Pulmonary Hypertension Associated with Congenital Heart Disease: What You Need to Know

Emma Olson, CPNP
Oregon Health & Science University
Portland, OR

Disclosures

• No financial disclosures
• I will be discussing the off-label use of several medications that are not FDA approved for use in pediatrics

Learning Objectives

• Review normal cardiac and pulmonary pressures
• Review pathophysiology and etiology for pulmonary hypertension associated with congenital heart disease
• Review both acute and chronic pulmonary hypertension treatment strategies

Normal Physiology Review

• Normal mean PA pressures at rest are <20mmHg
• Normal pulmonary wedge pressure (PAWP) is 5-12mmHg
• Normal transpulmonary gradient <10 mmHg
  \[ TPG = mPAP - PCWP \]
• Normal PVR is <2 Wood units
  \[ PVR = mPAP - PCWP/CO \]
• Left heart pressures vary with age
• Right heart pressures fairly constant after neonatal period
• NEVER normal for PA pressures to rise

Pulmonary Hypertension: Definitions

Pulmonary hypertension (PH)
  \[ mPAP \geq 25mmHg \text{ at rest} \]
Pulmonary arterial hypertension (PAH), a subgroup of PH.
  \[ mPAP \geq 25mmHg \text{ at rest} \]
  \[ \text{end-expiratory PA wedge (PAWP) } \leq 15mmHg, \]
  \[ \text{and a PVR } > 3 \text{ Wood units (after 3mon of age)} \]
Idiopathic or Isolated PAH (IPAH)
  \[ \text{PH with no underlying disease known to be associated with PAH} \]
  \[ \text{Referred to as HPAH with positive family history} \]
Persistent pulmonary hypertension of newborn (PPHN)
  \[ \text{dx only until 2-3 months of age} \]

Pediatric Classifications (Panama 2011): General Categories

1. Prenatal or developmental pulmonary hypertensive vascular disease
2. Perinatal pulmonary vascular maladaptation (PPHN)
3. Pediatric cardiovascular disease
4. Bronchopulmonary dysplasia
5. Isolated pediatric pulmonary hypertensive vascular disease (isolated pediatric PAH)
6. Multifactorial pulmonary hypertensive vascular disease in congenital malformation syndromes
7. Pediatric lung disease
8. Pediatric thromboembolic disease
9. Pediatric hypobaric hypoxic disease
10. Pediatric pulmonary vascular disease associated with other systemic disorders

Del Cerro et al, PVRI Pediatric Taskforce, Panama 2011
Pediatric Classifications

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8. Pediatric thrombotic disease
9. Pediatric hypoxic hypoxic exposure
10. Pediatric pulmonary vascular disease associated with other systemic disorders

Del Cerro et al, PVRI Pediatric Taskforce, Panama 2011

Pulmonary Vascular Disease Pathophysiology

- Increase in pulmonary blood pressure/flow and excessive pulmonary vasoconstriction
- Endothelial dysfunction (endothelial cells are the orchestrators of vascular pathology)
- Chronically impaired production of vasodilators (nitric oxide and prostacyclin)
- Prolonged overexpression of vasoconstrictors (endothelin-1)

Congenital Heart Disease associated PH

- Variable Alterations in pulmonary pressure and flow
- Pulmonary Vascular Changes Secondary to Increase Pulmonary Blood Flow
  - Shear stress to endothelial cells

<table>
<thead>
<tr>
<th>Defect</th>
<th>Risk of PH (%)</th>
<th>Age of onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>20%</td>
<td>&gt;20 years</td>
</tr>
<tr>
<td>VSD</td>
<td>15-20%</td>
<td>&gt;2 years</td>
</tr>
<tr>
<td>PDA</td>
<td>15-20%</td>
<td>&gt;2 years</td>
</tr>
<tr>
<td>Tetralogy</td>
<td>30-100%</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Atroventricular Canal</td>
<td>100%</td>
<td>&gt;2 years</td>
</tr>
<tr>
<td>Tricuspid Arteriosus</td>
<td>100%</td>
<td>&lt;2 years</td>
</tr>
</tbody>
</table>

Assessment of operability for shunt lesions in patients with congenital heart disease and PH

Eisenmenger Syndrome

- Left to right shunting of blood
- Increased pulmonary blood flow
- Irreversible pulmonary vascular injury
- Right to left shunting of blood

Assessment of operability for shunt lesions in patients with congenital heart disease and PH

Assessment of operability for shunt lesions in patients with congenital heart disease and PH

Steven H. Abman et al. Circulation. 2015;132:2037-2099
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General PH Management

- Prevent/treat active pulmonary vasoconstriction
- Support right ventricle
- Treat underlying condition
- Promote regression of structural disease

Pulmonary Hypertension Crisis

- Sudden and potentially lethal
- Acute right-sided heart failure
- Triggered by various stimuli
  - Pain, anxiety, suctioning, hypoxia, acidosis
- Highest risk periods
  - Post-operative period after CHD surgery
  - Rapid withdrawal of PH-specific therapy
  - Intercurrent illness or noncardiac causes
  - Acute lung injury or infection

Pulmonary hypertensive crisis

Recognition of PH Crises

- Sudden increase PA pressure
  - Ratio of PAP to systemic >0.75
  - Increase in CVP >20%
- Decrease in systemic and mixed venous saturation
- Hypotension
  - Decrease >20%
- +/- bronchoconstriction
  - Stiff chest wall, hard to ventilate

Acute Treatment of PH Crisis

- FiO₂ 100%
- Promote alkalosis
  - Hyperventilation
  - NaHCO₃
- Reduce postoperative stress response
  - Narcotic, sedative and muscle relaxant
- Inhaled pulmonary vasodilators
  - INO
  - nebulized PGI₂ (iloprost)
- ECMO

PH Treatment Pathways
**Nitric oxide pathway**

- **Nitric oxide (inhaled)**
  - Vasoreactivity in cardiac cath lab
  - In-patient treatment only

- **PDE 5 inhibitors** (oral):
  - Increases endogenous NO
  - Sildenafil (Revatio): TID or QID dosing (can be used short term for patients who do not tolerate iNO wean)
  - Tadalafil (Adcirca): daily dosing

**Endothelin Receptor Antagonists (ERAs)**

- **Bosentan** (BID dosing)
  - Tracleer – oral
  - Hepatotoxicity, anemia, teratogen
  - Decreases sildenafil effect (25%) (can be used short term for patients who do not tolerate iNO wean)
- **Ambrisentan** (daily dosing)
  - Letairis – oral
  - Hepatotoxicity, anemia, teratogen, edema
- **Macitentan** (daily dosing)
  - Opsumit – oral
  - Hepatotoxicity, anemia, teratogen, edema

**Prostacyclins**

- **Epoprostenol** (continuous IV)
  - Flolan, Veletri
  - Half-life 1-5 minutes
- **Treprostinil** (continuous IV or SQ, inhaled, and oral)
  - Remodulin (IV/SC), Tyvaso (inhaled), Opsumit (oral)
  - Half-life ~4 hours
- **Iloprost** (inhaled)
  - Ventavis
  - Half-life 20-30 min

**Prostacyclins: Side Effects**

- ALL prostacyclins
  - Hypotension, headache, nausea, diarrhea, jaw pain, bone pain, systemic vasodilation, bleeding, body aches, flushing
- Subcutaneous Remodulin
  - Pain at insertion site, worst first 2-7 days of new site
- Iloprost and Tyvaso
  - Cough, bronchospasm especially with URI

**Other PH Medications**

- **Milrinone**:
  - Phospodiesterase III inhibitor
  - Increases RV contractility
  - Reduces RV afterload by inducing pulmonary vasodilation
  - No significant increase in myocardial oxygen consumption

- **Calcium channel blockers**:
  - Consider for patients with adequate vasoreactivity
  - Do not use < 1 yr of age, high RA pressure, low CO

- **Digoxin**

- **Aspirin or Coumadin** (INR 1.5-2)

- **Diuretics**

- **Oxygen**
  - keep PaO2 >60mmHg (sat >92%)

**Support of the Right Ventricle**

- **Reduction in RV afterload**
  - Pulmonary vasodilators
  - Inotropes: milrinone, dobutamine

- **Optimization of RV volume**

- **Augmentation of RV contractility**
  - Inotropes: dopamine, epi, dobutamine, milrinone

- **Increase SVR**
  - Vasopressors: vasopressin, norepi, phenylephrine

- **Creation of right to left shunt**
  - Atrial septostomy, Pott's anastomosis
Questions?

References


Disclosures

• Speaker has no disclosures to report

Learning Objectives

• At the end of this presentation attendees will:
  – Recognize the need for pediatric palliative care for children with congenital heart disease throughout the trajectory
  – Be able to discuss the benefits of pediatric palliative care as it relates to the emergency department and the congenital heart team
  – Understand that a pediatric palliative care team effectively partners with the Emergency Department and Congenital Heart Program.

Pediatric Deaths & Congenital Heart Disease

• Congenital heart disease (CHD) is the most common major congenital anomaly worldwide
  – Heart defects equate to twenty-eight percent of all major congenital anomalies
• In the United States 42,328 children aged 0-19 died in 2013
  – 55% of these deaths were neonates and infants
  – 4.2% of neonatal deaths occur related to congenital heart disease
  – Infant deaths are primarily due to cardiovascular disease and defects
• An estimated 1.4 million adults and 1 million children are living with CHD in the U.S.
• Children and adults of all ages suffer from cardiovascular disease
  – Continues to rank high as cause of death through the lifespan

(References – Freibert & Williams, 2015; CDC, 2016; Gilboa et al, 2010)

Pediatric Palliative Care (PPC)

Palliative Care does NOT necessarily mean hospice...

• Definition of Pediatric Palliative Care
  – Multidisciplinary care that provides an added layer of support for children and their families who suffer from serious, complex, chronic and sometimes terminal disease.

• What can a PPC team do for you and your patients?
  – Care coordination experts
  – Provide multi-disciplinary family and patient support
  – Transition between hospital, home and hospice as needed
  – Provide support for providers and staff caring for seriously ill children
  – Goals of Care clarification
  – Advanced care planning conversations
  – Expert in pain and symptom management
  – Trained in facilitating difficult conversations and decision making

(References – Freibert & Williams, 2015; Weissman & Meier, 2011)

Pediatric Palliative Care

Treat all aspects of pain and suffering

References: Rome, Luminais, Bourgeois & Blais, 2011
Case Study – “Gabriela”

Past Medical and Birth History:
- Diagnosed with Trisomy 18 via prenatal amniocentesis at 4 month
  - Abnormal ultrasound prompted referral to a Maternal Fetal Medicine specialist at a major children’s medical center in Texas.
- 41 year old mother and father given diagnosis of hypoplastic left heart syndrome and double outlet right ventricle
  - They were told “nothing we can do” for her heart defect.
- Gabriela was born at a small regional hospital in coastal South Texas
  - She went home with mother at 3 days old with help of local hospice provider
- At 10 days old Gabriela arrives in our free standing childrens hospital emergency department in central Texas

**Emergency Department**

Current History
- Developed increased work of breathing and eye drainage at 3 days old
  - Oxygen via nasal cannula at home via hospice provider
- Parents were urged to go to our facility for a “second opinion” and treatment by family and friends
- Brought to the ED by car from more than 2 hours away
  - They brought medical records that included hospice and cardiology prenatal consult records
- Vital signs on arrival
  - Afebrile, HR 150’s, BP 85/64, RR 60-70’s, O2 Satuations 60% to 77% with severe subcostal retractions on 2 L nasal cannula oxygen
- ED attending contacts Pediatric Palliative Care on call for help…

“I don’t want to intubate this baby…”

- The ED physician asked for help with
  - Clarification of goals of Care
  - Advanced Care planning
  - Support for the family
- Palliative Care on call provider arrived in ED around 1am.
- Together we clarified social and spiritual history in the ED.
  - Parents are Spanish speaking only
  - 9 year old sister with them who speaks English and translates for parents.
  - Two other siblings in Mexico
  - Parents have strong Christian faith.
  - Strong support network of family, friends and spiritual/Church family.

Shared Decision Making

- Ethical Concepts in Pediatrics
  - Best interest of the child
  - Do no harm
- Shared Decision Making
  - This process “is dependent on collaborative communication and the exchange of information between the medical team and the family.” (Katz & Webb, 2010)
- What are the medical and clinical recommendations?
- Assess knowledge of situation by the parents, family

Goals of Care:
Are they really that different?

- “We want to do the right thing for Gabriela”
  - Wished for natural progression of her disease if there was no intervention that would “save her life.”
- Parents and providers want to prevent excessive “suffering”
  - Was their baby in pain? Was she suffering in any way
- Parents wanted to help Gabriela “live longer” if possible
  - But not if it prolonged her “suffering”.
- Parents worried they had made the “wrong decision” going home with hospice care?
  - Requested a second opinion

Decision Making & Advanced Care Planning

- Education by ED Attending MD, IMU Attending MD and PPC PNP.
  - Parents seemed unsure of diagnosis.
  - Reviewed pathophysiology of congenital heart disease with Trisomy 18.
- Reassurance given to parents by all providers.
- PPC introduces the concept of total "suffering" to the family.
  - Physical, social, psychological and spiritual
- NO code or intubation orders implemented in the ED.
  - Parents requested no more IV sticks

**Clinical Issues**

<table>
<thead>
<tr>
<th>Medical History</th>
<th>Diagnosis</th>
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<tr>
<td></td>
<td>Treatment risks/benefits</td>
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<tr>
<td></td>
<td>Chance ofsuccess</td>
</tr>
<tr>
<td></td>
<td>Treatment options</td>
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**Family Preferences**

- Who is the decision-maker for the child?
- What are you hoping for?
- What do you need right now?

**Contextual Issues**

- Social
- Financial
- Spiritual
- Cultural, Religious
- Legal

References:

Care Coordination: Admitted to Intermediate Care Unit (IMU)

- ED and PPC PNP agree on admission.
  - It was the right thing based on the goals of this family.
- What is the importance of the unit?
  - Nurses are experienced with end of life care.
  - Unit has frequent collaboration with the PPC team.
- PPC provided continuity of care between teams.
  - PNP contacted Cardiology urgently.
  - Educated IMU nursing, residents and attending physician about patient history and plan of care.

Reassessment of Goals: “We want to take Gabriela home…”

- PPC continually reassesses goals for the family after admission.
  - Parents hoped that Gabriela could die at home.
- PPC provides support in the IMU
  - Providers treated dyspnea and other symptoms
  - Care coordination facilitated between teams to ease transition.
  - Social Work helped coordinate with local hospice team.
  - Chaplain actively engaged with this devout Christian family.
  - Child life to help family with Gabriela’s 9 year old sister.

Care Coordination: Urgent Cardiology consult placed

- Early morning echocardiogram was performed.
  - It confirmed hypoplastic left heart syndrome & double outlet right ventricle
- Compassionate education by the Cardiology physician
  - He confirmed initial consult findings and no surgical options.
- He repeated the reassurances made to family earlier that they had “made the right decisions all along…”
  - Parents educated that she may survive weeks to months with her cardiac defect.

Care Coordination: “We want to take Gabriela home…”

- PPC coordinates transfer back to home in collaboration with Cardiology, IMU and hospice providers.
  - Oxygen tank for comfort
  - Morphine to ensure dyspnea and pain
  - Lasix BID PO or NG
  - Nasogastric tube for medications and nutrition
  - Oxygen for comfort
- Gabriela died in dad’s arms shortly after arrival to the home.

Multidisciplinary Support: For care providers

- Support providers for physicians/advanced practice providers, nursing and staff.
  - Goal of “cure” in the ED inconsistent with the outcomes of this case
  - Terminal diagnosis, difficult decisions and conversations
- Adult hospice team was not comfortable with pediatric end-of-life care.
  - Education provided to nurses about care of Gabriela in the home.
  - Reassurance and support to the team to make transitions home seamless.

Palliative Care Through the trajectory of illness...
A few final thoughts

- It isn’t just the child who suffers.
- Referrals to PPC can be made for any age child at any point in the trajectory of congenital heart disease.
- There IS a place for PPC in the Emergency Center.
- PPC teams are uniquely qualified to help both the Emergency Department and the Congenital Heart Teams.

Thank you!

- Contact Information:
  - Tandy A. Mellard, MSN, RN CPNP-PC/AC, CHPPN
  - Pediatric Nurse Practitioner
  - Pediatric Palliative Care
  - University Health System
  - 4502 Medical Drive, San Antonio, TX, 78229
  - tandy.mellard@ush-sa.com
  - 512-804-9439 (cell)

References

Pediatric Mechanical Circulatory Support

Cristina Clawson, MSN, RN, CPNP-AC
Heart Failure, Cardiomyopathy, and Cardiac Transplantation Nurse Practitioner
Department of Pediatric Cardiology, Texas Children’s Hospital
Adjunct Instructor of Pediatrics, Baylor College of Medicine

Disclosures

• I will be discussing off label use of mechanical circulatory support devices in children.

Learning Objectives

• After this session the learner will be able to identify the general risks and benefits of pediatric mechanical circulatory support for severe heart failure.

Overview of MCS

• A ventricular assist device (VAD) is a blood pump that can augment or replace the function of a failing ventricle.
  • The first successful VAD was reported by DeBakey in 1971.
    – General concept: drain left or right heart into pumping chamber followed by ejection of blood into aorta or pulmonary artery
  • VAD support in the adult population has been the standard of care for intractable heart failure for over a decade to provide circulatory support with usual improvement in end organ function
  • Pediatric VAD support options continue to evolve and change the clinical outlook of children with severe heart failure

Who is a VAD candidate?

- Inotropic dependent with suboptimal circulation
- Adequate end organ function
- Appropriate size to device match
- Anatomically feasible
- Able to undergo systemic anticoagulation
- Adequate immune system to minimize infectious complications
- Genetic and Neurologic impairments may preclude candidacy

Device Considerations

- Monitoring ability with accurate flow measurement
- Minimal blood damage in device design
- Manual operation in the event of a power failure or battery backup
- No dead space to cause stagnation or turbulence
- Ability to support cardiac function in a variety of patient sizes
- Amount of anticoagulation required for optimal device performance
Temporary Mechanical Circulatory Support

- Provides assistance to both heart AND lungs
- Can be placed peripherally
- Can cause permanent damage or loss of cervical vessels
- Limited ability for full support via peripheral cannulas often requires central cannulation
- High morbidity and mortality

Photo credit: https://www.nebraskamed.com

RotaFlow

- Only assists heart, lungs provide gas exchange
- Motor spins outside of body to increase blood flow and temporarily improve heart failure symptoms
- Can still provide hemodialysis and plasma exchange through circuit to support other end organs

Photo credit: https://www.maquet.com

Impella

- Percutaneous VAD can be placed in cath lab or OR
- Several different sizes
  - Smallest is 12 Fr at pump motor with max flow of 2.5 L/min
  - Largest can generate 5L/min of flows
- Helps pull blood from LV to aorta to minimize workload of LV

Photo courtesy of Abiomed.com

Durable Mechanical Circulatory Support

- Pulsatile Flow
- Continuous/Axial Flow

Berlin Heart

- First pediatric-specific VAD applied throughout North America for children of all sizes
- Sizes suitable for infants to adolescents
- Can provide biventricular support
- Inflow cannula leads to valved pumping chamber outside of the body and a return cannula
- Pump is driven by external compressor and suction source

Photos courtesy of BerlinHeart, Inc.
Berlin Heart
- Blood enters pumping unit via one way valve. Inside the pumping unit there is a chamber for blood separated from a pressure/suction chamber with a flexible diaphragm.
- Has a programmable percent systole and percent diastole as well as heart rate to optimize patient support.
- Pump chamber can be exchanged for larger size or in the event of clot formation but not without risk.
- Large surface area and pulsatile flow create high risk of thrombosis.

HeartMate II
- Continuous flow with axial design.
- Surgically placed within the chest cavity with inflow connected to LV and outflow connected to aorta.
- Driveline tunnels from patient abdomen to controller and battery pack for mobility.
- Lower incidence of thromboembolic events due to continuous flow.
- Allows for improved rehabilitation and lifestyle, able to be discharged, return to school/work.

HeartWare HVAD
- Continuous flow with centrifugal design.
- Integrated inflow and outflow attachment with only one moving part.
- Delivers up to 10L/min of flow.
- Preload dependent and afterload sensitive to ensure adequate flows.
- Much smaller than HeartMate II.

Total Artificial Heart
- Replaces both failing ventricles and four heart valves eliminating source of end stage biventricular heart failure.
- Can be used for biventricular heart failure, transplant coronary vasculopathy, transplant rejection, large ventricular clot burden, restrictive disease, or need for complex cardiac repairs.
- Can be discharged home via use of Freedom Driver.
- Smallest pump size is 50 cc allowing use down to BSA of 0.9 m² (determined by virtual fit imaging).

In summary
- Pediatric MCS is constantly evolving with need for more stable, smaller sized devices to support all patient sizes.
- Earlier implantation can lead to improved rehabilitation and end organ recovery and ultimately better transplant candidacy.
- All devices will carry some degree of thromboembolic risk associated with artificial hardware and anticoagulation.
- Better durability leads to improved outpatient VAD management and need for outpatient subspecialty care for pediatric patients with more complex needs (dialysis, rehabilitation, hematologic needs).

On the horizon...

Jarvik Infant
- Continuous flow device
- 15 mm in diameter – about the size of one AA battery
- Blood flow can be increased via pump speed to adjust for growth of patient
- Designed for patients under one year of age up to about age ten

HeartMate III
- Continuous flow device with magnetically levitated rotor
- Provides between 2.5 and 10 L/min of flow
- Artificial pulse feature to presumably reduce thrombus formation in device

HeartWare MVAD
- Inflow cannula size identical to that of HVAD
- Pump housing is smaller
- More compact size -> improved use in smaller children

Questions

References
- HeartWare, Inc. https://www.heartware.com
- JarvikHeart, Inc. http://www.jarvikheart.com
- SynCardiaSystems, LLN. http://www.syncardia.com
Pediatric Heart Transplant Complications

Cristina Clawson, MSN, RN, CPNP-AC
Heart Failure, Cardiomyopathy, and Cardiac Transplantation Nurse Practitioner
Department of Pediatric Cardiology, Texas Children’s Hospital
Adjunct Instructor of Pediatrics, Baylor College of Medicine

Disclosures

- I will be discussing the off label use of medications in children.

Learning Objective

- After this session the learner will be able to identify signs and symptoms of a post-transplant complication in a pediatric patient.

Orthotopic Heart Transplant History

- First infant heart transplant by Kantrowitz in late 1967 - survived 6 hours post transplant
- Cyclosporine introduced as immunosuppressant in 1980
- October 26, 1984 Loma Linda performed a xenotransplant in an infant using a baboon heart.
- On November 1, 1984 the Texas Heart Institute performed the first successful infant orthotropic heart transplant in an 8-month-old female.

Heart Transplant Process

Transplant Complications

- Infection
- Rejection
  - Acute and Chronic
  - Antibody and Cellular Rejection
- Side effects of immunosuppression
- Cardiac allograft vasculopathy (CAV)
- Post transplant lymphoproliferative disorder (PTLD)
- Non-specific graft failure
Post-transplant infectious issues

Early Infections

Late Infections

Common Colds

Acute Rejection

• Routine biopsies in post transplant period help detect rejection
• Echocardiogram may show change in function
• Endomyocardial biopsy is gold standard for detecting acute rejection, it is then assessed for both cellular and antibody mediated rejection
  • Cellular rejection: ISHLT Scale 0R – 3R
  • Antibody mediated rejection: Immunohistochemical and Immunofluorescence staining (positive or negative depending on pattern)
  • Monitoring of Donor Specific Antibodies

Acute Rejection Signs and Symptoms

• Findings can be subtle or severe
  - Asymptomatic
  - Unexplained fevers (low grade)
  - Decreased appetite
  - Nausea/vomiting
  - Fatigue
  - Shortness of breath
  - Change in activity level
  - Arrhythmias
  - Elevated BNP, with or without symptoms
  - Gallop rhythm
  - Sudden death event

Treatment for Rejection

• Cellular Rejection:
  - High-dose steroid pulse (oral or IV) x 2-3 days
    • s/e: hyperglycemia, GI upset, hypertension
  - Thymoglobulin (rATG) for steroid resistant cellular rejection
    • s./e: thrombocytopenia, leukopenia, anemia, infusion reactions (premedicate)
  - High dose IVIG
    • s/e: fevers, chills, arthralgias, dyspnea, hypertension, injection site reactions, renal dysfunction

• Antibody Mediated Rejection
  - Rituximab – targets circulating B-cells
  - s/e: infusion reactions, maculopapular rash
  - Plasmapheresis – mechanical removal of antibodies
    • s/e: hypotension, transfusion reactions, nausea, fatigue

Immunosuppression Side Effects

• Calcineurin inhibitors: block T-cell cytokine gene expression
  - tacrolimus (Prograf, Sandimmune)
    • Hypertension, tremors, renal insufficiency, abdominal upset, headaches, hyperglycemia, hyperuricemia, seizures, hirsutism, gingival hyperplasia, facial dysmorphism
  - cyclosporine (Neoral, Gengraf, Sandimmune)
    • Hypertension, tremors, renal insufficiency, abdominal upset, headaches, hyperglycemia, hyperuricemia, seizures, hirsutism, gingival hyperplasia, facial dysmorphism

Photos from: Society for Cardiovascular Pathology
Immunosuppression Side Effects

• Corticosteroids: suppress cell-mediated immunity as well as humoral immunity
  – methylprednisolone (Solumedrol),
  – prednisone (Deltasone)
  – prednisolone (Orapred)
- weight gain, steroid induced diabetes, growth retardation, crouched appearance, acne, mood swings, increased appetite, osteoporosis, adrenal insufficiency

Antiproliferative agents: prevent rejection by interfering with purine synthesis resulting in anti-proliferative effects on T and B cells
- azathioprine (Imuran)
- bone marrow suppression, hepatotoxicity, photosensitivity, alopecia, cutaneous malignancy
- mycophenolate mofetil (CellCept)
- GI symptoms, bone marrow suppression (anemia), hypertension, headache, fever, increased risk of lymphomas

mTOR inhibitors: inhibits target or rapamycin preventing proliferation of activated T-cells
- Sirolimus (Rapamune)
- hyperlipidemia, bone marrow suppression, mouth sores, poor wound healing, anemia
- may decrease graft vasculopathy, less nephrotoxic

Cardiac allograft vasculopathy
• Diagnosed via coronary angiography or intravascular ultrasound
• Signs and Symptoms
  – New onset arrhythmias
  – Unexplained/recurrent chest or abdominal pain
  – CHF symptoms
  – New onset systolic or diastolic dysfunction
  – Sudden death
• Prevention:
  – Statin therapy (MAY help prevent development): anti-inflammatory properties and lipid lowering
  – Healthy lifestyle
• Treatment:
  – Re-transplant (if candidate)
  – Medical management: pain control, pravastatin, heart failure management

Post-transplant lymphoproliferative disorder
• Complication related to the EBV virus usually with chronic immunosuppression in organ transplant patients
• Can be serious or fatal ranging from isolated lymphadenopathy to fulminant systemic disease
• Higher frequency of rejection episodes is a risk factor for PTLD (more rejection = increased immunosuppression)
• Presentation:
  – Tonsillar or adenoidal hypertrophy
  – Single enlarged lymph nodes
  – Invasive mass in abdomen, thorax, or anywhere lymphoid tissue resides
• Treatment:
  – Decrease immunosuppressive regimen
  – Surgical resection
  – Possible chemotherapy/radiation (Rituximab + high dose steroids)

Non-specific graft failure
• Diagnosis of exclusion
• No evidence of active rejection
• May have history of acute rejection events
• No evidence of coronary artery vasculopathy
• No evidence of infection
• Medical management of failing graft with heart failure medications
• Consideration for re-transplantation
Questions


References