Colon Cancer Metastasized to the Liver—Now What?

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• No Relevant Financial Relationship Reported
Objectives

• Describe colorectal cancer (CRC) and statistics of the disease
• Identify the evolution of colon cancer
• Discuss the treatment options of colon cancer that metastasizes to the liver
• Emphasize the role of the Interventional Radiology nurse and technologist in assisting with treatment options, educating and supporting the patient/significant others
 Colon Cancer - A Formidable Enemy

In the United States:
- 3rd most common cancer (behind lung, prostate and breast cancer)
- 2nd most common cause of cancer death (behind lung cancer)

Estimated Statistics, 2014:
- 136,830 new cases of CRC
- 50,310 deaths caused by CRC

SEER, 2014
Stage at Diagnosis

- 39% Localized
- 36% Regional
- 19% Distant
- 6% Unknown

Legend:
- Unknown
- Localized
- Regional
- Distant
Adenoma to Carcinoma Pathway

Normal Epithelium → Hyper-proliferation → Early Adenoma → Intermediate Adenoma → Late Adenoma → Cancer

Sidney J. Winawer, M.D., 2003
Metastatic Colon Cancer

50-60% diagnosed will develop metastatic disease

15-25% with synchronous lesions

5-year survival >50% if resectable liver mets

Over 50% colon cancer deaths have liver mets

What’s the Point?

NCCN Guidelines 2010
Presentation of Patient

- Newly diagnosed colon cancer
- Newly diagnosed colon cancer with metastatic disease
- Colon cancer that has progressed to metastatic disease
- Recurrence of colon cancer
- Recurrence of metastatic disease
Patient Presentation to Clinic

- Fearful
- Anxious
- Angry
- Guilty
How is Colorectal Cancer/Recurrence Diagnosed?

- Diagnosis is confirmed with a biopsy
- Blood tests
  - Carcinoembryonic Antigen (CEA)

How is Colorectal Cancer Staged?

- Clinical stage versus pathologic stage
  - **Clinical Stage:**
    - Physical Exam
    - CT chest, abdomen, and pelvis
    - Endorectal Ultrasound (ERUS) or Rectal MRI
  - **Pathologic Stage:**
    - Surgical specimen
    - Need adequate number of lymph nodes (at least 12)

NCCN Guidelines, 2010
TMN Staging of Colon Cancer

- **Tumor (T)** looks at how far the primary tumor has grown into the wall of the colon or rectum, and if it has expanded into nearby areas.
- **Lymph node (N)** examines the extent of the cancer spread to nearby lymph nodes.
- **Metastasis (M)** refers to whether cancer has spread to other parts of the body, such as the liver, lungs or brain.
Stages of Colorectal Cancer

Stage 0

Stage I

Stage II

Stage III

Stage IV

ASCO 2010
5 Year Related Survival

- Localized: 90.3%
- Regional: 70.4%
- Distant: 12.5%
- Unstaged: 33.6%

SEER, 2013
How is Colorectal Cancer Metastatic to the Liver Treated?

- Stage/location dependent
  - Surgery
  - Chemotherapy
  - Embolization of liver lesions
  - Radiofrequency ablation (RFA) and thermal ablation
  - Radiation therapy
  - Targeted therapies, such as bevacizumab (Avastin), cetuximab (Erbitux), and panitumumab (Vectibix)

- More than one treatment may be used

- Colon cancer is treated somewhat differently from rectal cancer
Steps to Excellent Surgical Cancer Care

• Diagnosis

• Staging

• Evaluation of medical fitness

• Surgery

• Follow-up care/evaluations
Cancer Treatment: Surgery

• Foundation of curative therapy

• The tumor, along with the adjacent healthy colon or rectum and lymph nodes, is typically removed to offer the best chance for cure

• May require temporary or permanent colostomy

• 5-year survival rate following resection of liver metastases exceeds 50%
Right Hemicolectomy

Abdominoperineal Resection (APR)

Total Mesorectal Excision (TME) for Rectal

Left Hemicolectomy

Low Anterior Resection (LAR)
Who Gets Chemotherapy?

- Pathologic Stage
  - Tis, T1, N0, MO; T2, NO, MO
  - T3, NO, MO (no risk features)
  - T3, NO, MO (high risk for reoccurrence) or T4, NO, M0; or T3 with localized perforation or close, indeterminate or positive margins
  - T1-3, N 1-2 M0 or T4, N1-2, M0
  - Any T, any N, M1

- Adjuvant Therapy
  - None
  - Consider capecitabine or 5FU/leucovorin or Clinical trial or Observation
  - 5-FU/leucovorin/oxaliplatin or capecitabine or 5FU/leucovorin or Clinical Trial or Observation
  - FOLFOX or CapeOx or FLOX or Clinical Trial or Observation
  - see NCCN Guidelines

**Adjuvant therapy is indicated if lymph nodes are positive**

NCCN Guidelines, 2014
<table>
<thead>
<tr>
<th>Surveillance</th>
<th>ASCO Recommendation</th>
<th>NCCN guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H&amp;P</strong></td>
<td>Every 3 to 6 mos x 3 yrs Every 6 mos during year 4 and 5</td>
<td>Every 3 mos x 2 yrs Every 6 mos year 3 to 5</td>
</tr>
<tr>
<td><strong>CEA</strong></td>
<td>Every 3 mos x 3 yrs for stage II and III and rectal cancer</td>
<td>For T2 Tumors or higher Every 3 to 6 mos x 2 yrs Every 6 mos year 3 to 5</td>
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<tr>
<td></td>
<td>Start surveillance after completion of chemotherapy</td>
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<tr>
<td><strong>CBC, LFTs</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>CXR</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
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<tr>
<td><strong>FBOT</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>CT Chest</strong></td>
<td>Stage II or III yearly CT x 5 yrs</td>
<td>Consider CT CAP x 3 years if stage II or III</td>
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<tr>
<td><strong>Abdomen</strong></td>
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<tr>
<td><strong>CT pelvis</strong></td>
<td>Annual CT for 3 years if rectal cancer</td>
<td></td>
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<tr>
<td><strong>Colonoscopy</strong></td>
<td>Full colonoscopy Preoperative or preoperative If obstruction at presentation within 6 mos of surgery High risk yearly, if normal every 3 yrs</td>
<td>Colonoscopy in 1 year, if abnormal repeat in 1 year. If negative for polyps every 3 years. If preoperative obstruction within 6 mos</td>
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</table>
Colorectal Liver Metastasis

• Up to 20% of patients with CRC present with liver metastasis
  – Synchronous lesions

• Liver is the most common site of metastasis
  – Synchronous lesions
  – Metachronous lesions

• Uncontrolled CRC liver metastasis is the most common cause of death
What About Resectable Synchronous Lesions?

- Colectomy with staged liver resection
- Neoadjuvant therapy, then synchronous or staged colectomy and liver lesion resection (if converted)
- Colectomy, then chemotherapy (2-3 months), then resection liver lesion

NCCN Guidelines, 2010
Metachronous Liver Metastases

• Resectable
  – Consider PET-CT scan
  – Resection, followed by active chemotherapy regime (6 months) or
  – Neoadjuvant chemotherapy (2-3 months), followed by resection

• Unresectable
  – Active chemotherapy regime, dependent on chemotherapy history
    • Re-evaluate for conversion to resectable every 2 months if surgery reasonable goal
    • Continue active chemotherapy regime
Resection of CRC Liver Metastasis

Prognostic Factors

- Number of metastasis
- Resection margin status
- High pre-op CEA
- Size of largest tumor
- Stage of primary tumor
- Disease-free interval
- Synchronous disease
- Extrahepatic disease
- Periportal lymph node
Right Hepatic Lobectomy
Liver Metastasis

Unresectable

- Remaining liver after resection too small for adequate function
- Tumor contiguous to essential intrahepatic vascular structures
- Comorbidities of patient
How can we increase the number of patients eligible for liver surgery?

- Reduce tumor size
- Increase hepatic reserve
- Combine resection with other local therapy modalities
  - Radiofrequency ablation/thermal ablation
  - Stereotactic body radiation therapy
  - Chemoembolization
  - Radioembolization
Cancer Treatment: Chemotherapy

• Use of drugs to kill cancer cells
• Typical medications include: fluorouracil (5-FU, Adrucil), leucovorin (Wellcovorin), oxaliplatin (Eloxatin), irinotecan (Camptosar), and capecitabine (Xeloda)
• A combination of medications is often used (FOLFOX, FOLFIRI)
• Considerations prior to chemotherapy
  – Prognostic features of disease
  – Assessment of performance status, comorbidities and life expectancy
  – Anticipated survival benefits
  – Intentions of treatment
  – Response rates
  – Safety/toxicity of medications
• Discussion with patient/informed consent mandatory
  – Potential risks versus potential benefits of chemotherapy
Neoadjuvant Chemotherapy

• Allows downstaging of the tumor
• Optimal timing of surgery is unknown
  – prolonged chemotherapy increases liver toxicities and increases the rate of postoperative complications
• FOLFOX or FOLFIRI +/- Bevacizumab (Avastin®) is recommended
• 12 to 25% of patients have sufficient response to undergo subsequent resection
• 5-year survival rate is ~ 30 to 35% depending on series
• Generally offered to patients with
  – More than 4 liver metastasis
  – Bilobar involvement
Neoadjuvant Chemotherapy for Metastatic Disease

Advantages

• Earlier treatment of micrometastatic disease
• Determination of response to chemotherapy
• Avoidance of local therapy for those with early disease progression

Disadvantages

• Chemotherapy induced liver injury
• Missing “window” for resection through achievement of complete response or through disease progression, making resection areas difficult to ascertain
  – Evaluation every two months imperative post initiation of chemotherapy
Adjuvant Chemotherapy Post Liver Resection

• The best postoperative strategy is unknown
• NCCN recommendations:
  – 4 to 6 cycles post-operatively
  – Chemotherapy may be shortened post-op if patient received pre-op chemotherapy
  – FOLFOX or FOLFIRI +/- Bevacizumab is recommended

Timing Matters!!!
New Therapies: Targeted Therapy

- Treatment designed to target cancer cells while minimizing damage to healthy cells

- Cetuximab (Erbitux®) and panitumumab (Vectibix®) block colorectal cancer cell growth
  - Recent studies show that these two treatments are not effective for patients with tumors that have specific changes (mutations) to the KRAS gene
  - According to the U.S. FDA, cetuximab and panitumumab are only used to treat tumors that have a non-mutated KRAS gene
New Therapies: Antiangiogenesis Therapy

• “Starves” the tumor by disrupting its blood supply

• This therapy is given along with chemotherapy

• Bevacizumab (Avastin ®) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of stage IV colorectal cancer
Radiofrequency Ablation (RFA)/Thermal Ablation

Use of heat energy to cook and kill cancer cells

- Indicated for treatment of metastatic colon cancer and other malignancies
  - Multiple neoplasms
  - Dependent on position and size
  - Adjunct to surgery
  - Adjunct to other medical treatment

Procedure

- Small needle electrode inserted directly into tumor
- Wattage and current supplied by generator
- Each treatment:
  - Time of active ablation varies; dependent on needle used and size of lesion
  - One cm margin around treated lesion ideal
- Ablation margins critical to success
pre RFA of liver lesion

needle probe into lesion

post RFA margin around lesion
Hepatic Artery Chemoembolization

• Injection into the blood vessels of microspheres mixed with chemotherapy supplying the tumor
  – While delivering chemotherapy, cuts off the blood supply to the tumor, killing cells and reducing tumor size

• Indications
  – Metastatic colon cancer, hepatocellular cancer and other metastatic diseases
  – Patient selection
    • Chemotherapy resistant/refractory disease
    • Predominant liver metastases

Courtesy-BioSphere Medical, Inc.
pre-chemoembolization

post-chemoembolization
Radiation Therapy

• May be delivered concurrently with chemotherapy
• Includes tumor bed defined by radiological imaging or surgical clips
• Clinical situations determine type of radiation delivery
  – Stereotactic body radiation therapy (SBRT)
    • Image guided radiation therapy (IGRT)
    • Intensity modulated radiotherapy (IMRT)
  – Intra-arterial embolization using Yttrium-90 microspheres
Marker Placement for Radiation Delivery

Radiographic placement of coils through needle into target site

• Indications
  – Guide for future therapeutic procedures to mark area for accurate targeted therapy
  • In GI world, used for radiation treatment, accounting for variations in breathing
Radioembolization

• Description
• Indications
• Considerations for use
• Pre-procedure planning
• Treatment day
  – Discharge instructions
• Side effects
• Effects of treatment
About Advanced/Disseminated Disease

• Use of single or combination of agents
  – Chemotherapy
  – Interference with DNA replication
  – Inhibition of activities of vascular endothelial growth factor (VEGF) and epidermal growth factor (EGF) receptors

• All therapies represent a continuum of care; chemotherapy history paramount in regime choice
  – Doses, scheduling, methods of administration, regime intent, and patient performance status
  – Considerations include altering therapy in presence or absence of disease progression and presence of toxicities
End of Life

• Warning signals
  – Surveillance/evaluation testing results
  – Intolerance to treatment
  – Patient performance status

• Palliative treatment/best supportive care
  – May include continuation of treatment
  – Management of symptoms – pain, ascites, weakness, appetite, dehydration
  – Comfort care

• Hospice
  – Patient, family voice imperative
Case Study #1

- 62 year old male presented in 2/2006 with rectal bleeding; last colonoscopy at age 50
- Colonoscopy revealed adenocarcinoma sigmoid colon; CT’s and PET scan negative for metastatic disease; CEA level 6.0; sigmoid resection done, T2 N0 lesion; no need for adjuvant chemotherapy
- Patient complied with surveillance recommendations; CEA level returned to normal at 1.0; normal CT’s and CEA level until 4/2009
- 4/2009 rising CEA level to 6.0; CT’s and PET revealed solitary lesion to right lobe liver; deemed unresectable; downstaged with chemo
- To surgery for exploratory laparoscopy 6/2009; intraop RFA and wedge resection performed
- Adjuvant chemo given end of 7/2009 to 1/2010
- Patient complying with surveillance recommendations; serial CEA levels normal, CT’s free of disease; patient continues to enjoy activities of daily living with no limitations 12/2014
Case Study #2

- 54 year old female first diagnosed 1/2006, presented with right upper quadrant pain; no family history of colon cancer; no previous colonoscopy
- Colonoscopy revealed colon cancer, CT revealed metastatic disease to the liver
  - Resection primary tumor and hepatic mets at time of presentation
  - TheraSphere© to right hepatic lobe 1/2007, to left hepatic lobe 4/2007
  - Resection right lobe 5/2008
  - Post op chemo FOLFOX, then FOXFIRI to 10/2008
  - Repeat liver resection segment 6 and 7, no viable tumor present-abdomen negative for tumor 10/2008
  - Xeloda and Avastin until progression 7/2009
  - RFA and wedge resection of liver mets and abdominal surgeries due to encasement of left ureter 7/19/2010
  - Irinotecan and Avastin 4/2010 to 5/2010-discontinued due to disease progression
  - Enrollment in clinical trial-discontinued due to hyperbilirubinemia, cholangitis
    - Biliary stent, serial paracentesesises
- Succumbed to disease 1/2011
CT 4/2008
CT 10/2008
CT 5/2010
CT 12/2010
PET 4/2008
PET 10/2008
PET 5/2010
Biliary obstruction 7/2010
How Can We As Technologists and Nurses and Make a Difference in Statistics/Patient Care?

• Participate in colon cancer awareness programs
• Know colon cancer screening guidelines/follow-up
• Stress importance of colonoscopy results/recommendations
  — Discharge instructions in endoscopy
  — Follow-up appointments
• Education of self and peers
  — Radiology, SGNA courses
  — Interdisciplinary educational offerings
• Know and use resources available to patients and families
• Use opportunity for teachable moments
  — Effects of regular exercise if permitted
  — Effects of good dietary choices
Moffitt Cancer Center-Colon Cancer Awareness
Saturday, March 29, 2014

2014 Tampa Undy 5000!
Saturday, February 8, 2014
Al Lopez Park
Tampa, Fla
Conclusions

• Colorectal cancer is a leading cause of death
• There are effective treatments of metastatic disease, giving patients increased survival and quality of life
• The Interventional Radiology Team can be an enormous source of knowledge, encouragement, and support for patients and families facing colorectal cancer that has metastasized to the liver
• New strategies to prevent and treat colorectal cancer offer hope of winning the fight against this disease
References


References


References