Colon Cancer
Follow-up and Management

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Kings County Hospital Center
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Case Presentation

- **CC:** left abdominal wall mass

- **HPI:** This is a 59 y/o female who had undergone a laparoscopic extended right hemicolecetomy in 2009 for adenocarcinoma who was lost to follow-up after her procedure. She subsequently presented to clinic in 2010 with a painful left lower quadrant mass at a previously placed trocar site and a rising CEA level.
• Colonoscopy ’09: 75-99% circumferential mass in distal transverse colon, biopsy: infiltrating colonic adenocarcinoma, moderately differentiated

• CT Chest: negative

CT Abd/Pelvis: thickened segment of colon with adjacent fatty infiltration at the proximal descending colon
• Pathology: moderately differentiated adenocarcinoma, invading through muscularis propria and pericolonic fat, no lymphovascular invasion, negative proximal and distal margins, 0/20 LN negative for tumor; T3N0Mx; Stage IIA

• Oncology consult: no adjuvant chemotherapy indicated
• PMHx: colon cancer, placenta accreta
• PSHx: laparoscopic colon resection ‘09, D & C ‘78
• Allergies: shellfish
• Meds: none
• SHx: non-contributory
• FHx: non-contributory
• Vitals: Temp 98.6°F   BP 126/68   HR 71   RR 18

• Physical Exam:
  General: AAOx3
  HEENT: NCAT, EOMI
  Chest: CTA bilaterally
  CVS: S1S2, rrr
  Abdomen: previous scars well healed, ND, +BS, palpable, tender LLQ mass
  Rectal: good tone, no gross blood
• Labs:
  CBC: 5.37 / 13.1 / 38.9 / 268
  Chem: 142 / 4.3 / 106 / 23 / 11 / 0.83 / 87
  Coags: 10.1 / 26.9 / 0.9
  Type & Screen: O+

  CEA: 12/09 – 13.17 (0 – 3.0)
      4/10 – 2.7
      6/10 – 5.74
      9/10 – 11.20
      10/10 – 3.61
• Radiologic Studies:

  CXR: negative for pulmonary pathology

  CT Abd/Pelvis: soft tissue nodules within mesenteric fat and anterior to IVC as well as at the trocar site in LLQ suspicious for recurrent disease
• Radiologic Studies: CT scan of Abd/Pelvis
• Radiologic Studies:

   PET Scan: increased uptake corresponding to right hepatic serosal implants, retroperitoneal and mesenteric adenopathy and LLQ subcutaneous implant
- Radiologic Studies: PET Scan
• **pre-op:** exploratory laparotomy, excision of LLQ mass, possible resection of intra-abdominal mass/tumor

• **post-op course was uneventful.** The patient tolerated the procedure well and was discharged home on **POD #5**

• **pathology:** abdominal wall mass - metastatic colonic adenocarcinoma, negative margins
• pathology: cont’d
  small bowel, anastomotic and colonic resection- metastatic colonic adenocarcinoma, margins negative, 0/15 LN negative for tumor
  Pouch of Douglas mass- metastatic colonic adenocarcinoma, positive margins; T4N0M1; Stage 4

• Oncology: follow-up as outpatient for systemic chemotherapy (FOLFOX + Avastin)
## TNM Classification for Colorectal Cancer Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Classification</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Tis, N0, M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td></td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3, N0, M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4, N0, M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1, N1, M0</td>
</tr>
<tr>
<td></td>
<td>T2, N1, M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3, N1, M0</td>
</tr>
<tr>
<td></td>
<td>T4, N1, M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>Any T, N2, M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T, Any N, M1</td>
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</table>
• Adjuvant Therapy:
  current standard recommendations – all node +
  patients (Stage III) receive systemic therapy

• Trend to advocate adjuvant therapy for Stage II patients is
  based on poor prognostic factors:
    poorly differentiated histology
    vascular or lymphatic invasion
    bowel obstruction
    <12 LN evaluated
• Approx. 40% of patients will present with recurrent disease

• Surveillance is performed to identify recurrent disease at an early stage and at a time of potential resectability for cure

• Guidelines developed for follow-up include:
  - history and physical
  - CEA levels
  - colonoscopy
  - imaging studies (CT)
Colon Cancer: Follow-up

National Comprehensive Cancer Network Practice Guidelines for Surveillance

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Frequency</th>
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</table>
| History & Physical | Every 3 months for 2 years  
Then every 6 months for 5 years                                    |
| CEA                | Every 3 months for 2 years  
Then every 6 months for 5 years ($\geq T2$)                        |
| Colonoscopy        | Do in 1 year; If abnormal, repeat in 1 year  
If normal repeat every 2–3 years                                    |
| CT scan            | Consider annually for high risk of recurrence  
Post metastectomy for synchronous liver mets, increase to every 3–6 months |
• CEA
  - approx. 70% of pts with asymptomatic recurrent disease have an elevated level
  - PPV of 89%, NPV 100%

• CT Scan Chest/Abd/Pelvis evaluate for recurrent local or distant disease

• PET scan
  - localize recurrent and distant metastatic lesions
  - differentiate among scar, fibrosis or viable tumor
  - helpful in determining resectability of recurrent disease
Medical

• 5-FU (anti-folate), cornerstone of chemotherapy since 1960s
  - interferes with DNA synthesis by inhibiting thymidylate synthase (TS)
  - incorporates into RNA disrupting protein synthesis

• Biomodulator – leucovorin (folinic acid)
  - increases cytotoxicity by stabilizing 5-FU/TS complex

• Combination of both has led to clinical benefit in terms of disease free survival
Medical

- Oral therapy: Capecitabine
  - fluoropyrimidine that is converted to 5-FU via enzymatic pathway

  - highly selective; final conversion to 5-FU occurs with thymidine phosphorylase which is expressed only in neoplastic cells

  - avoids long-term IV access complications, cost-effective in comparison to continuous IV infusion of 5-FU, decrease in neutropenia and stomatitis
Medical

- **Oxaliplatin**
  - cross-links DNA and induces apoptosis
  - synergistic effect when combined with 5-FU/LV (FOLFOX)
  - MOSAIC trial: increased benefit in terms of disease free survival (DFS)

- **Irinotecan**
  - inhibits topoisomerase I by stabilizing DNA breaks
  - improves survival when given with 5-FU/LV (FOLFIRI)
  - neutropenia, neutropenic fever, death
### Adjuvant Chemotherapy for Colon Cancer

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>Description</th>
<th>N</th>
<th>3-year DFS</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP C-03</td>
<td>Intravenous 5-FU (Roswell Park Regimen) vs. methyl CCNU, vincristine, and 5-FU</td>
<td>1081 patients with Duke's B/C colon cancer</td>
<td>73% vs. 64%</td>
<td>.004</td>
</tr>
<tr>
<td>X-ACT</td>
<td>Capecitabine 1250 mg/m² orally twice daily vs. bolus intravenous 5-FU (Mayo Regimen)</td>
<td>1987 patients with resected stage III colon cancer (noninferiority trial)</td>
<td>64.2% vs. 60.6%</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>MOSAIC</td>
<td>FOLFOX-4 vs. infusional 5-FU/LV</td>
<td>2246 patients with stage II/III colon cancer</td>
<td>78.2% vs. 72.9%</td>
<td>.002</td>
</tr>
<tr>
<td>NSABP C-07</td>
<td>FLOX vs. bolus weekly 5-FU/LV</td>
<td>2407 patients with stage II/III colon cancer</td>
<td>76.5% vs. 71.6%</td>
<td>&lt;0.004</td>
</tr>
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Medical – Targeted Agents

• **Bevacizumab (Avastin)**
  - VEGF receptor; interferes with tumor-feeding blood vessel growth
  - improves DFS and OS when added to FOLFOX and FOLFIRI
  - side effects: bleeding, HTN, clot formation

• **Cetuximab (Erbitux)**
  - EGFR; inhibits multiple growth signaling pathways
  - treatment for irinotecan-resistant metastatic disease
Surgical

- Appropriately aggressive approach towards tumor debulking and potentially complete resection

Categories of Recurrence

- Perianastomotic (mural)
- Mesenteric (regional nodal)
- Retroperitoneal (drop mets, distant nodal, residual)
- Peritoneal
Surgical Management of Locally Advanced and Locally Recurrent Colon Cancer

Landmann, RG and Weiser, MR; Clinics in Colon and Rectal Surgery 2005; vol 18, pgs. 182-189

• 100 pts MSKCC presented with locoregional recurrence and underwent attempted salvage surgery

• hypothesis: recurrence occurred due to incomplete resection of infiltrating tumor

• symptoms: pain, bleeding, obstruction

• elevated CEA levels 51% pts

• work-up included CT scan, PET, colonoscopy
Surgical Management of Locally Advanced and Locally Recurrent Colon Cancer
Landmann, RG and Weiser, MR; Clinics in Colon and Rectal Surgery
2005; vol 18, pgs. 182-189

- 56 complete resection, 30 incomplete resection, 14 unresectable
- 41 pts underwent extensive en bloc resection
- 5 yr. survival was associated with completeness of resection
  - R0 resection: 58%
  - R1 resection: 5%
  - R2 resection: 0%
Surgical Management of Locally Advanced and Locally Recurrent Colon Cancer

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- R0 resection: single site of disease, perianastomotic recurrence, low presalvage CEA, absence of distant mets; useful in patient selection for operative intervention
- Systemic therapy: FOLFOX + Avastin for recurrent and metastatic disease
- Conclusion: locoregional recurrent disease, complete resection along with adjuvant therapy can lead to long-term survival
Cytoreduction and HIPEC

- Surgical technique for peritoneal surface malignancy
- Peritoneal Carcinomatosis Index (PCI): determines extent of disease; patient selection
- Peritonectomy: visceral and parietal stripping of peritoneum (complete cytoreduction)
  - spleen, gallbladder, greater and lesser omentum
Cytoreduction and HIPEC

- Hyperthermic Intraperitoneal Chemotherapy
  - hyperthermia increases penetration and cytotoxicity of CT to tissues
  - infused via catheter at 42-44 °C over 90 mins.

- Can lead to improvement in survival of appropriately selected patients if complete cytoreduction is achieved
Colon Cancer: Management

Survival based on PCI

Survival based on cytoreduction
Conclusions:
- rising CEA level post-op warrants high suspicion of recurrent disease and further evaluation
- management of recurrent disease is a combined approach (surgically, medically)
- regardless of surgical approach, complete resectability is the goal for long-term survival
References


2. Townsend, Beauchamp et al. Sabiston Textbook of Surgery 17th Ed. pgs. 1443-1462


5. www.NCCN.org