Intraoperative Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Volodymyr Labinskyy MD
KCHC
8/29/13
• 52 y.o. F presented with severe pain in the right back and right flank, sharp, 8 out of 10, for 7 days. Also with complaints of SOB.
• PMX: No significant Hx
• PSH: None
• Allergies: NKDA
Labs:

- CBC: 12.51 <7.8/25.4> 464
- BMP: 133/4.3/95/21/14/0.44/105
- Mg 1.8 Phos 3.3
- CEA: 18.7
7/22/13 Abdomen/Pelvic CT: Large low-density 12 cm mass in the right lower quadrant inseparable from the colon, right adnexa and surrounding pelvic and abdominal wall musculature.

7/22/13 Chest CT negative for mets. Bilateral segmental PE.

7/25/13 Colonoscopy: Adenocarcinoma, well differentiated, with mucinous features.
Operative procedure 8/13/13: Intraoperative right ureteral stent placement, right colon resection, retroperitoneal dissection, right salpingo-oophorectomy, intraoperative HIPEC procedure.

Postoperative period was non complicated. Clears on post-op day #14, discharged home on post-op day #16.
Ileum, cecum, ascending colon:

- Invasive mucinous adenocarcinoma of the cecum, low grade
- Size 12 cm
- Gross tumor perforation
- Tumor invades through muscularis propria into pericolic fat
- Negative for lymphovascular/perineural invasion
- Tumor deposits in the pericolic fat
- Proximal and distal margins are negative
- Lymph nodes negative 0/20

Pathological stage: pT4pN0pMx

- Separately submitted margins are negative
- Right ovary and fallopian tube are negative
Hyperthermic intraperitoneal chemotherapy (HIPEC)
A change of strategy in the war on cancer

Patients and politicians anxiously await and increasingly demand a ‘cure’ for cancer. But trying to control the disease may prove a better plan than striving to cure it, says Robert A. Gatenby.

Nature 2009
• New treatment for carcinomatosis in the last 10 years:
• Complete cytoreductive surgery + hyperthermic intraperitoneal chemotherapy
• 5 year survival increased from 10% to 30-40%
Multimodality Treatment
Cytoreductive Surgery (CRS)
Peritoneectomy Procedures

- Peritoneectomy RUQ
- Lesser omentectomy CHE
- Right colectomy
- Peritoneectomy LUQ
- Omentectomy
- Splenectomy
- Gastrectomy
- Anterior parietal peritoneectomy

Peritoneectomy small pelvis, Rectosigmoid resection, Hysterectomy

Sugarbaker et al, Ann Surg 1999
How is PC usually diagnosed?

Table 2. Modes of Carcinomatosis Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Incidental finding (laparotomy or laparoscopy)</td>
<td>439</td>
<td>34</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>251</td>
<td>19.5</td>
</tr>
<tr>
<td>Radiologic examinations</td>
<td>138</td>
<td>10.3</td>
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<tr>
<td>Ascites or increased abdominal girth</td>
<td>124</td>
<td>9.2</td>
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<tr>
<td>Weight loss or lethargy</td>
<td>67</td>
<td>5.1</td>
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<tr>
<td>Intestinal obstruction</td>
<td>50</td>
<td>3.7</td>
</tr>
<tr>
<td>Elevated tumor markers</td>
<td>20</td>
<td>1.5</td>
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<tr>
<td>Symptomatic hernia</td>
<td>19</td>
<td>1.4</td>
</tr>
<tr>
<td>Anemia or gastrointestinal hemorrhage</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Appendicitis or peritonitis</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Constipation or diarrhea</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

Glehen et al. Cancer 2010
Rationale for Hyperthermic intraperitoneal chemotherapy (HIPEC)

**IP Chemotherapy**
- Pharmacokinetic argument: peritoneal plasma barrier higher dose feasible
- Maximal effect immediately after cytoreduction
- Limited systemic resorption / toxicity

**Hyperthermia**
- Pharmacodynamic argument: increased drug penetration
- Selective cytotoxicity of hyperthermia
- Synergism with chemotherapy and radiotherapy
Indications

- PC arising from colorectal carcinoma
- Pseudomyxoma peritonei
- PC arising from gastric cancer
- Malignant peritoneal mesothelioma
- PC arising from ovarian cancer
- Peritoneal sarcomatosis
- Adjuvant HIPEC (R0-Resection of colorectal and gastric cancer)
- Palliative HIPEC due to irreductible ascites
- Uncertain indications (CUP, desmoplastic tumor etc)
Morbidity: 27-56%; Mortality: 2.5-11%
<table>
<thead>
<tr>
<th>Year</th>
<th>National *</th>
<th>UPMC</th>
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<tbody>
<tr>
<td>2002</td>
<td>400</td>
<td>24</td>
</tr>
<tr>
<td>2003</td>
<td>425</td>
<td>60</td>
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<td>2004</td>
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<td>1050</td>
<td>163</td>
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<tr>
<td>2011</td>
<td>1200</td>
<td>145</td>
</tr>
<tr>
<td>2012</td>
<td>1350</td>
<td>176</td>
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</tbody>
</table>

* Estimated
HIPEC for colorectal carcinomatosis: indications

- good general condition
- biological age < 70 years
- no ascites
- no obstruction
- no or limited liver metastases
- motivation
‘Coliseum’ technique
Limitations of HIPEC

• Local toxicity
  – Bleeding (oxaliplatin)
  – Increased risk of anastomotic leakage
  – Prolonged ileus
  – Pleural effusion

• Systemic toxicity
  – Renal (cisplatin)
  – Bone marrow

• Limited tissue penetration (3 mm)
• Limited contact time
• Only non cell cycle specific chemotherapy
Prognostic Variables

- Disease histology
- (Near) complete cytoreduction feasible
- Not progressive under systemic chemotherapy
- Absence of ascites
- Long interval with primary surgery
- Performance status
- median survival 13 - 29 months
- complete cytoreduction: median survival 28 - 60 months
- mortality rate ranged from 0% to 12%.
8-Year Follow-up of Randomized Trial: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy Versus Systemic Chemotherapy in Patients with Peritoneal Carcinomatosis of Colorectal Cancer

Vic J. Verwaal, MD, PhD, Sjoerd Bruin, MD, Henk Boot, MD, PhD, Gooi van Slooten, MD, and Harm van Tinteren, ScM

Kaplan–Meier survival estimates, by arm

- arm = Standard
- arm = HIPEC

12.6 m versus 22.2 m, \( P = 0.028 \)
Comparison with ‘best’ systemic chemotherapy

25% of stage II and III T4 tumors developed peritoneal carcinomatosis as the only site of metastases. This defines the window of opportunity for adjuvant HIPEC to prevent peritoneal recurrence.
• Currently 103 ASPSM members, 52 from the U.S. and 51 from the 12 other countries.

• There are currently approximately 64 hospitals in the United States that have the capabilities of performing cytoreductive surgery and HIPEC.
American Society of peritoneal Surface Malignancies
standardized HIPEC delivery in patients with colorectal cancer with peritoneal dissemination

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<thead>
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<tbody>
<tr>
<td>1</td>
<td>HIPEC method</td>
</tr>
<tr>
<td>2</td>
<td>Drug</td>
</tr>
<tr>
<td>3</td>
<td>Dosage</td>
</tr>
<tr>
<td>4</td>
<td>Timing of drug delivery</td>
</tr>
<tr>
<td>5</td>
<td>Volume of perfusate</td>
</tr>
<tr>
<td>6</td>
<td>Inflow temperature</td>
</tr>
<tr>
<td>7</td>
<td>Duration of perfusion</td>
</tr>
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Conclusions

1) In selected PC patients, surgery with IP chemo can significantly prolong survival, but cure is rare

2) Possible role of ‘preventive’ HIPEC in high risk patients

3) Systemic chemotherapy is active in PC and should be seen as complementary, not competitive

4) More evidence is needed to ascertain:
   – Role of hyperthermic perfusion in addition to surgery
   – Role of (neo)adjuvant chemotherapy and/or targeted therapy
Thank You!

www.downstatesurgery.org
1. HIPEC in T4a colon cancer: a defendable treatment to improve oncologic outcome?  

2. Consensus Statement on the Loco Regional Treatment of Colorectal Cancer With Peritoneal Dissemination; JESUS ESQUIVEL, MD, FACS,1* DOMINIQUE ELIAS, MD,2 DARIO BARATTI, MD,3 SHIGEKI KUSAMURA, MD, PhD,3 AND MARCELLO DERACO, MD; Journal of Surgical Oncology 2008;98:263–267

3. 8-Year Follow-up of Randomized Trial: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy Versus Systemic Chemotherapy in Patients with Peritoneal Carcinomatosis of Colorectal Cancer; Vic J. Verwaal, MD, PhD,1 Sjoerd Bruin, MD,1 Henk Boot, MD, PhD,2 Gooike van Slooten, MD,1 and Harm van Tinteren, ScM; Annals of Surgical Oncology 15(9):2426–2432

4. Summary of Current Therapeutic Options for Peritoneal Metastases From Colorectal Cancer; TERENCE C. CHUA, BscMed (Hons), MBBS,1,2 JESUS ESQUIVEL, MD,2 JOERG O.W. PELZ, MD,3 AND DAVID L. MORRIS, MD, PhD1; Journal of Surgical Oncology 2013;107:566–573
Emerging indications for cytoreduction and intraperitoneal chemotherapy

**Ovarian cancer**: secondary cytoreduction; primary cytoreduction with minimal residual disease

**CRC**: approximately 3% of CRC patients will develop resectable PC without distant metastasis

**Pseudomyxoma peritonei (PMP)**; appendiceal neoplasms: rare

**Peritoneal mesothelioma**