Renal Pathology Specialty Conference

Case 1

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Clinical History

- A 56 y.o. male with ESLD due to idiopathic pulmonary fibrosis underwent a left lung transplant in 2009
  - Immunosuppressive regimen
    - Anti-thymocyte globulin followed by Tacrolimus, MMF and Prednisone
  - Prophylaxis
    - Valganciclovir and TMP-SMX
  - Social History
    - Works as a cattle rancher with herding dogs x 30 years

- 1 week post-transplant, he developed ACR with humoral component treated with steroids and rituximab
  - Lung biopsies x 2 GMS and AFB stains negative for organisms
  - Rejection resolved over 6 weeks
Post Transplant Period

- **4 months**
  - Episodic fevers and persistent dry cough
  - Lung biopsy: GMS & AFB stains negative

- **5.5 months**
  - Admitted for fever, cough, altered mental status, diarrhea
    - Chest CT: small ground glass infiltrates LLL
    - Brain MRI: unrevealing (CSF w/u negative for bacteria, AFB, fungi, virus)
    - Colonoscopy and stool cultures: negative
    - Blood, urine, sputum cultures: negative for bacteria, AFB and fungi
    - Serum studies negative: Hepatitis B and C, HIV, CMV, EBV, HSV, coccidiomycosis antibody, ANA and ANCA
  - Empiric therapy: Vancomycin, Cefepime, Acyclovir
  - Renal function worsened: Creatinine 1.2-2.6 mg/dl
Post Transplant Period

- **6.5 months**
  - Admitted with fever, cough, confusion, acute renal failure (peak Cr 4.3 mg/dl)
  - Diarrhea resolved.
    - Blood, urine, stool, sputum, CSF cultures: negative
    - Tacrolimus blood levels ↑ (11-23 ng/ml)
    - Renal function transiently improved with ↓ Tacrolimus dose
    - BK and JC virus PCR: negative
    - Urinalysis: sterile pyuria, rod-shaped organisms and tubular epithelial cells with inclusions

- **7 months**
  - Renal Biopsy performed
Allograft Biopsy Results

- Acute granulomatous interstitial nephritis
- Normocellular glomeruli
- Severe interstitial fibrosis and tubular atrophy
Granulomatous infiltrate

Interstitium

- Interstitial granulomatous infiltrate
- Poorly formed granulomas admixed with lymphs, monocytes and a few neutrophils
- Occasional well-formed granulomas

Poorly formed granulomas

Well-formed granulomas
Tubules

- Few tubules with tubulitis
- TEC with enlarged hyperchromatic nuclei
- Partial to complete tubular necrosis

Granulomatous infiltrate

Hyperchromatic nuclei

Disrupt TBM

Polyomavirus IHC negative
Vessels

- Granulomatous inflammation surrounds vessels with fibrinoid necrosis of wall

- Tacrolimus effect: arteriolar hyalinization with beaded hyalinization

Focal necrosis

Beaded hyaline

PAS stain
Organisms

- Small purplish pleomorphic rod-shaped organisms in tubular lumens and epithelial cells
- Granulomas with organisms in histiocytes
**Special Stains**

- **Urine re-examine**

  - **Gram stain (Brown & Brenn)**: irregularly stained gram positive pleomorphic rod-shaped organisms.

  - **Organisms intracellular and in lumens show:** Transverse dark band or “belt-like stripe”

  - **Tubular lumens**

  - **Gram Chromotrope stain**

  - **Modified trichrome stain**

  ![Image of stained tissue](image-url)
Special stains

Renal Biopsy

GMS stain - negative

AFB stain - negative

PAS stain – dot pattern

Organisms show single pink dot that corresponds to “posterior vacuole”
Electron Microscopy – Diagnostic!

*Encephalitozoon cuniculi*

- Organisms develop in parasitophorous vacuole in host cell
- Vacuole has all stages of development:
  - Meront
  - Sporont
  - Spores

![Tubular epithelial cell](image1)

- Parasitophorous vacuole
- Extruded polar tubule

![Spores](image2)

- Spores
- Polar tubules
- Posterior vacuole

![Meronts and Sporonts](image3)

- Meronts
- Sporonts
- Spores
- Parasitophorous vacuole
CDC Testing

(Rows: 1-2 wk after biopsy)

PCR Analysis: urine sediment positive for *E. cuniculi* using species-specific primer set (lane 1)

- **Lane 1:** *E. cuniculi* positive specimen amplified with PCR primers ECUNF/ECUNR, diagnostic band size: 549 bp.
- **Lane 2:** *E. hellem* template amplified with PCR primers EHELF/EHEL, diagnostic band size: 547 bp.
- **Lane 3:** template amplified with PCR primers SINTF1/SINTR, diagnostic band size: 547 bp.
- **Lane 4:** *Enterocytozoon bieneusi* template amplified with PCR primers EBIEF1/EBIER, diagnostic band: 607 bp.
- **Lane 5:** *Vittaforma cornae* template amplified with PCR primers NCORF1/NCOR, diagnostic band size: 375 bp.

Urine culture: positive for *E. cuniculi* (mammalian cell culture IF with *E. cuniculi* Ab)

Calcofluor White Stain: Spores bluish white 2-3 μm

2% Agarose gel

PCR shown with permission from DPDx: CDC’s website for parasite identification; www.dpd.cdc.gov/dpdx/
Lung biopsy at 4 months re-examine

Clusters of organisms in bronchial epithelial cells

- H&E – no inflammation
- Gram Stain: Gram-positive rods
- Warthin Starry Stain: Solid black rods
Renal Biopsy Diagnosis:

- Acute granulomatous interstitial nephritis due to *Encephalitozoon cuniculi*
- Infection-related arterial and arteriolar focal necrosis
- Interstitial fibrosis and tubular atrophy, severe, due to ongoing interstitial nephritis
- Arteriolar hyalinosis, beaded, Tacrolimus-related
Pathology of E. cuniculi

Spectrum of pathologic changes in the kidney

- HIV negative kidney transplants
  - Mohindra AR et al., 2002: Tubulointerstitial infiltrate and coccoid organisms in renal tubules
  - Gamboa-Dominguez A et al., 2003: Abscesses with tubular necrosis
  - Mahmood MN et al., 2003: Tubules with round structures and surrounding neutrophilic infiltrates

- HIV positive native kidney cases
  - Tosini A et al., 2002: Tubulointerstitial nephritis and granulomatous reaction; spores in necrotic tubules
  - Other reports: No inflammatory response in tissues

- Animals
  - Kunzel F et al., 2010: Granulomatous interstitial nephritis, necrosis
  - Vasculitis with fibrinoid necrosis in various tissues
Differential Diagnosis of Granulomatous Interstitial Nephritis (GIN)

- **Drug hypersensitivity**
  - Antibiotics: Ampicillin, Vancomycin
  - Antiinflammatory agents
  - Thiazide diuretics
  - Other: Acyclovir

- **Sarcoidosis**

- **ANCA-associated vasculitis**
  - Granulomatosis with polyangiitis (Wegener)
  - Microscopic polyangiitis

- **Crystal deposits with FBGC reaction**
  - Gout
  - Calcium oxalate

- **Intravesical bacillus Calmette-Guerin therapy**

- **Xanthogranulomatous pyelonephritis**

- **TIN with uveitis (TINU syndrome)**

- **Infection**
  - Bacterial
    - Mycobacteria*
    - Rhodococcus*
    - E. coli
  - Fungal
    - Histoplasma*
    - Cryptococcus*
    - Candida albicans
  - Viral
    - CMV*
    - Adenovirus*
    - Polyoma virus

*Infections with initial pulmonary involvement that may disseminate
Disorders Associated With GIN

- 3 retrospective studies evaluated the cause of GIN
- GIN is uncommon in native kidneys and organ transplant recipients

Disorder | Avg %
--- | ---
Drug-induced | 33.6%
Sarcoidosis | 21.0%
Wegener's | 12.7%
Tuberculosis | 3.1%
Misc. Infection | 8.3%
Foreign body GCR | 4.2%
BCG therapy | 0.9%
Xantho. Pyelo. | 0.9%
Idiopathic | 14.5%

Retrospective studies of GIN (mainly native kidneys)

Viero RM et al., Hum Pathol 26:1347, 1995
Mignon E et al., Adv Nephrol 13:219, 1984
Differential Diagnosis #1

- Rhodococcus
  - Clinical:
    Acquired by animal contact (horses, cows) or inhalation of Rhodococcus in soil
    1 case in allograft kidney: lung infection and sepsis, disseminated to kidney
    Culture: blood, sputum, urine positive for *Rhodococcus equi*
  - Pathology
    Multiple noncaseating granulomas with giant cells
    Macrophages contain gram positive 2-3 μm pleomorphic coccobacilli

Botucato SP., 2004

Gram stain
Phylum Microsporidia

- Obligate intracellular, spore-forming parasites, related to fungi; identified in 1857 as cause of silkworm disease
- Infect vertebrate and invertebrate hosts: rodents, insects, birds, fish, mammals including cattle and dogs (domestic and wild)
- Responsible for infectious disease problems and economic losses in the fishing, honeybee and silkworm industries
- 1959 first human case of microsporidiosis; 1985 emerged as cause of opportunistic infections in HIV patients
- Phylum contains 1,200 species with 14 known to infect humans; 2 most common:
  - *Enterocytozoon bieneusi* (diarrhea in AIDS patients and travelers)
  - *Encephalitozoon sp.* (*E. intestinalis*, *E. cuniculi*, *E. hellem*)
Epidemiology

- World wide distribution
- Most commonly occurs in immunosuppressed patients:
  - Immunocompromised patients with AIDS (15%)
  - Immunocompromised patients without AIDS – Organ transplant recipients, patients with malignancies, diabetics
- Increasingly reported in immunocompetent patients:
  - Children and Elderly
  - Travelers
  - Subset of asymptomatic humans may harbor latent infection
- Mode of transmission:
  - Fecal-oral
  - Ingestion of contaminated water/food
  - Inhalation of contaminated aerosols
  - Person-to-person
  - Contact with animal (Zoonotic infection)
# Classification & Clinical Features

- 14 species are known to infect humans
- Clinical presentation varies depending on site of infection

## Species

<table>
<thead>
<tr>
<th>Species</th>
<th>Sites of Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. bieneusi</em></td>
<td>Intestine, biliary, respiratory, urinary tract</td>
</tr>
<tr>
<td><em>E. intestinalis</em></td>
<td>Systemic, intestine, respiratory/urinary/biliary tract</td>
</tr>
<tr>
<td><em>E. cuniculi</em></td>
<td>Systemic, eye, respiratory/urinary/GI tract, liver</td>
</tr>
<tr>
<td><em>E. hellem</em></td>
<td>Systemic, eye, respiratory/urinary tract, intestine</td>
</tr>
<tr>
<td><em>N. connori</em></td>
<td>Systemic</td>
</tr>
<tr>
<td><em>T. anthro.</em></td>
<td>Systemic, eye, brain</td>
</tr>
<tr>
<td><em>T. hominis</em></td>
<td>Systemic, eye, skeletal muscle</td>
</tr>
<tr>
<td><em>B. algerae</em></td>
<td>Eye, skeletal muscle, skin</td>
</tr>
<tr>
<td><em>M. ceylonensis</em></td>
<td>Eye</td>
</tr>
<tr>
<td><em>M. africanum</em></td>
<td>Eye</td>
</tr>
<tr>
<td><em>N. ocularium</em></td>
<td>Eye</td>
</tr>
<tr>
<td><em>V. corneae</em></td>
<td>Eye, urinary tract</td>
</tr>
<tr>
<td><em>Pleistophora Sp.</em></td>
<td>Skeletal muscle</td>
</tr>
<tr>
<td><em>B. vesicularum</em></td>
<td>Skeletal muscle</td>
</tr>
</tbody>
</table>

## Clinical Presentation

- Enteritis/Diarrhea
- Cholecystitis/Hepatitis
- Bronchitis/Pneumonia
- Cystitis/Nephritis
- Keratoconjunctivitis
- Myositis
- Encephalitis
- Disseminated

*Curr Opin Infect Dis 24:490, 2011*
Morphology and Cellular Infection

**E. Cuniculi spore:** - Oval 2-3μm diameter  
- Electron-dense exospore (Ex) (glyoprotein)  
- Electron-lucent endospore (En) (chitin)

- Cytoplasm: Nucleus  
  Posterior vacuole (Pv)  
  Polar tubule (Pt) 5-7 coils

**Cellular Infection by E. cuniculi**
1. Infective spore
2. Spore extends Pt - infects cell
3. Sporoplasm injected into cell
4. Organisms divide in parasitophorous vacuole
5. Organisms differentiate and mature to spores
6. Spores disrupt cell and released

Shown with permission from DPDx: CDC's website for parasite identification
Comparative Morphology

- Distinct features of *E. cuniculi* by EM

*E. cuniculi* or *E. hellem*
- Parasitophorous vacuole - Nonseptated

*E. intestinalis*
- Parasitophorous vacuole - Septated

*Enterocytozoon bieneusi*
- Parasitophorous vacuole - None

Developmental stages: meronts (M) → sporonts (ST), → sporoblasts (SB) → spores(S).

Mechanisms of Host Defense

Cell- and Humoral-mediated immunity contribute to host defense against infection:

- Human studies: ↑ severity of disease in AIDS patients with declining CD4+ T cells
- Mouse studies: ↑ mortality of mice infected with *E. cuniculi* and depleted of T cells
  - Importance of CD4+ T cells is shown SCID mice orally infected with *E. cuniculi*
    - Survival improved by adoptive transfer of CD4+ T cells from WT mice
    - Survival of mice reconstituted with CD4+ T cells was further prolonged by administration of anti-*E. cuniculi* antibody

Macrophage function is also important for host defense against infection

Clin Microbiol Rev 15:401, 2002
Diagnostic Tests

- Histochemical Methods

  1. Clinical Fluids (detect spores in stool, urine, sputum, tissue imprint):
     - Chemofluorescent agents: calcofluor white
     - Modified trichrome (chromotrope-based) stains (pink spores /belt stripe)
     - Hot gram chromotrope stain (rapid stain)
     - Gram stain (Brown & Brenn) (blue spores but variable staining)
     - Immunofluorescent stain: species-specific antibodies

  2. Tissue Paraffin Sections
     - Gram stain (blue spores with belt stripe)
     - PAS-fungal stain (posterior vacuole as pink dot)
     - Silver stain (Warthin-Starry) (solid black rods)
     - Immunohistochemistry using species-specific antibodies

- Serology (detect carriers; not routine in immunocompromised patients)
Diagnostic Tests

- **Molecular Techniques** (PCR of DNA extract from fluids or tissues)
  - Specific primer sets for 5 species including *E. cuniculi*
    - Amplify the small subunit rDNA gene specific for each species
  - Genotype: DNA sequence of Internal Transcriber Spacer (ITS) region of rDNA
    - 4 types of *E. Cuniculi*: type I, II, III, IV; type III is “dog strain”

- **In vitro culture** (special conditions); Routine culture is negative
  - Innoculate fresh specimen into mammalian cultures

![Diagram showing the process of diagnostic tests](image)
## Microsporidiosis in HIV Negative Transplant Recipients

<table>
<thead>
<tr>
<th>Case (Ref#)</th>
<th>Type of Transplant (no. of patients)</th>
<th>Species/genotype</th>
<th>Immunosuppressive Treatment Agent(s)</th>
<th>Clinical Features</th>
<th>Treatment/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (25)</td>
<td>Heart-lung (1); Kidney (6); liver (1)</td>
<td><em>E. bieneusi</em></td>
<td>NA</td>
<td>Diarrhea</td>
<td>NA</td>
</tr>
<tr>
<td>2 (34)</td>
<td>Heart; lung</td>
<td><em>E. bieneusi</em></td>
<td>CS, AZ, Pred</td>
<td>Intestinal,</td>
<td>Metronidazole/recovery</td>
</tr>
<tr>
<td>3 (35)</td>
<td>Heart and/or lung (4); Kidney (14); liver (5)</td>
<td><em>E. bieneusi</em></td>
<td>ATG, CS, AZ, MMF, Tacrolimus</td>
<td>Asymptomatic,</td>
<td>Albendazole/Fumagillin</td>
</tr>
<tr>
<td>4 (16)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>AZ, CS, Pred, MMF, Tacrolimus, Pred, MMF</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>5 (16)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus, Pred, MMF</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>6 (29)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus, MMF</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>7 (31)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Steroids, Tacrolimus, MMF</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>8 (22)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus, MMF</td>
<td>Intestinal</td>
<td>Fumagillin/recovery</td>
</tr>
<tr>
<td>9 (Galvan)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>10 (Galvan)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Steroids, Tacrolimus, MMF</td>
<td>Intestinal</td>
<td>Fumagillin/recovery</td>
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<tr>
<td>11 (46)</td>
<td>Kidney</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus</td>
<td>Intestinal</td>
<td>Fumagillin/recovery</td>
</tr>
<tr>
<td>12 (Champion)</td>
<td>Kidney (10)</td>
<td><em>E. bieneusi</em></td>
<td>CS, everolimus</td>
<td>Intestinal,</td>
<td>Topical ciprofloxacine</td>
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<tr>
<td>13 (41)</td>
<td>Liver</td>
<td><em>E. bieneusi</em></td>
<td>L-asp, Vin, Daun, Pred, CS</td>
<td>Intestinal,</td>
<td>Metronidazole/recovery</td>
</tr>
<tr>
<td>14 (15)</td>
<td>Liver</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>15 (31)</td>
<td>Liver</td>
<td><em>E. bieneusi</em></td>
<td>CS, AZ, Pred</td>
<td>NA</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>16 (22)</td>
<td>Heart</td>
<td><em>E. bieneusi</em></td>
<td>Pred</td>
<td>Intestinal</td>
<td>Albendazole/recovery</td>
</tr>
<tr>
<td>17 (17)</td>
<td>Heart</td>
<td><em>E. bieneusi</em></td>
<td>Tacrolimus, Pred</td>
<td>Intestinal,</td>
<td>Disseminated</td>
</tr>
<tr>
<td>18 (20)</td>
<td>Bone marrow</td>
<td>Undetermined</td>
<td>Pred</td>
<td>Intestinal,</td>
<td>Postmortem diagnosis</td>
</tr>
<tr>
<td>19 (19)</td>
<td>Cornea</td>
<td>Undetermined</td>
<td>Tacrolimus</td>
<td>Intestinal</td>
<td>Disseminated</td>
</tr>
<tr>
<td>20 (40)</td>
<td>Liver</td>
<td>Undetermined</td>
<td>AZ, CS, Pred</td>
<td>Intestinal</td>
<td>Disseminated</td>
</tr>
<tr>
<td>21 (23)</td>
<td>Kidney</td>
<td><em>Encephalitozoon sp.</em></td>
<td>Tacrolimus, MMF, Pred, AZ</td>
<td>Intestinal</td>
<td>Disseminated</td>
</tr>
<tr>
<td>22 (4)</td>
<td>Pancreas; kidney</td>
<td><em>Encephalitozoon sp.</em></td>
<td>Pred</td>
<td>Intestinal,</td>
<td>Disseminated</td>
</tr>
<tr>
<td>23 (30)</td>
<td>Kidney</td>
<td>*E. cuniculi/III strain</td>
<td>Rapamycin, CS, Pred</td>
<td>Disseminated</td>
<td>Albendazole/death</td>
</tr>
<tr>
<td>24 (14)</td>
<td>Kidney</td>
<td><em>E. cuniculi</em></td>
<td>Steroids</td>
<td>Disseminated</td>
<td>Albendazole/release</td>
</tr>
<tr>
<td>25 (28)</td>
<td>Kidney</td>
<td><em>E. cuniculi</em></td>
<td>Thiotepa, CYP, ATG, CS</td>
<td>Disseminated</td>
<td>Antimicrobial/death</td>
</tr>
<tr>
<td>26 (33,45)</td>
<td>Bone marrow</td>
<td>*E. cuniculi/III strain</td>
<td>TG, MMF, CsA</td>
<td>Disseminated</td>
<td>Pulmonary</td>
</tr>
<tr>
<td>27 (44)</td>
<td>Kidney</td>
<td>*E. cuniculi/IV strain</td>
<td>TG, Tacrolimus, MMF, Pred, Butuximab</td>
<td>Disseminated</td>
<td>Disseminated</td>
</tr>
<tr>
<td>28</td>
<td>Lung (current case)</td>
<td><em>E. cuniculi</em></td>
<td>Pred</td>
<td>Disseminated</td>
<td>Albendazole/recovery</td>
</tr>
</tbody>
</table>

CS, cyclosporine; AZ, azathioprine; MMF, mycophenolate mofetile; CsA, cyclosporine A; CYP, cyclophosphamide; ATG, antilymphocyte globulin; TG, thymoglobulin; Vin, vincristin; Pred, prednisone; Daun, daunomycin; L-asp, L-asparaginase; NA, not available.

Microsporidiosis in HIV negative Transplant Recipients

- Few cases of microsporidiosis are reported in HIV negative organ transplant recipients (OTR) - 70 cases including ours

- *E. bieneusi* is most common species; diarrhea is the most common symptom

- Infection occurred from 19 days up to 7 yrs post transplant

- Only 5 cases of *E. cuniculi* infection are reported in HIV negative OTR
  - 4/5: Renal transplants - disseminated disease
  - 1/5: Bone marrow transplant - pulmonary disease

*E. bieneusi is the only species reported in lung transplants; our case is first report of* *E. cuniculi in lung transplant recipient*
Treatment of *E. cuniculi*

- CDC recommends Albendazole for *E. cuniculi* infection
  - Leads to clinical improvement/clearance of parasites in cases of *Encephalitozoon* infection. Fumagillin is effective for *E. bieneusi*.
  - Side effects are rare: hypersensitivity, neutropenia, thrombocytopenia
  - Also: lower or transiently discontinue immunosuppressive therapy

♦ Randomized, double-blind, placebo controlled study:
  - Albendazole (400 mg bid x 3 weeks) for Rx and prophylaxis of *E. intestinalis* in AIDS patients (J Inf Dis 177:1373, 1998)

♦ Results
  - Clearance of parasite and clinical benefit:
    - Albendazole: 4/4  Placebo: 0/4  \( p = 0.01 \)
    - (All 4 cases cleared microsporidia with albendazole)
  - Prevention of relapse: All 8 patients randomized to:
    - Albendazole (400 mg/bid) x 12 months vs No Rx
      - Albendazole: 0/3 recurred (6-9 mo)  No Rx: 3/5 recurred
Clinical Course

- Albendazole 400 mg bid x 4 wks
  Immunosuppression was reduced

- Urine and sputum were monitored for spores using the Calcofluor white stain

- After 5 days: pt responded to therapy, afebrile, reduction in *E. cuniculi* spores
  1 wk later: Aspergillus pneumonia and expired

- 8 months autopsy: disseminated *E. cuniculi* in lung, kidney, brain, liver, spleen
Summary:

- 56 y.o. lung transplant recipient: heavy immunosuppressive therapy and history of direct contact with cattle/dogs
  \[\text{At risk for microsporidia}\]

- 4 months post-transplant: fever, cough, lung infiltrate, +lung biopsy (in retrospect) for *E. cuniculi*
  \[\text{Probably acquired zoonotic infection}\]

- 5.5 to 7 months post-transplant: persistent fever, cough, confusion, renal failure. Cultures/serology negative
  \[\text{R/O Tacrolimus vs ATIN}\]
  \[\text{*E. cuniculi* spread to kidney}\]
  \[\text{Granulomatous Interstitial Nephritis due to *E. cuniculi*}\]
  \[\text{Albendazole, ↓Immunosuppression}\]

- 8 months autopsy: Aspergillus pneumonia and disseminated *E. cuniculi*
Conclusions:

- Our case is the first report of disseminated *E. cuniculi* in an HIV negative lung transplant recipient.
- HIV patients and immunocompromised non-HIV transplant recipients should be considered risk groups for microsporidia.
- Microsporidia should be considered in cases of FUO and/or multiorgan infection, especially with renal failure, after other causes are excluded.
- Examine urine carefully; if organisms are identified but cultures are negative, screen for microsporidia (calcofluor white/modified trichrome).
- In certain cases, serotesting of donors may be useful to detect carriers of microsporidiosis to prevent donor-related infection.
- Further studies to elucidate the cellular mechanisms by which microsporidia infect tissues may lead to new therapeutic strategies.
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  - William McClain, M.D., Department of Pathology
  - Fermin Tio, M.D., Department of Pathology
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