Peritonitis with Atypical Organisms

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Conflict Of Interest

• None
Objectives
- Atypical Mycobacteria
- Fungal
- Viral
- Zoonotic infections

PD related infections
1. PD-related peritonitis
2. PD catheter-related infections:
   - Exit site infection (ESI)
   - Tunnel infection

Continuous Ambulatory Peritoneal Dialysis

Process of CAPD
- PD fluid enters abdomen
- Waste products mix with PD fluid
- PD fluid with waste products exits
- PD fluid in abdomen
### Diagnosis of PD Peritonitis

When at least two* of the following are present:

- Clinical features consistent with peritonitis, i.e., abdominal pain and/or cloudy dialysis effluent
- Dialysis effluent white cell count above 100/μL or with over 50% of poly leukocyte in the differential count
- However, among patients with fungal peritonitis, the peritoneal WBC is almost always >200 cells/μL, with a PMN predominance
- Identification of infective organisms by dialysis effluent gram stain or culture

*Cloudy PD effluent

### Common organisms

**Gram positive**
- Coagulase-negative Staphylococcus (S. epidermidis)
- Streptococcus spp
- *S. aureus*
- Enterococcus spp
- Corynebacterium spp.

**Gram negative**
- Escherichia coli
- Klebsiella spp
- Pseudomonas aeruginosa
Peritonitis with Atypical Organisms

- Although uncommon
- Delay in recognition of PD peritonitis
- Delay in diagnosis and implementation of appropriate treatment
- Atypical organisms can lead to poor patient outcomes

On Day #3:

- If clinical improvement
  - narrow down antibiotics (discontinue gram negative coverage) based on local antibiogram

- If no bacteria identified on PD effluent culture
  - Repeat PD fluid WBC, differential, cultures
  - Duration of the dwell and whether or not peritoneal lavage was performed prior to sample collection

- If the culture-negative peritonitis is not resolving at day# 3
  - Special culture techniques should be considered for isolation of unusual/atypical organisms

Mycobacterium

- M. tuberculosis
- MAC (avium)
- Non- tuberculosis
  - Mycobacteria (NTM) = Atypical

- Mycobacterium tuberculosis
- Mycobacterium avium complex
- Mycobacterium abscessus
- Mycobacterium chelonae
- Mycobacterium fortuitum
- Mycobacterium gastri
- Mycobacterium gordoniae
- Mycobacterium kansasii
- Mycobacterium phlei
- Mycobacterium rhinoscleromatis
- Mycobacterium xenopi
Atypical Mycobacteria - PD peritonitis

• First case: in 1982
• > 50 case reports so far (geographical publication bias and variation in accurate diagnosis)
• Can be misidentified as gram-positive diphtheroids
• In immunosuppressed states: Diabetes, Bone Marrow transplant, HIV and auto-immune disease
• A frequent history of bacterial peritonitis episodes or concomitant bacterial/fungal infections
• Exit site infection with atypical organism
• Signs/symptoms: Not much different than other causes of peritonitis

Case....

• 69 Y old female
Medical History of HTN, DM, Ischemic heart disease, on APD ~ 40 months
• Recurrent culture negative exit site infections x 3 months
(Rx with topical gentamicin and oral antibiotics)
Several tunnel ultrasounds: sub-centimeter tunnel abscess
• Patient preferred to continue PD
• Subsequent exit site: grew M. abscessus after 12 days
Sensitive to only Amikacin and Clarithromycin
(No IV access: Amikacin couldn’t be given)
• Rx: Clarithromycin + Ethambutol
Ethambutol was stopped due to drug induced psychosis
• PD fluid cultures remain negative
• Completed 6 weeks of monotherapy with Clarithromycin
• Converted back to APD

The Role of Non-Tuberculous Mycobacteria in Peritoneal Dialysis-Related Infections: A Literature Review.

• 10 years data, retrospective, observational (Tokyo, Japan)2018
• # patients: 44
• NTM peritonitis:
  • Catheter removal: in 92.2%
  • Withdrawal of PD: in 91.9%.
  • Overall mortality rate: 12.4% (including unrelated deaths)
• NTM exit site infections:
  • Developed peritonitis: 33.3%
  • Catheter removal: 50.0%.
  • Patients stopped PD when the catheter was removed without developing peritonitis (37.5%)
  • Patients stopped PD when it was removed after the onset of peritonitis (91.9%)
  • Changing the exit site: in 12.5%

CJ Renaud et al. Nephrology. © 2010
Asian Pacific Society of Nephrology

Rx

The treatment regimen for non-tuberculous mycobacterial peritonitis is **not** well established and requires individualized protocols based on susceptibility testing.

Fungal Peritonitis

- Non-candida species
- Some unusual Fungi i.e. Cryptococcus/Aspergillus
- Usually delay in diagnosis
- Red flag: Lymphocytes and/or mononuclear cells in the peritoneal dialysate
- PD fluid: almost always > 200 cells/μL with PMN cells predominance
- Rx: Most anti-fungal agents should be given systemically
Fungal Peritonitis

- High rates of hospitalization
- Catheter removal
- Transfer to hemodialysis
- Higher morbidity and mortality than bacterial infections

Causes of contamination:
- Breaks in sterile technique
- Infections at the cutaneous site of catheter entry
- Intestinal perforation
- Peritoneovaginal fistula
- Transmigration of fungi across the bowel wall into the peritoneum (avoid constipation)

ISPD

- Unlike bacterial peritonitis, IP anti-fungal agent has no preferential role over systemic therapy
- Suggests the use of echinocandins (e.g., caspofungin) for Aspergillus and non-albicans Candida species
- Second-generation azoles (e.g., posaconazole and voriconazole) for filamentous fungi
- Intravenous voriconazole contains cyclodextrin as solvent, which may accumulate in renal failure patients and cause neurotoxicity
**Fungal Peritonitis**

**ISPD**

We recommend immediate catheter removal when fungi are identified in PD effluent (1C).

We suggest that treatment with an appropriate anti-fungal agent be continued for at least 2 weeks after catheter removal (2C).

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**Case..**

- 65 year old farmer; presented outpatient with abdominal pain
- On CAPD ~ 4 years, ESRD from DM
- Previous PD history:
  - Staph. aureus PD related peritonitis in 1st year on CAPD
  - 1 PD catheter exit site infection after 2 years on CAPD
  - Pneumonia treated with broad spectrum antibiotics 6 months ago
  - He had PD catheter damaged during catheter care and it was replaced 1 month ago
- Exam and peripheral blood labs: was unremarkable
- PD fluid: WBC 431/ul; PD peritonitis was suspected, PD fluid culture were sent
  - 2 gm IP vancomycin was administered with follow up
  - No improvement next day ➔ now has fever, BP 110/80 mmHg, Temp. 36 C
  - Subcutaneous tunnel and exit site were unremarkable
  - Peritoneal fluid is now cloudy: WBC 5664/ul.
  - RX: IP vancomycin + Cefazolin ➔ only mild clinical improvement


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**Case conti..**

- Day#5: worsened clinical picture, increased abdominal pain, febrile 38.2 C
- PD fluid WBC of 9742/ul while on antibiotics
  - Culture obtained on Day #5 and 8 were negative
  - Day #14 (while no +ve culture were reported)
  - Clinically deteriorated, T 39.6, HR 120bpm, Blood WBC 14 x 103/ul.
  - Day #15: Aspergillus was reported on sample from day #9 (A. oryzae)
  - Day #15 and 20: Same grew from day #13 (after 6 days)
  - RX: IV Amphotericin B as 1 mg/kg of body weight + Caspofungin (LD 70 mg day 1; MD 50 mg), PD catheter was removed, transitioned to HD 3/week
  - 28 days of Amphotericin + Caspofungin ➔ Itraconazole 200mg daily PD x 6 months
  - Discharged on Day #45
  - Doing well on HD on 2 years follow up
Treatment

Goal:
• Eradication of infection and preservation of peritoneum for future use of dialysis
• Team approach with Infectious disease specialist
• Rx: Prolonged course of anti-fungal +/- PD catheter removal
• PD catheter removal
• Look before removing: is there an alternate access available/or can be created or not)
• Continuation of PD is possible (Use your best clinical judgment)

Antifungal Prophylaxis

❖ Routine antifungal prophylaxis is not recommended for all PD patients
❖ It can be given in patients receiving prolonged antibiotic therapy
  – Nystatin (400,000 to 500,000 units PO TID) OR
  – Fluconazole (200 mg every other day or 100 mg PO daily)
• Optimal duration of prophylaxis is unclear
  ✓ Usually administered for duration of antibiotic
  ✓ Extend for additional 3 days in case of Aminoglycosides
  ✓ Extend for additional 7 days in case of vancomycin
  ✓ (as these antibiotics have a prolonged half lives in patients on PD)
Viral Peritonitis

- Fever, malaise (+/- sick contacts with similar features)
- Negative bacterial and mycobacterial cultures
- Slight leukopenia
- PD effluent monocytosis (or absence of polymorphonuclear leukocytes)
- PD effluent (+ Blood/serum): PCR/ antibody titer/ viral cultures (as appropriate)

- Enterovirus (Echovirus type II): Antibodies titers
- Coxsackie virus B1: Antibodies titers
- HSV type I and II: Intra- nuclear viral particles
- HZV: Antibodies titers
- CMV: Antibodies titers

Case...

- 42 year F. ESRD from Diabetes, on CAPD for ~ 1 year
- Medical History: Failed kidney transplant due to chronic rejection
- 3 bacterial peritonitis in last year (Stap. Epidermidis, Strep. Mitis and N. Pharyngis)
- Presented with abdominal pain - started after 1 weeks history of her 11 year old son had high fever and headache for few days
- Cloudy dialysate with WBC 100/ul, on day #1,
- No response with antibiotics; It remained cloudy. Cultures negative for bacteria.
- Day#3: Dialysate WBC 400/ul and atypical bodies in leukocytes on gram stain
- Day #10: Enterovirus was isolated from dialysate (Echovirus type II)
- Day13: Fecal cultures +ve as well, Antibodies titers 1:64
- Follow up:
  Day#30 : WBC resolved to 20/ul.
  Day#41: WBC 0/ul.
  Day #43: Antibodies titers 1:16
- Clinical improvement with resolution of culture positivity from dialysate and faeces

DGS: Stuijt, Nephron 1986
**Zoonotic**

- Be aware that PD effluent culture results from zoonotic organisms can take 3–7 days
- Consider a zoonotic cause in culture-negative peritonitis
- Consider mandatory exclusion of pets from room where dialysis takes place

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**Identify mode of transmission**

<table>
<thead>
<tr>
<th>Contact with an animal is EVIDENT at time of peritonitis</th>
<th>Without animal contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bite, scratch, or perforation of tubing</td>
<td>Ingestion of contaminated food</td>
</tr>
<tr>
<td>Lack of hygienic measures before/after exchange</td>
<td>Skin contamination</td>
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<tr>
<td></td>
<td>Bad hand hygiene in general</td>
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**Tube bite by cat**

- B-lactam antibiotics+ B lactamase
- 2nd generation cephalosporin
- 2nd generation Fluoroquinolone

<table>
<thead>
<tr>
<th>Dog</th>
<th>Pasturella, Capnocytophaga, Neisseria</th>
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</thead>
<tbody>
<tr>
<td>Same as above</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th></th>
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<tbody>
<tr>
<td>Diarrhea</td>
<td>Salmonella or campylobacter</td>
</tr>
<tr>
<td>2nd generation</td>
<td>Fluoroquinolone</td>
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Broughton et al. Seminars in Dialysis 201
Zoonotic

Due to vast diversity of infective agents that are potentially transmitted by different animals:

it is difficult to make general antibiotic guidelines

Catheter removal

- Refractory peritonitis (failure of the effluent to clear after 5 days (not 96 h as used previously) of appropriate antibiotics (ISPD)
- Relapsing peritonitis
- Refractory exit site and tunnel infection
- Fungal peritonitis
- Repeat peritonitis, Mycobacterial peritonitis, and peritonitis caused by multiple enteric organisms

Catheter Removal and Re-Insertion

**ISPD**

We recommend that PD catheters be removed for refractory, relapsing, or fungal peritonitis unless there are clinical contraindications (1C).

We suggest that it is appropriate to consider return to PD for many patients who have had their catheter removed for refractory, relapsing, or fungal peritonitis (2C).

We suggest that if re-insertion of a new catheter is attempted after a PD catheter is removed for refractory, relapsing, or fungal peritonitis, it be performed at least 2 weeks after catheter removal and complete resolution of peritoneal symptoms (2D).
Refractory PD-related peritonitis

- Antibiotic-resistant bacteria
- Fungal peritonitis
- Biofilm formation in PD catheters
- Bacterial translocation from the gastrointestinal tract
- Encapsulating peritoneal sclerosis

Terminology for Peritonitis

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<tr>
<th>Time elapsed since completing antibiotics for prior peritonitis episode</th>
<th>Same organism</th>
<th>Different organism</th>
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<tbody>
<tr>
<td>≤4 weeks</td>
<td>Relapsing</td>
<td>Recurrent</td>
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<tr>
<td>&gt;4 weeks</td>
<td>Repeat</td>
<td>Reinfection</td>
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</tbody>
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Important

- Break in technique
- No clean space available
- Physical functional status/ vision/dexterity/ new neurological issues
- Burden of home dialysis
- Pets
- Personal life issues/partner dependence
- Care taker fatigue
- Depression
- Compliance issues
- Etc..
Thank you

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Thank you & Stay warm