Objectives

• To understand rarer contemporary scenarios in donor derived infections that may affect screening decisions
• To articulate steps in epidemiologic investigation that improve patient safety
• To elaborate what perioperative transplant professionals can do to mitigate the risk of disease transmission
Disclosures

None
Case: Something to fear?

The ugly

- Transplant recipient identified with post-transplant HCV and HIV infection with no obvious risk factors. Negative pre-transplant testing
- Reported to OPO, UNOS, and CDC
- Donor – Look-back Assessment
  - Negative serology for HIV & HCV
  - Appropriately labeled as “high risk” by PHS Guidelines
  - Subsequent testing of post-transfusion serum was + for HIV and HCV by PCR
- All other recipients tested + for HIV & HCV

Case: Something near?

The good

- Patient is a 56 year-old W male
- Underwent OLT
- CMV D+/R–
- Prophylaxis: Valganciclovir
- 9 days post-transplant
- Donor has + blood cultures drawn the day prior to donation
- Positive for Pseudomonas aeruginosa – generally easily treated
Case 1

• Male patient s/p deceased donor kidney transplant
• 17 months later: Presents to ED with R hip pain and radiation to the lower extremity
• 4 days later: Admitted with fever, diaphoresis, nausea, right lower extremity weakness, abdominal pain
• Eventually progressed to bilateral lower extremity weakness with ascending paresthesias
Case 1
Which is the culprit?
Case 1: Something rare?

The bad

- Patient eventually developed encephalopathy, excessive salivation, hemodynamic instability
- Died 22 days after admission
- Rabies virus RNA detected in saliva, nuchal skin biopsy, postmortem CNS tissues
- Donor: Admitted with upper extremity paresthesias, seizure, autonomic instability
- Donor brain tissue archived: Rabies virus antigen detected. Raccoon rabies variant
- 3 other recipients well (heart, kidney, liver)

Vora et al, JAMA 2013; 310(4)
Questions to consider when accepting a potential donor with CNS process

• What is the potential donor’s age and cause of brain death?
• Did the potential donor have a fever at presentation of illness?
• Were altered mental status and/or seizures part of the presentation that led to the donor’s hospitalization?
• Was a CT of the head or MRI of the head or lumbar puncture consistent with an infectious process?
• Was the donor immunosuppressed?
• Did the donor have any unique environmental exposures?

http://optn.transplant.hrsa.gov/
Case
Which of these organisms are safe?
Case 2

- Organ donor: Hispanic female in early 40s with history of migraines
- Unresolving headache despite therapy
  - CT-angiogram of head: Right carotid cavernous fistula
  - Coiling and embolization
  - Intracranial bleed and craniotomy
  - Brain death
    - No autopsy performed
Case 2
Organ recipients

- **Right Kidney**
  - 6 weeks post-transplant: fever, myoclonus, abnormal gait, altered mental status
  - Died; autopsy performed

- **Heart/Left kidney**
  - 6 weeks post-transplant: fatigue, nausea, vomiting, confusion, myoclonus, fever, and mild aphasia.

- **Liver**
  - Post-transplant diarrhea, tremor, and altered gait

- **Transplant center testing**
  - Only notable finding +measles IgG and IgM in heart/L kidney recipient (CSF)
Case 2

Microsporidium investigation slides
Case 2
CDC Investigation

- Lymphocytic choriomeningitis virus and measles
  - Negative
- Right kidney recipient autopsy
  - Microsporidia by H & E and immunohistochemistry
- Heart/left kidney recipient and liver recipient
  - Urine PCR
- Organ donor
  - Investigational serology
- Evidence of Microsporidiosis infection identified in donor and all recipients
Case 2
Back in San Francisco

• 64 year-old male with a history of HCV cirrhosis and HCC s/p liver transplantation 2/10/14
• 5/13/14 pt complains of tremor in clinic
• Call from CTDN (local OPO)
• CDC to the rescue
• 6/1/14 pt started on albendazole for potential disseminated microsporidium
• 6/18/14 pt admitted with abdominal pain, nausea, vomiting found to have 5cm abdominal aortic aneurysm
• True, true and unrelated?
Case 3

- 34 year-old W male with DM s/p kidney pancreas transplant 6 weeks prior
- Gram negative rod sepsis and abdominal rash
- U.S. born, no foreign travel. From Fresno, CA
- Donor was immigrant from Mexico. Immigrated 6 years ago. Farmer
Case 4

- 45 year-old kidney transplant recipient presents with abdominal pain, shortness of breath and this rash on his buttocks
Cases 3 & 4

- **Strongyloides** rhabditiform larvae complete life cycle via peri-anal skin in IS hosts.
- Spread to lungs, skin, other areas
- Can cause bacteremia with GI bugs. Mortality rate is high
- Often no eosinophilia
Recent outbreaks reported to CDC and DTAC

- Three donors from Strongyloides endemic areas
- Transmission 1
  - 5 organs transplanted; 1 recipient affected (CTDN)
- Transmission 2
  - 5 organs; 2 recipients dead. Results known but not reported to TC
- Transmission 3
  - 4 organs; donor tested prior to transplantation; all recipients treated. No disease (NYODN)
- CDC
  - Since 2009, 7 other clusters; 20 recipients; 2 deaths
- NYODN
  - Screening since 2010
  - 10 positive donors
  - 355 screened

Abanyie F et al, 2014
Case
Which of these organisms are safe?

Chin-Hong et al, Am J Transplant. 2011; (11)4
Roy et al, Am J Transplant. 2014; (14)1
Kumar et al, Am J Transplant. 2010; (10)1
Chin-Hong et al, ATC 2013
Potential donor derived transmission events
DTAC 2005=2012
## Reported cases to DTAC
### 2005-2012

<table>
<thead>
<tr>
<th>Disease Types</th>
<th># of Donor Reports</th>
<th># of Recipients w/ Confirmed Tx</th>
<th># of DDD-Attributable Recipients Deaths</th>
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<tbody>
<tr>
<td>Malignancies</td>
<td>282</td>
<td>69</td>
<td>25</td>
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<tr>
<td>Viruses</td>
<td>205</td>
<td>58</td>
<td>17</td>
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<tr>
<td>Bacteria</td>
<td>152</td>
<td>42</td>
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<tr>
<td>Fungi</td>
<td>106</td>
<td>37</td>
<td>13</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>63</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Parasites</td>
<td>47</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>Other Diseases</td>
<td>47</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>902</strong></td>
<td><strong>252</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>
Lessons learned: DTAC data

• Bacterial Transmissions
  – Likely under-recognized & under-reported
  – Often involves resistant bacteria
  – Follow-up of outstanding culture data

• Fungal Transmissions
  – Endemic mycoses & Cryptococcus increasing
  – High morbidity and mortality

• Mycobacteria Transmissions

• Parasite Transmissions
  – Increase in Strongyloides, Chagas, & Amoeba

• Viral Transmissions
  – Increased recognition of PB19, LCMV
  – Need to use NAT to diagnose transmission, esp for HCV
Lessons learned: DTAC data

• Communications
  – Inefficient system currently in place in the US
• Poor systems for recognizing donor-derived disease transmissions
  – No cluster analysis
  – Severe outcomes not recognized by all recipient teams
  – Variable recognition and report
  – Management of positive cultures/result information locally
• Increased risk donors
  – Variable definitions used across US
  – Variable understanding of risk by clinicians and patients
  – Variable follow-up of recipients
• Human errors
• Living donors are not spared
What transplant professionals can do peri-operatively

- Ensure **donor screening** performed
  - Review medical & social history
  - Physical examination
  - Screening of blood samples of donor and recipient
  - Serology
  - Nucleic Acid Testing (NAT)

- Define the **increased risk** donor
  - OPTN-defined increased risk donor
  - New definitions
  - Increased risk of transmission of other infections may affect peri-transplant antimicrobials

- Screen high-risk recipients **post-transplant**
Screening 123

1. The **Big 3**: HIV, Hep B, Hep C
2. The **givens**: CMV, EBV, HSV, VZV, toxoplasma, syphilis, bacteria
3. The **Next 3**: TB, Chagas, endemic mycoses
4. More **a la carte**: Strongyloides, West Nile
5. The **impossibles**: LCMV, microsporidia

Hocevar S et al, Ann Intern Med; 2014; 160(4)
Kotton C, Ann Intern Med; 2014; 160(4)
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