Solid Organ Transplants
Preserving the Gift

The Gift of Life

Jason Folt, MD
Senior Staff Physician
Henry Ford Health System
Review Topics

• General principles of the transplant patient
• Specific Solid Organ Transplants
• Transplant Drugs
• ED Pearls
Solid Organ Transplants

• Subtle signs and symptoms are the norm
  – Devoid of native innervations
  – Surgical anastomoses to many different structures
• Patients are immunosuppressed
• Search for surgical complications related to specific transplanted organ
• Heavy reliance on baseline physiologic capacity of the allograft
Solid Organ Transplants

• Anatomic Complications
  – Vascular
    • Arterial and venous thrombosis
    • Arterial stenosis
    • Pseudoaneurysms
  – Nonvascular anastomosis
    • Leaks and obstructions
  – Surgical Complications
Solid Organ Transplants

• Infection
  – Primary cause of mortality after transplantation
  – Typical signs of infection may not be present
  – Sources
    • Pretransplant
    • Community acquired
    • Nosocomial
    • Transmission from donor
  – Timing may help predict etiology
Infection: First Month

Primarily Healthcare Associated Infections

- Aspiration
- Catheter/Lines related
- Wound infections
- C. Diff, MRSA, VRE, fungal infections
Infection: 1-6 Months Out

Patients without CMV/PCP Prophylaxis

- Immunomodulating Viruses
  - CMV
    - Primary or reactivation from latent virus found in lymphocytes
    - Gancyclovir and CMV immunoglobulin improve survival
  - EBV
- PCP
- HSV, VZV
- *Listeria, Nocardia, Toxoplasma, Trypanosoma, Strongyloides*
Infection: 1-6 Months Out

Patients with CMV/PCP prophylaxis

– Activation of latent infections and opportunistic infections

• HCV
• Influenza
• Cryptococcus
• TB
• Polyomavirus BK
• Adenovirus
• C. difficile
Infection: 6+ Months Out

• Increased susceptibility to community acquired infections
  – Pneumonia and UTIs most common
• Fungal Infections
• Late Viral Infections
  – CMV, HBV, HCV, HSV, West Nile, VZV
Pop Quiz

1. Which of these vaccines are not safe in transplant patients?

A. Influenza
B. Rabies
C. Tetanus
D. Vaccinia
E. Pneumococcal
REJECTION
It starts from an early age. Get used to it!
Allograft Rejection

- Typically a lifelong wax/wane of immune response to allograft
- Differentiating infection and rejection is extremely difficult
- Hyperacute Rejection – immediate
- Acute Rejection – months +
- Chronic Rejection – months to years
Renal Transplantation
Renal Transplantation

Anatomic Complications

– Renal Artery/Vein Thrombosis
  • 1st post transplant week
  • Oligouria and renal failure
  • Dx: doppler US

– Hematoma
  • Severe pain over allograft
  • Drop in H/H, Rising Cr
  • CT imaging for diagnosis
Renal Transplantation

Anatomic Complications

- Urinary Leak
  - Disruption of anastomosis from ureter to bladder
  - Extravasation of urine and renal failure
  - CT imaging for diagnosis

- Lymphocele
  - Peritransplant fluid collection
  - May exert pressure on ureter, bladder or iliac veins
  - US for diagnosis
Renal Transplantation

Infection: 1 month
  • Usual postoperative infections
    – Pneumonia, wound infections, line sepsis, UTIs
    – High risk for pyelonephritis

Infection: 1-6 months
  • Pyelonephritis
  • Opportunistic infections
    – CMV, regional fungal infections

Infection: 6+ Months
  • Community acquire infections unrelated to immunosuppression become more common
  • Opportunistic infections may still occur
Renal Transplantation

Acute Rejection

- Worsening renal function, decreased UOP
  - T lymphocytes, B lymphocytes and macrophages invade allograft
  - Microvascular lesions impair perfusion of organ
- DDX: cyclosporine/tacrolimus toxicity, ATN, renal artery stenosis, obstruction, UTI
- TX: High dose steroids after speaking with transplant team
Renal Transplantation

Chronic Rejection/Chronic Allograft Dysfunction

– Slowly progressive nephrosclerosis
– Proliferation of vascular intima of renal vessels with decrease in lumen size
– Nonimmunologic factors contribute
  • HTN, HLD, drug toxicity
Renal Transplantation

Special Concerns

• ARF if creatinine rises 20%
• CAD increased 3-5x compared to general population
• Keep a watchful eye for hyperkalemia
  – Combination of fragile renal dysfunction with meds (tacrolimus/cyclosporine) which decrease excretion of K
• Carefully consider use of contrast agents: CT dye as well as gadolinium
Liver Transplantation

1. Suprahepatic IVC Anastomosis
2. Gallbladder Fossa
3. Infrahepatic IVC Anastomosis
4. Hepatic Artery Anastomosis
5. Portal Vein Anastomosis
6. Celiac Trunk
7. Choledochocholedochostomy Anastomosis
Liver Transplantation

Anatomic Complications

• Biliary Complications
  – Bile Leaks
    • Occur in first 1-3 months
    • Fever, RUQ pain, elevation in Alk Phos, GGT, Bilis
    • Biloma may cause obstruction
    • Dx: US, CT or MRI
    • Most are treated nonoperatively
Liver Transplantation

Anatomic Complications

• Biliary Complications
  – Biliary Strictures
    • 2-6 months post transplantation
    • Many are associated with Hepatic Artery Thrombosis
    • Elevated LFTs, Bilis, Alk Phos
    • Dx: US or cholangiography
    • Tx: Endoscopic dilation and stenting
2. Who or what is Budd Chiari?

A. Herniation of cerebellar tonsils
B. An English Internist
C. Obstruction of hepatic vein
D. An Austrian Pathologist
E. Occlusion of hepatic artery
Anatomic Complications

- Hepatic Vein Thrombosis
  - Rare except for patients transplanted due to Budd Chiari Syndrome
  - Recurrence develops months to years after transplantation
  - Often with subtherapeutic INR
Liver Transplantation

Anatomic Complications

- Hepatic Artery
  - Stenosis
  - Thrombosis
    - Associated with cholangitis and abscess secondary to ischemia of biliary tree
    - If tolerated, leads to biliary strictures
    - Dx: US, CT
  - Aneurysm
Liver Transplantation

Anatomic Complications

• Portal Vein Thrombosis
  – Usually asymptomatic
  – Related to hypercoagulability or mechanical venous problems
  – Manifest as varices, ascites and enlarged spleen
  – Dx: US or CT
Liver Transplantation

Infection: 1 month

- Usual postoperative infections
  - Pneumonia, wound infections, line sepsis, UTIs

Infection: 1-6 months

- Opportunistic infections
  - CMV, HSV, regional fungal infections, atypical bacteria
- Ascending cholangitis due to colonization of biliary stents
- Liver abscesses from biopsies

Infection: 6+ Months

- Community acquire infections unrelated to immunosuppression become more common
- Opportunistic infections may still occur
• Acute Rejection
  – Most occur within 1 weeks to 1 year
  – Fever, RUQ pain, elevated LFTs, Bilis
  – Dx: Biopsy, r/o infectious and anatomic causes
  – Tx: Steroids and increased immunosuppression

• Chronic Rejection
  – < 5% of Liver transplants due to improved detection and immunosuppression
  – Usually after episodes of acute rejection unresponsive to steroids or recurrent episodes
Liver Transplantation

Special Concerns

• Watch for bleeding/coagulopathy as a sign of graft dysfunction

• Increased risk of new malignancy
  – Squamous cell carcinoma, lymphoma, posttransplant lymphoproliferative disorder
  – No increase in lung, colon, breast or prostate
  – Hepatobiliary cancer is rare unless reoccurrence
Pop Quiz

3. Who is this guy?
4. Why do we care?
Cardiac Transplantation
Cardiac Transplantation
Pop Quiz

5. Resting heart rate after cardiac transplant is most likely:

A. 60 bpm
B. 80 bpm
C. 100 bpm
D. 120 bpm
Cardiac Transplantation

Post Transplantation Physiology

• Denervated heart with resting atrial rate 90-100 bpm
• Cardiac response is blunted
• No centrally mediated response to stress or exercise
• Relies on circulating catecholamines
• Normal to depressed cardiac output at rest
Cardiac Transplantation

Post Transplantation Physiology
Cardiac Transplantation

Specific Complications

• Dysrhythmias
  – Often due to rejection, arrange for quick biopsy
  – If unstable, treat with high dose steroids
  – Atrial dysrhythmias
    • Calcium channel blockers, digoxin
  – Ventricular dysrhythmias
    • Lidocaine or class Ic agents (flecainide)

• Cardiac Arrest
  – Typical CPR
  – Vagally induced bradycardia does not occur – no role for atropine
Cardiac Transplantation

Specific Complications

• Sinus Node Dysfunction
  – Occurs in 5% of patients
  – May have sinus bradycardia or sinus standstill with junctional escape beats
  – Occurs in early postoperative period and usually resolves
  – Tx: theophylline or pacemaker if no resolution
Cardiac Transplantation

Infection: 1 month

- Usual postoperative infections
  - Pneumonia, wound infections, line sepsis, UTIs
- **Infectious endocarditis 100X more common than general population**

Infection: 1-6 months

- Opportunistic infections
  - CMV, HSV, regional fungal infections, atypical bacteria

Infection: 6+ Months

- Community acquire infections unrelated to immunosuppression become more common
- Opportunistic infections may still occur
• Acute Rejection
  – 75-85% of patients within first 3 months
  – Classically, rejection presents with decreased QRS voltage, new S3, new onset CHF or arrythmias
  – May just present with fatigue or CHF
  – Dx: made by endomyocardial biopsy
  – Frequent biopsies are performed as monitoring; 3-6 months
  – Tx: steroids and increasing immunosuppression regimen
• Chronic Rejection
  – Diffuse graft atherosclerosis
  – Myocardial infarction does not present with angina due to denervation
  – Traditional stents/revascularization may not work
Cardiac Transplantation

Special Concerns

• Baseline tachycardia is expected
• No pericardium but tamponade is possible!
• Rejection may mimic viral syndrome/gastro
• Myocardial ischemia will not have angina
Lung Tranplantation
Lung Transplantation

Anatomic Complications

• Airway dehiscence
  – Within 3 weeks of transplantation
• Bronchial stenosis
  – Occurs later after transplantation
  – Limits clearance of secretions
  – Increases risk of postobstructive pneumonia
• Spontaneous pneumothorax
  – Possible at any time
Lung Transplantation

Infection

• **Bacterial Pneumonia**
  - Most common complication in first 3 months
  - Result of decreased mucociliary clearance, decreased cough reflex, reperfusion injury and immunosuppression
  - Pseudomonas, Staph, Strep, Mycobacterium

• **Viral**
  - CMV
    • Most common viral infection
    • Most common 3 weeks – 4 months post transplant
    • CMV pneumonitis
  - HSV, EBV are also implicated

• **Fungal**
  - Aspergillus and Candida
• Acute Rejection
  – Few days to years after transplantation
  – Mimics infection
  – Cough, dyspnea, fever, hypoxia
  – Infiltrates on CXR
  – Dx: Transbronchial biopsy showing lymphocytic infiltration
• Chronic Rejection
  – Previous acute rejection and CMV are risk factors
  – May mimic URI or bronchitis
  – Bronchiolitis obliterans
Bronchiolitis Obliterans

- Most frequent cause of death after year 2
- Chronic allograft dysfunction and airflow limitation
- Prevalence 20-50% in long term patients
- Chronic rejection, CMV, toxic fumes all contribute
- Dx: Fall of FEV1 > 20% without other etiologies
- Bronchoscopy and biopsy are low yield
Transplant Drugs

Calcineurin Inhibitors

• Cyclosporine
  – Inhibits cellular and humoral immunity
  – Potent suppression of helper-induced T cells
  – Nephrotoxic
  – Worsens HLD, HTN, gout, DM
  – Significant drug interactions via cytochrome P450

• Tacrolimus (Prograf)
  – Binds to lymphocyte proteins and inhibits cytokine synthesis
  – Nephrotoxic, neurotoxic
  – Must avoid macrolide antibiotics
Transplant Drugs

Antimetabolites

• Azathioprine (Imuran)
  – Inhibits DNA and RNA, suppressing lymphocytic proliferation
  – Neutropenia, hepatic dysfunction, pancreatitis

• Mycophenolate Mofetil (CellCept)
  – Potent and selective inhibition of lymphocytic proliferation
  – Low side effect profile
  – Leukopenia, thrombocytopenia
Transplant Drugs

Corticosteroids

• Combination therapy used in effort to decrease reliance on steroids
• Osteoporosis, GI bleeding, DM, adrenal suppression, cushing syndrome
• Muscle wasting
  – Check for pressure sores
The Transplant Patient

• Presents atypically and with subtle findings
• Be concerned with small changes in allograft function
• Rejection/infection are difficult to tell apart
• Be wary of drug-drug interactions
  – Use our pharmacists
• Always involve the transplant teams, and early
References


