When to refer, when to list Pediatric PH patients for Lung Transplantation?

Overview

- Setting the Stage
- PAH survival and quality of life 2013
- Ins and Outs of Lung Transplantation in 2013
- Assessing the Individual PH Patient
- Knowing your Transplant Centers
- Transparency and Eschewing Paternalism

Definitions

- HLT = heart-lung transplantation
- BLT = bilateral lung transplantation
- SLT = single lung transplantation
- TXP = transplant

Disclosures

- Honorarium for consultation with Actelion, Inc
Pediatric PH Clinical Care in 2013
- Challenge of timely diagnosis remains, except in many NICU settings
- Clinical experience and published commentaries have mushroomed in the past decade
- Experience with and number of therapies available have increased with understandable clinical optimism about improvement in morbidity and mortality
- Exciting research into mechanisms of disease and new avenues of therapy

Reality of PH Clinical Care and Therapy in 2013
- Mortality is still common among the pediatric PH population and the ultimate outcome of a sizable portion of our patients
- Predictability is still often difficult
- Higher absolute and relative mortality on lung transplant lists for PH compared with PH or any other cause
- Lung transplant remains the only curative therapy for PH

Key Aspects of Pediatric PH Relevant to Lung Transplantation
- Subsets with unique pathophysiology and more rapid disease progression
- Pulmonary vein stenosis, especially idiopathic type
  - Pharmacotherapy – which agents, how long?
  - STL transplant experience with lung transplant
- Early childhood idiopathic PAH: more rapidly progressive?
- PVOD in childhood
- ALK-1 mutations of HHT
- Use of pharmacotherapy with accumulating experience in the pediatric age group

More Challenges of Pediatric PH
- Van Loon and Berger, 2009: commonly associated with co-morbidities and syndromes
- Beghetti, 2011: CHD-associated PH carries anatomic issues and previous surgery
- Lammers 2011: functional class is a huge challenge across childhood; comparability across age ranges?
Experience with Lung Transplantation for Pediatric PH
- 23 recipients from 25 centers between 1996 and 2006
- 19/23 on epoprostenol, 14 in WHO FC IV, 6 in WHO FC III, 2 on ECMO
- After transplantation, median time on vent 9 days, time in ICU 11 days, hospital 30 days
- 91% survival at 6 mos
- Median survival was 45 months

Schaellibaum, Pediatr Pulmonol, 2011

Pulmonary Vein Stenosis vs Pulmonary Atresia in St. Louis

Therapies for Pulmonary Arterial Hypertension
- Pharmacotherapy options in 2013 largely slow the progression of a fatal disease in idiopathic and familial PAH with marked inter-individual variation
- New therapeutic options on the horizon
- Lung transplantation alone cures PH albeit in return for a new and daunting life-limiting health situation

Trends in Pediatric Lung Transplantation in the USA over Time
Volume of HLT vs BLT vs SLT 1991-2011: All Ages Worldwide

AGE DISTRIBUTION OF PEDIATRIC HEART-LUNG RECIPIENTS BY YEAR

Comparative Survival after Adult Lung Transplantation by Underlying Dx

Transplants for PAH by Operation over Time: all ages

Conclusions: fewer transplants for PAH over time and more BLT; HLT is becoming a rare operation.
Operative Options in 2013 for Pulmonary Hypertension

- Experience with single lung transplantation and HLT now has given way to bilateral lung transplantation
- Even though early post-transplant period can be very rocky with higher incidence of primary graft dysfunction, bilateral lung transplant has been adopted in most centers
- Severe right ventricular dysfunction is almost always recoverable
- Few surgeons have a deep abiding affection for heart-lung transplantation

Assessing the Individual Pediatric Patient with PAH

- Prognostication from the onset
  - Pulmonary vein stenosis, when idiopathic and progressive, has very poor prognosis
  - Pulmonary veno-occlusive disease
  - Diagnosis with severe RV failure
- Every newly diagnosed child with IPAH should know therapeutic options—pharmacotherapy and lung transplantation

Initial Education of the Child with IPAH

- Indication for lung transplantation for any disease process is worsening disease in the face of maximal medical therapy
- Contraindications: HLA sensitization with RV conduit, homografts and blood transfusions, pulmonary atresia with MAPCAs
- Adequate familial resources, including insurance
The Child with Severe RV Failure at diagnosis

- High mortality
- Role of VA ECMO – usually a contraindication in most programs, destination therapy to rest right ventricle and institute therapy??
- Berlin Heart as a right ventricular assist device
- LPA to aortic vascular shunt
- NovaLung with central cannulation
  - Pulmonary circulation largely circumvented
  - Patient can be ambulatory
  - Inherent danger of hemorrhage (STL and TCH)

The PH Lung Transplant Candidate

- Medical therapy optimized = most patients will be on parenteral prostanoid and at least one oral agent with relentless RV failure
- No other major co-morbidities
- Viable surgical approach
- Committed family support system
- A record of adherence to complex regimen

Child with Progressive PAH: The trajectory of disease

- Assessing RV function serially – multiple modalities
- Growth and development
- Assessing exercise capacity
- Measuring quality of life

Assessing Pediatric Lung Transplant Centers

- Assess patient volume: waiting list size and duration of wait, patients transplanted per year, deaths on the wait list, access to trustworthy clinicians caring for patient on the list, post-operative survival
- Look at age range for transplant centers
- Join patient and family on conference call with transplant center if appropriate
Pediatric Lung Transplant Volume Dominated by Adolescents

JHLT, October 2012

Transplants versus Waiting List Deaths
US Pediatric Lung Transplant Programs, 2007-2011

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Conclusions:
- Impressive differences among centers in terms of risk of death versus likelihood of transplant.
- More active centers have lower death rate on waiting list.
- Death on wait list correlates with size of wait list.
- Referring physicians and families often not provided this information although readily available on UNOS.org.

Kaplan-Meier Survival Curve for Lung Transplantation: Adult versus Pediatric

Aurora P. J Heart Lung Transplant, 2011

HLT and BLT in Children < 5 yrs of age in Six US Pediatric Centers, 2006-2012
The Spectrum of Pediatric Lung Transplantation in USA

- Marked variation in volume, waiting time, deaths on waiting list and avidity for young transplant recipients among centers
- Insurers may narrow family choice
- Geographic concerns may narrow choice
- Need for new centers
  - Cincinnati
  - UCSF

Survival after Lung Transplant

- Survival has improved over time but remains significantly below achievements in other organs
- Most survivors have high quality of life
- Biology of the transplanted lung remains daunting in terms of rejection and infection
- Easy for physicians to underestimate parental valuation of the dream of conquering a child’s disease and the value of a few years of health

Transparency

- PH clinicians need to be honest with themselves and families, treading between over-optimism and over-pessimism in treatment and prognosis
- Transplant centers need to be transparent with referring physicians and patients/families
- UNOS data quite revealing if accessed
- Beware the temptation of paternalism
- Refer early, especially age < 12 yrs
Conclusions

- Despite advances, pediatric PH is often a lethal diagnosis
- There are few pediatric lung transplant centers worldwide and marked variations in activity and policy among centers
- Lung transplantation is only cure for PH
- Advances in survival have been disappointing even as the quality of life of most survivors is high
- Improvement in care and survival will continue