An Uncommon Use of High Dose Steroid in a CAPD patient

Hau Kai Ching, Kwan Tze Hoi
Tuen Mun Hospital
LKK, 63M

- HT, IHD, DM, ESRF on PD since 14, August, 2003
- Bilateral inguinal hernia with repair done in December, 2004
- 1 episode of CAPD peritonitis in May, 2005
- Recurrent admission due to fluid overload requiring stepping up PD fluid to 2.5% 3 times per day
He developed recurrent abdominal pain since early 2006

Colonoscopy: multiple diverticuli over ascending colon

In view of the multiple diverticuli and underdialysis, he was shifted to chronic HD in Feb 2006

Tenckhoff catheter was removed on 23rd Feb, 2006
He began to experience recurrent episode of intestinal obstruction ....
He experienced the 3rd episode of IO in March 2006 and irreducible left indirect inguinal hernia was noticed.

Therefore urgent laparotomy was performed which revealed:

- Small bowel segment densely adhered to the previous prolene mesh causing marked proximal small bowel dilatation up to DJ
- Small bowel resection and repair of hernia was performed
- Path: serosal fibrosis + gangrenous bowel
2 more episodes of IO occurred in April, 2006

He also experienced progressive abdominal distension with tense ascites despite treating the underlying intestinal obstruction

Tapping was performed six times over 1 month
Content of the abdominal fluid revealed:
- WBC: 91/mm³
- Negative culture for bacteria, AFB and fungus
- Cytology: abundant lymphocyte but no malignant cells are seen
- Total Protein 26 (Serum TP: 49)
- Ferritin: 990 pmol/l
- CRP: 11.1 mg/dL
Cr: 760 (pre-HD), R/LFT: normal, Alb: 21
Ca: 2.30, PO4: 1.79
Hb: 9.0, WBC: 3.39, Plt: 493
USG(20/4/2006):
- ascites without collections
- Gallstone

CT abdomen was performed for persistent ascites:
• 4 months ago
Diagnosis: Encapsulating Peritoneal Sclerosis

Prednisolone 25mg BD was started

Response to treatment can be summarized in the following:
Prednisolone 50mg daily

- Ferritin
- CRP
- Albumin

Prednisolone dosage:
- 30mg
- 20mg
- 15mg
- 10mg

Dates:
- 5/23
- 6/12
- 7/2
- 7/22
- 8/11
- 8/31
- 9/20
Prednisolone 50mg daily

Weight

Abd Circ

<table>
<thead>
<tr>
<th>Date</th>
<th>Weight</th>
<th>Abd Circ</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-Mar-06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-Apr-06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-May-06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23-May-06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2L 2.7L 3.7L 2.8L 5L
Outcome

- Receiving 3x per week HD through retrocath
- Pending AVF creation
- No more vomiting, abdominal distension
- Appetite very good
- Enjoys good life, returning to pre-EPS life
- Complicated with 1 episode of line sepsis
- Reduction of prednisolone stepwise to 5mg BD (about 10 mg reduction per 4 weeks)
Summary

- Tenckhoff removal
- Recurrent IO
- Tense Ascites
- Steroid Started
- Nutrition & Ascites improved

EPS diagnosed

March → May → July
Encapsulating Peritoneal Sclerosis
Definition

EPS is a syndrome involving persistent, intermittent, and/or recurrent adhesive bowel obstruction (ileus) caused by wide ranging adhesion of the diffusely hypertrophied peritoneum

Morphologically, peritoneal thickening and/or sclerosis are observed:

- Peritoneal thickening: the state of peritoneal fibrosis and sclerosis
- Sclerosing peritonitis: peritoneal thickness accompanied by infiltration by certain inflammatory cells

Japanese Sclerosing Encapsulating Peritonitis Study Group 1998
Fatal complications of PD

Not all cases are related to PD

Best limited survey comes from a survey of 18 surgical centers in France

32 operated cases during 16 year

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>5</td>
<td>15.6</td>
</tr>
<tr>
<td>Post surgical</td>
<td>19</td>
<td>59.4</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>4</td>
<td>12.5</td>
</tr>
<tr>
<td>Cirrhosis + ascites</td>
<td>4</td>
<td>12.5</td>
</tr>
<tr>
<td>Generalized peritonitis</td>
<td>3</td>
<td>9.4</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>3</td>
<td>9.4</td>
</tr>
<tr>
<td>Total cases(^a)</td>
<td>32</td>
<td>100</td>
</tr>
</tbody>
</table>

\(^a\)PDI V20, S4
Hypothesis of EPS development

Two Hit Theory

1\textsuperscript{st} Hit
- Bacterial Peritonitis
- Chronic Peritonitis
- Excessive reaction after discontinuation of PD

2\textsuperscript{nd} Hit
- Peritoneal deterioration fibrosis and/or sclerosis
- Inflammation
- Encapulation
- Bowel obstruction

Kawanishi H et al, Adv PD 2002
Hypothesis of EPS in pathologic findings

Non-biocompatible dialysate, glucose, GDPs, AGEs, Osm + inflammation

TGF beta

Fibrosis

Peritoneal Thickening

EPS

VEGF

Neoangiogenesis

Inc permeability

Fibrin deposition

Encapsulation
Light Microscopy

- 250X
- Normal Peritoneum 450X
- Simple sclerosis 100x
- Arterial occlusion 450X
• Sclerosing peritonitis; areas of inflammation. Note giant cell in one area and amorphous material in other areas, as well as vascular sclerosis (LM, ×100).

• Note clusters of inflammatory cells and fibroblasts (LM, ×250).
• Normal

• EPS

9 months post PD
## Prevalence & Mortality of EPS

<table>
<thead>
<tr>
<th>Study</th>
<th>Prevalence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDTA, Oules 1988</td>
<td>0.03 – 0.31%</td>
<td>69%</td>
</tr>
<tr>
<td>Australia, Rigby 1998</td>
<td>0.7%</td>
<td>56%</td>
</tr>
<tr>
<td>Japan, Nomoto 1996</td>
<td>1.7%</td>
<td>44%</td>
</tr>
<tr>
<td>Japan, Kawanishi 2000</td>
<td>2.8%</td>
<td>42%</td>
</tr>
<tr>
<td>Korea, Kim 2005</td>
<td>0.8%</td>
<td>24%</td>
</tr>
</tbody>
</table>

**Prospective Kawanishi, AJKD 2004, Japan**

- 1958 pts followed 4 yrs: 2.5% 38%
- EPS developed from withdrawal of PD: 70%
## Prevalance and Mortality

<table>
<thead>
<tr>
<th>Time on PD</th>
<th>EPS cases(%)</th>
<th>Mortality(%)</th>
<th>Recover(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 years</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3 to 5 years</td>
<td>4(0.7%)</td>
<td>0(0%)</td>
<td>4(100%)</td>
</tr>
<tr>
<td>5 to 8 years</td>
<td>12(2.1%)</td>
<td>1(8.3%)</td>
<td>10(83.3%)</td>
</tr>
<tr>
<td>8 to 10 years</td>
<td>14(5.9%)</td>
<td>4(28.6%)</td>
<td>6(42.9%)</td>
</tr>
<tr>
<td>10 to 15 yrs</td>
<td>13(5.8%)</td>
<td>8(61.5%)</td>
<td>2(15.3%)</td>
</tr>
<tr>
<td>&gt;=15 years</td>
<td>5(17.2%)</td>
<td>5(100%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>48(2.5%)</strong></td>
<td><strong>18(37.5%)</strong></td>
<td><strong>22(45.8%)</strong></td>
</tr>
</tbody>
</table>

Kawanishi H et al, AJKD 44: 729, 2004

>= 10 yrs: Incidence 7.1%, mortality 72%
The Risk of EPS was high in pts on PD > 8 years
Diagnosis of EPS

When PD patients with peritoneal deteriorations complains of GI symptoms, EPS has to be suspected.

Symptoms

- Relating to bowel obstruction
  - Nausea, vomiting, abdominal pain
  - Malnutrition, diarrhoea, constipation, abdominal mass
- Bloody effluent, severe ascites
- Low grade fever
Blood tests
- Elevated CRP
- Low albumin
- EPO resistant anemia
- Effluent: Increased IL-6 & FDP

Imaging examinations
- Abdominal CT
- Intestinal fluoroscopy, Barium enema
- USG
- Laparoscopy
• Sclerotic calcification of peritoneum in AXR
- Peritoneal Calcification in CT
- Cacooning of bowel

NEJM 2002
Figure 1 — Computed tomographic scan demonstrating thickening of the peritoneum, fixed bowel, and anterior loculation of peritoneal dialysis fluid.  

Due to thinness of fibrous tissue, SPS gives no particular findings.

Increased thickness of the peritoneal membrane with a characteristic trilaminar appearance is the typical finding.
Figure 1
Intraoperative photograph: a fibrotic, cocoon-like membrane covering enteric loops.
Diagnostic dilemma

25% of cases of EPS was related to peritonitis either as a persistent or severe infection despite treatment according to the ISPD guidelines of peritonitis therapy.

Some form of “fulminant” peritonitis converting to EPS later had been reported.

Difficult to judge infection and inflammation, particularly in the early inflammatory stage.

Keep a High degree of suspicion in case of resistant peritonitis

Can start treatment for EPS if repeated septic workup was negative
Stages of EPS

Importance for understanding disease progression and treatment:

- **Inflammatory stage:**
  - Inflammation is suddenly noted; elevated C-reactive protein and fibrin degradation products in the effluent; bloody effluent

- **Encapsulating stage:**
  - Inflammation decreases; adhesions and sclerosis progress; ileus appears

- **Ileus stage:**
  - Inflammation disappears, but ileus progresses
Treatment

**Inflammatory stage:**

- Discontinuation of PD
- A steroid should be simultaneously administered.
- If, within 1 month, the steroid is ineffective, then the steroid is decreased, and the condition is managed using total parenteral nutrition (TPN)
Encapsulating stage:

To suppress inflammation, manage the condition using TPN

Ileus stage:

In leading this stage, total intestinal enterolysis should be performed.
Corticosteroid

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawanashi, AJKD, 2004</td>
<td>39</td>
<td>15 (38.5%)</td>
</tr>
<tr>
<td>Kawanashi, PDI, 2001, S6</td>
<td>12</td>
<td>7 (58.3%)</td>
</tr>
</tbody>
</table>

- Studies are mainly case series only
- Recommended dosage was about 0.5 - 1mg/kg/day
- Most useful in the inflammatory stage of EPS
- Also better response in shorter duration of PD
Pulse steroid is tried in some centres (0.5-1g/Day)

Combination of Steroid + Azathiopine

- Based on the improvement of EPS after transplant in some patients
- Studies are currently limited to case report

Dosage:
- Prednisolone ~ 0.5mg/kg/day
- Azathiopine ~ 1.5mg/kg/day
Use of tamoxifen to treat well-established EPS is limited to case series only:

**TABLE 1**  
Tamoxifen in Encapsulating Peritoneal Sclerosis (EPS)

<table>
<thead>
<tr>
<th>Case report (Ref.)</th>
<th>Allaria et al. (4)</th>
<th>Turner et al. (5)</th>
<th>Pollock (6)</th>
<th>Evrenkaya et al. (7)</th>
<th>Eltoum et al. (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients [n (sex)]</td>
<td>1 (female)</td>
<td>1 (male)</td>
<td>1 (female)</td>
<td>1 (female)</td>
<td>4 (3 males; 1 female)</td>
</tr>
<tr>
<td>Duration of PD (months)</td>
<td>92</td>
<td>N/S</td>
<td>84</td>
<td>N/S</td>
<td>52–97</td>
</tr>
<tr>
<td>Presentation of EPS with peritonitis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes in 3 cases</td>
</tr>
<tr>
<td>Prior episodes of peritonitis</td>
<td>8</td>
<td>Recurrent</td>
<td>8</td>
<td>N/S</td>
<td>1–2</td>
</tr>
<tr>
<td>Ultrafiltration failure</td>
<td>Yes</td>
<td>N/S</td>
<td>Yes</td>
<td>N/S</td>
<td>Yes</td>
</tr>
<tr>
<td>Total parenteral nutrition required</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dose of tamoxifen</td>
<td>10 mg q.d.</td>
<td>10 mg b.i.d.</td>
<td>10 mg q.d.</td>
<td>10 mg q.d.</td>
<td>20 mg q.d.</td>
</tr>
<tr>
<td>Duration of tamoxifen before recovery</td>
<td>3 months</td>
<td>N/S</td>
<td>N/S</td>
<td>2 months</td>
<td>2 months</td>
</tr>
<tr>
<td>Concurrent steroids</td>
<td>No</td>
<td>No</td>
<td>20 mg q.d.</td>
<td>0.5 mg/kg/day</td>
<td>No</td>
</tr>
</tbody>
</table>

PD = peritoneal dialysis; q.d. = once daily; N/S = not specified; b.i.d. = twice daily.
Tamoxifem as Prevention/ Early Treatment?

- Tamoxifem was also studied as preventive/early treatment for EPS (Adv in PD, 2003, Peso)
  - Case control studies involving patients with sclerosing peritonitis (early stages of EPS, no cacooning of bowel and mainly inflammatory state)
  - Tamoxifem group vs control group (similar baseline)
  - 4 develop encapsulation in control while non develop encapsulation in tamoxifem group
  - Mortality is higher in control group (71% vs 22%)
  - Mild thrombocytopenia is the only adverse reaction noticed in treatment group
Same group performs a newer study on patient with early stage of EPS (PDI, 2006, S2):

- 14 patients treated with tamoxifen 20mg/12h versus 15 patients of historical control
- Baseline characteristics are similar
- 13 patients from CG and 6 from TG develop EPS (p=0.013)
- Causes of death were related to EPS in 6 patients in CG and 1 in TG group (p=0.039)
- Mortality relating to EPS was significantly higher in patients not treated with tamoxifen (p=0.038)
Surgical Treatment

- Acute ablation of capsules and intestinal adhesions
- Cases of success have been reported
- Variable outcomes in difference studies:

<table>
<thead>
<tr>
<th>Author</th>
<th>Number</th>
<th>Success</th>
<th>Failure</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawanashi, Adv in PD, 2002</td>
<td>27</td>
<td>24</td>
<td>3</td>
<td>3.7%</td>
</tr>
<tr>
<td>Yamamoto, Adv in PD, 2002</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>25%</td>
</tr>
<tr>
<td>Kawanashi, AJKD, 2004</td>
<td>12</td>
<td>7</td>
<td>4</td>
<td>25%</td>
</tr>
<tr>
<td>Summers, KI, 2005</td>
<td>13</td>
<td>9</td>
<td>4</td>
<td>30.8%</td>
</tr>
<tr>
<td>Kawanashi, Adv in PD, 2006</td>
<td>86</td>
<td>78</td>
<td>8</td>
<td>9.3%</td>
</tr>
</tbody>
</table>
Conclusion

- Treatments showed variable outcomes
- Mortality is high even after treatment
- Most important part of management is prevention and early recognition
- Early initiation of steroid can be life-saving