoAll:
  - Pace of deposition very slow
  - Affected organ replacement effective
  - May benefit from liver transplant