PD Related Infections: Case Vignette

Jeffrey Perl MD SM FRCP(C)  
Division of Nephrology, St. Michael’s Hospital  
Associate Professor of Medicine  
Toronto, ON  
Jeffrey.Perl@Unityhelth.to
The Case

- 43 year old electrician
  - ESRD due to PKD
  - PD catheter insertion laparoscopically
  - 3 weeks later receives PD training
  - Starts APD 2L X 5 x 9 hours day dry
  - RKF 2.8 L per day, GFR 7ml/min
  - Weight 80 kg, BMI 32 kg/m²
The Case

- One month later presents to PD clinic with cloudy fluid and abdominal pain

- PD effluent sampled
  - Cell count 3500
  - Neutrophils 88%

- Exit site and tunnel are normal

- What would you do now?
Options

1. IP cefazolin and Ceftazidime
2. IP cefazolin and Gentamicin
3. IP Vanco and Ceftazidime
4. IP Vanco and Gentamicin
Is vancomycin or cefazolin the empiric antibiotic of choice?

- Meta analysis
  - glycopeptide (vanco or tecoplainin) achieved a higher cure rate compared to cefazolin
  - 1.66 [1.01, 2.72] 3 trials 28/189 vs. 37/181

- Driven by one study in which cefazolin was dosed lower than ISPD guideline recommendations (50 vs 125 mg/mL)

- Both for HD (Cather related bacteremia) and PD guidelines empiric choice should be dictated by a “threshold level” of methicillin resistance

- In HD continuing empiric vancomycin in the context of methicillin sensitivity has a higher risk of treatment failure compared to switching to cefazolin.

---

4. Li et al PDI 2016 - VOL. 36, NO. 5
5. Stryjewski et al. CID 2007
The Case Continues

• Initially treated with IP cefazolin and ceftaz (one dwell per day x 6 hours)

• By day 5 cell count < 100, < 50% neutrophils, culture is negative

• Culture grows CNST sensitive to Vanco (ancef resistant)
What would you do

1. **Keep cefazolin and stop ceftaz**
   - The cell count and culture are negative so the cefazolin is effective at these high intraperitoneal doses

2. **Stop cefazolin switch to vanco**
   - The organism is reported as cefazolin resistant by the lab

3. **Add vanco keep cefazolin**
   - Because of the initial response cefazolin is effective but add vanco because of resistance pattern
MR-CNST: Vancomycin vs. Cefazolin
Ariano et al PDI 2002
Heywood et al Adv in Perit Dial 2010

**Ongoing therapy** with vancomycin vs. cefazolin for methicillin resistant CNST when the cell count has normalized:

- Ariano et al showed no difference in:
  - Treatment success 26/31 (84%) vs. 14/17 (82%)
  - Did not examine relapse rate
  - Intermittent administration of cefazolin vs. Intermittent vancomycin

- Bargman et al
  - Cephalosporin-treated throughout:
    - 4/10 (40%) relapse rate
  - Vancomycin (initial or subsequent) treated:
    - 2/28 (7%) relapse rate
The Case Continues

• Switched to Vanco monotherapy 1.5 g IP every four days

• Completes two weeks of therapy

• Nystatin is added 500 000 po QID for three weeks

• Retraining Reveals ‘‘not wearing mask occasionally’’
The Case Continues

• Three weeks later re-presents to PD unit with cloudy fluid

• Initially started on vancomycin 1.5 g IP and Ceftaz

• Culture grows MR-CNST again

• Nystatin is added 500 000 po QID restarted

• Admits that may have had one wet contamination episode and did not report that to the unit.
Wet Contamination

1. Exit site and titanium connector
2. Transfer set
3. "Bad" PD Bag

1. Exit site and titanium connector
Where the Wet Contamination Can Happen

Catheter

Titanium Adapter

Open twist clamp

Crack Along Transfer Set
Management of Wet Contamination

• Have patient come into ER or home dialysis unit
• Transfer set to be changed
• Prophylactic antibiotics (cefazolin or vanco IP or oral cefalexin)
• Review of Technique if needed
What should have been done differently to prevent this relapse?

1. Extend treatment for a total of three weeks
2. Monitoring of Vancomycin levels
3. Switch to hemodialysis given poor technique
4. Treatment of wet contamination
5. 2 and 4
The Case Continues

- Vancomycin levels drawn at day 3 and were 14.2
  - Likely underdosed due to body size and residual kidney function

- Vancomycin dose increased and frequency increased

- Completes 3 weeks of therapy (one week extended due to relapse)

- Follow up sample cell count and culture after treatment negative.
The Case Continues

- Three weeks later represents with cloudy fluid and mild abdominal pain

- Started on Vancomycin 2.0 g IP q 3 days with levels to be checked

- Nystatin added

- Cell count normalizes by day three and culture becomes negative

- Technique reviewed and patient appears to be performing the dialysis using sterile procedure principals
What would you do now for this second relapse?

1. Remove the catheter transfer the patient to hemodialysis as this is a second relapse

2. Treat and keep the catheter as the patient is responding to therapy

3. Remove and reinsert the catheter in the same procedure under antibiotic coverage
Relapsing Peritonitis X 2

Relapsing peritonitis with a “skin bug”

Exit site/Tunnel Infection Ruled Out

Reinfection: poor technique
Biofilm on catheter
Biofilm Formation on PD Catheters

Single Bacteria

Biofilm
What is A Biofilm?

- Defence for bacteria too thrive
- Aggregated communities enmeshed in an extracellular matrix of microbial and host-derived components
- Demonstrated by microscopy and culture
- DNA fragments in the dialysis fluid
What is a Biofilm?

- Bacteria survive better under hostile environmental conditions
- Intra-and extraluminal biofilm on PD catheter
- *ica*AD genes associated with biofilm production in CNST predictive of relapses or repeat episodes

Simultaneous Removal and Reinsertion of PD Catheters

- Removal of catheter in reinsertion in same procedure
- Minimizes eliminates the need for temporary HD during catheter removal
- For peritonitis, refractory exit site tunnel infections
- Successful reports in United States (n=55), France (n=11)
Use of TPA for biofilm

- Use of TPA to dislodge and disrupt biofilm

- Stand alone or adjunct therapy in addition to catheter removal reinsertion

- Only addresses intraluminal biofilm (not extraluminal)

- Previous randomized trial confirmed the superiority of catheter removal and reinsertion over urokinase

Williams Perit Dial Int. 1989;9(1):65-7
Removal and Reinsertion for Peritonitis: Important Points

- Not for peritonitis due to enteric organisms fungi, pseudomonas, or mycobacteria
- Peritonitis must be clinically, biochemically and microbiologically resolved
- Under and continued antibiotic coverage (duration not studied probably 7 days ok)
- Clean catheter first, old PD catheter removed second
The Case Continues

• Patient undergoes simultaneous catheter removal and reinsertion

• Treated with vancomycin for total of 7 days (some IV)

• Three days after catheter insertion starts low volume supine night cycler

• Returns back to usually prescription by two weeks
The Case Continues

• Two years later patient comes to ER on the weekend
  • Abdominal pain
  • Nausea and Vomiting, Fever
  • Cloudy Fluid

• PD fluid cell count c/w peritonitis

• Hemodynamically stable, admitted to hospital for pain control

• Started on IP Vancomycin and Ceftazidime and nystatin
The Case Continues

• PD fluid grows enterococcus faecalis sensitive to ampicillin and vancomycin

• Ceftazidime stopped vancomycin continued targeting trough levels above 15.

• Day 1 - cell count 5000
• Day 2 – cell count 6000
• Day 3 – cell count 5800
Is abdominal imaging (i.e. CT Scan) warranted at this time?

1. Yes because the cell count is climbing
2. Yes because the patient presented with fever, nausea and vomiting which is unusual with PD peritonitis
3. Yes because it is a ‘bowel’ bug
4. All of the above
Who would I Image?

- Polymicrobial enteric organisms
- Enteric Organism not responding to appropriate treatment clinically and biochemically
  - Persistent/Rising cell count
  - Persistent abdominal pain
  - Persistent culture positivity
- Hypotension / Hemodynamic Instability
- Accompanying Bacteremia
- Other severe GI symptoms – N/V, obstipation
- Other abnormal bloodwork
  - Lipase, transaminases.
The Case Continues

- CT scan done on day three with contrast no acute findings
- Oral amoxicillin 500 mg po bid added to therapy
- Could have switched to CAPD and ampicillin in every exchange but didn’t
- Peritoneal Rest (PD held for 24 hours)
  - Some evidence that may reduce risk of treatment failure
  - Rationale that microperforations can heal
- PD rechallenged on day 5 cell count drastically drops to 450 (from 5800)
- Considered adding gentamicin as synergy to vancomycin
- Day 5 culture grows enterococcus again
What Would You Do Now

1. The cell count is improving dramatically continue antibiotic therapy until culture and cell count negative

2. Remove the catheter with simultaneous reinsertion

3. Remove the catheter with no simultaneous reinsertion
Indications for Catheter Removal During Peritonitis

• **Urgent**
  • Secondary peritonitis – i.e., bowel perforation
  • Fungal peritonitis
  • Refractory peritonitis (DAY 5)

• **Semi-Elective**
  • Relapsing / Repeating peritonitis
    • (if responding to IP antibiotics)
  • Concomitant exit-site and tunnel infection
  • May entertain in and out
    • Under antibiotic coverage, organism dependent
The Risk of Catheter Loss Varies By Organism
Mujais et al KI 2006

![Bar chart showing the percentage of episodes and the percentage of catheters resolved or removed for different organisms.](chart.png)
The Case Continues

- PD catheter removed, HD initiated, vancomycin continued for a total of 3 weeks
- Patient is keen to return to PD
- Is return possible or advised?
PD After Catheter Removal: The Hong Kong Experience

100 Patients between 1995-2000

PD Catheter Removed After an Episode of Peritonitis

Catheter Reinsertion Attempt in all

Successful (n=51) Unsuccessful (n=49)

Szeto et al JASN, 2002
Successful vs. Unsuccessful PD

- Failed reinsertion in 49 patients due to "peritoneal adhesions" or ultrafiltration failure due to peritoneal sclerosis

- Catheter inserted via open surgical method (not laparoscopic)

- Catheter not removed until failure of effluent to clear by 10 days

Szeto et al JASN, 2002
Successful vs. Unsuccessful PD

- Greater dialysis vintage in the failed group:
  - 41 ± 29 months vs. 29.7 ± 17 months

- Greater proportion of fungal peritonitis in the failed group:
  - 16% vs. 4%

Szeto et al JASN, 2002
Return to PD Is Possible After Catheter Removal and Should Not Be Discouraged
Cho et al NDT 2014
Return to PD Is Possible After Catheter Removal and Should Not Be Discouraged
Cho et al NDT 2014
What have we learnt: Clinical Perls (I)

- Choice of empiric antibiotics (vancomycin vs. cefazolin)
- Role of antibiotic level monitoring and proper dosing
- Management of wet contamination
- Management of relapsing peritonitis and role simultaneous in and out procedure for PD catheter removal/reinsertion
What have we learnt : Clinical Perls (I)

• Role for abdominal imaging for peritonitis

• Management of enterococcal peritonitis and role of bowel rest

• Impact and success of return to PD after peritonitis resulting in catheter removal