ARROCase
Rectal Cancer

Mark Zaki, MD
Faculty Advisor: Peter Paximadis, MD

Detroit Medical Center
Karmanos Cancer Center
Wayne State University School of Medicine
Detroit, MI

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Case: Clinical Presentation

- 57 y/o male with a 2 month history of hematochezia, mainly with bowel movements
- Decrease in stool caliber over last 2 months
- Tenesmus
- Good appetite; weight stable
- KPS 90
Work-up: Colonoscopy

- Near circumferential, partially obstructing, malignant appearing mass 10cm from the anal verge, measuring 4cm in size

- Remainder of the colon was normal

- Biopsy was performed, revealing moderately differentiated invasive adenocarcinoma
Work-Up: Endoscopic Ultrasound

• Hypoechoic lesion extending through the muscularis propria into pericolorectal tissues
• No abnormal lymphadenopathy was noted, confirming the lesion to be **T3 N0**
• No gross invasion into surrounding structures was noted
Work-Up: PET/CT Scan

• Focal area of FDG uptake is demonstrated in the rectum, measuring 3.9 x 4.2 cm, with maximal SUV of 11.4

• Few subcentimeter lymph nodes in the pelvis bilaterally which demonstrate faint FDG uptake

• No evidence of distal metastases
Epidemiology

- Colorectal cancer: 3rd most common cancer and 2nd leading cause of cancer-related death in men and women in the United States
- Estimated number of cases in the U.S. in 2016
  - 95,270 new cases of colon cancer
  - 39,220 new cases of rectal cancer
  - 49,190 expected deaths
- Lifetime risk is 1 in 21 (4.7%) for men and 1 in 23 (4.4%) for women

1American Cancer Society
Risk Factors

• Modifiable
  – Obesity
  – Sedentary lifestyle
  – Diet high in red meat or processed meat
  – Smoking
  – Alcohol

• Non-modifiable
  – Age >50
  – Inflammatory bowel disease (IBD)
  – Family history
  – Inherited syndromes (FAP, HNPCC, Turcot & Peutz-Jeghers syndromes)
  – Type II diabetes mellitus

1American Cancer Society
Screening

- Malignant transformation takes several years
- Screening – detection/treatment of benign, premalignant, and curable-stage cancers
- Average-risk population: Start at 50 years old with one of the following:
  - Colonoscopy every 10 years (preferably)
  - Flexible sigmoidoscopy every 5 years
  - Fecal occult blood test (FOBT) or fecal immunochemical testing (FIT) every year

\(^2\)NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening. Version 1.2015
Anatomy

• The rectum is about 15 cm long (anorectal ring to peritoneal reflection)

• Reference point (anal verge or the dentate line/anorectal ring) should be stated
  – Anal verge - lowermost portion of the anal canal
  – Anorectal ring - is at the level of the puborectalis sling and levators, representing the pelvic floor

• Anterior peritoneal reflexion represents the point at which the rectum exits the peritoneal cavity (~12-15 cm from the anal verge)

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Histology

• Adenocarcinoma >90% of colorectal cancers
  – Poorly differentiated tumors - worse prognosis
  – Signet-ring cell subtype (1-2%) - poor prognosis

• Other histologic types are rare
  – Carcinoid tumors
  – Leiomyosarcomas
  – Lymphomas
  – Squamous cell cancers

³Bruce D. Minsky, Claus M. Rödel and Vincenzo Valentini. Clinical Radiation Oncology, Chapter 51, 992-1018.e6.
Clinical Presentation

• Hematochezia
• Change in bowel habits
  – Constipation
  – Diarrhea
  – Decreased stool caliber
• Urgency, inadequate emptying, and tenesmus may occur in cases with extensive transmural penetration
• Urinary symptoms and/or perineal pain from posterior extension are grave signs

Diagnosis/Work-Up

• H&P
  – DRE – evaluate for sphincter function
• Rigid Proctoscopy – assess primary tumor and biopsy
• Colonoscopy – detect possible synchronous primaries
• CT (chest, abdomen, and pelvis)
• Endorectal ultrasound (ERUS)
• MRI
  – Both ERUS and MRI are accurate in predicting T stage
  – PET scan is accurate in identifying nodal disease, though not routinely indicated
• CBC, CEA

\(^3\)Bruce D. Minsky, Claus M. Rödel and Vincenzo Valentini. Clinical Radiation Oncology, Chapter 51, 992-1018.e6.
# TNM Staging, AJCC 7th Edition

## Primary Tumor

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: intraepithelial or invasion of lamina propria</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into pericolorectal tissues</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor penetrates to the surface of the visceral peritoneum</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor directly invades or is adherent to other organs or structures</td>
</tr>
</tbody>
</table>

## Regional Lymph Nodes

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1–3 regional lymph nodes</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis in one regional lymph node</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastasis in 2–3 regional lymph nodes</td>
</tr>
<tr>
<td>N1c</td>
<td>Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in 4–6 regional lymph nodes</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in 7 or more regional lymph nodes</td>
</tr>
</tbody>
</table>

## Distant Metastasis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node)</td>
</tr>
<tr>
<td>M1b</td>
<td>Metastases in more than one organ/site or the peritoneum</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-T2</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3-T4a</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2-T3</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1-T2</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td>IIIIC</td>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3-T4a</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1-N2</td>
<td>M0</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
</tbody>
</table>

Treatment: T1-2, N0

• cT1 N0 – Transanal excision (if appropriate*)
  – *<30% circumference of bowel; <3cm in size; margin clear
    >3mm, mobile, non-fixed, within 8cm of anal verge, no LVSI or PNI; well to moderately differentiated; no lymphadenopathy

• cT1-2 N0 – Transabdominal resection

• Advantage of upfront surgery is complete pathologic staging and avoiding overtreatment with preoperative therapy
  – 18% in post-op arm of German Rectal Cancer Trial were overstaged preoperatively and found to have pT1-2, N0 disease at surgery

Adjuvant Treatment

• ChemoRT for pT3-4 N0 or N+

• GITSG 7175 – 227 patients (pT3-4 or N+) randomized to: surgery vs. post-op chemo vs. post-op RT vs. post-op chemoRT
  – Compared to surgery alone, postop ChemoRT improved 10-year OS (45% vs. 27%) and LF (10% vs. 25%)
  – *Underpowered to show benefit, unequal randomization, and not analyzed by intent to treat

• Intergroup/NCCTG 79-47-51 – 204 patients (pT3-4 or N+) randomized to post-op RT vs. post-op chemoRT
  – Post-op ChemoRT improved 5-year OS (55% vs. 45%) and LR (14% vs. 25%)

Treatment: T3 N0 or N+

• Neoadjuvant
  – Capecitabine/long-course RT (category 1/preferred) or
  – Infusional 5-FU/long-course RT (category 1/preferred) or
  – Bolus 5-FU/Leucovorin/long-course RT or
  – Short course RT (not recommended for T4 tumors)

• Primary Treatment
  – Transabdominal resection

• Adjuvant Chemotherapy
  – FOLFOX (preferred) or
  – CapeOx (preferred) or
  – FLOX or 5-FU/Leucovorin or Capecitabine

Swedish Rectal Cancer Trial

• 1168 patients randomized to:
  – Pre-op RT (25 Gy in 5 fx) followed by surgery vs.
  – Surgery alone

• Pre-op RT improved 13-year OS: (38% vs. 30%),
  CSS (72% vs. 62%), and LR (9% vs. 26%)

• Criticism: high recurrence rate in surgery-alone arm (26%)
  since total mesorectal excision (TME) surgery not used

• TME - entire specimen removed by sharp dissection along the mesorectal plane

Dutch CKVO 95-04 TME Trial

• 1805 patients randomized to:
  – Pre-op RT (25 Gy in 5 fx) followed by surgery vs.
  – TME alone (post-op RT if positive margins)

• RT improved 10-year LR (5% vs. 11%)
• No difference in OS
  – Unplanned subgroup analysis: RT significantly improved 10-year OS (50% vs. 40%) in stage III patients with a negative circumferential margin

\(^8\text{van Gijn W, Lancet Oncol. 2011 Jun;12(6):575-82.}\)
German Rectal Cancer Study
CAO/ARO/AIO-94

- 823 patients cT3-4 or N+ randomized to:
  - Pre-op chemoRT: ChemoRT (50.4 Gy/5-FU) followed by TME vs.
  - Post-op chemoRT: TME followed by chemoRT (55.8 Gy/5-FU)
    - Both arms received 4 additional cycles of bolus 5-FU after 4 weeks
- pCR rate in the pre-op group 8%
- No difference in 10-yr OS (59.6% vs. 59.9%)
- Pre-op RT improved 10-yr LR (7.1% vs. 10.1%)
- Increased rate of sphincter-preserving surgery (39% vs. 19%) in pre-op group

Treatment Planning

• CT Simulation
  – IV contrast may be used to delineate GTV and pelvic blood vessels
  – Supine with body immobilization or
  – Prone with use of a belly board for anterior displacement of bowel
Target Volumes

• CTVA: always treated for rectal cancer: internal iliac, pre-sacral, and peri-rectal
• CTVB: external iliac nodal region
• CTVC: inguinal nodal region
• For rectal cancer, in most cases, CTVA would be the only volume to receive elective RT
  – For certain presentations (e.g. extension into GU structures, extension to the peri-anal skin) one could consider adding the external iliac (CTVB) and even the inguinal regions (CTVC)

12https://www.nrgoncology.org/Portals/0/Resources/Atlases/AnorectalContouringGuidelines.pdf
Target Volumes: CTVA

- **Inferior**
  - At least 2 cm caudad to gross disease, including coverage of the entire mesorectum to the pelvic floor

- **Posterior and lateral**
  - Lateral pelvic sidewall musculature or, where absent, the bone

- **Anterior**
  - ~1 cm into the posterior bladder and the posterior portion of the internal obturator vessels

- **Superior**
  - Primary: the rectosigmoid junction or 2 cm proximal to the superior extent of macroscopic disease
  - LN: where the common iliac vessels bifurcate into external/internal iliacs (approximate boney landmark: sacral promontory)

- PTV margin should be ~0.7 to 1.0 cm, except at skin.

12https://www.nrgoncology.org/Portals/0/Resources/Atlases/AnorectalContouringGuidelines.pdf
Contours (See accompanying ARROContour)
3-field plan: PA and opposed lateral fields
3-field Plan:
dose color wash
<table>
<thead>
<tr>
<th>Dose Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Small Bowel</strong></td>
</tr>
<tr>
<td>QUANTEC</td>
</tr>
<tr>
<td>V15Gy &lt;120cc (Individual loops)</td>
</tr>
<tr>
<td>V45Gy &lt;195cc (potential space within peritoneal cavity)</td>
</tr>
<tr>
<td><strong>RTOG 0822 (IMRT)</strong></td>
</tr>
<tr>
<td>V35Gy &lt;180cc</td>
</tr>
<tr>
<td>V40Gy &lt;100cc</td>
</tr>
<tr>
<td>V45Gy &lt;65cc</td>
</tr>
<tr>
<td>Dmax &lt;50Gy</td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
</tr>
<tr>
<td>QUANTEC</td>
</tr>
<tr>
<td>Dmax &lt;65 Gy</td>
</tr>
<tr>
<td>V65Gy &lt;50%</td>
</tr>
<tr>
<td><strong>RTOG 0822 (IMRT)</strong></td>
</tr>
<tr>
<td>V40Gy &lt;40%</td>
</tr>
<tr>
<td>V45Gy &lt;15%</td>
</tr>
<tr>
<td>Dmax &lt;50Gy</td>
</tr>
<tr>
<td><strong>Femoral Heads</strong></td>
</tr>
<tr>
<td><strong>RTOG 0822 (IMRT)</strong></td>
</tr>
<tr>
<td>V40Gy &lt;40%</td>
</tr>
<tr>
<td>V45Gy &lt;25%</td>
</tr>
<tr>
<td>Dmax &lt;50Gy</td>
</tr>
</tbody>
</table>

Cumulative DVH
Cumulative DVH (Structure Volumes)
Post-treatment Assessment: PET Scan

- Complete resolution of the previously demonstrated FDG uptake in the rectum and small FDG avid lymph nodes in the pelvis

- No suspicious findings to suggest active malignant process

Before neoadjuvant therapy

3 weeks after neoadjuvant therapy
Post-treatment Assessment: Flexible Sigmoidoscopy

- Minimal residual erythema and granularity at the site of malignancy without any evidence of gross residual malignant tissue

- The rest of the examination was unremarkable
Surgery

• Low anterior resection (TME)
  – 8 weeks after completion of neoadjuvant chemoRT
  – Operative report: “No obviously palpable mass was noted. The tumor apparently had an excellent response to the preoperative radiation and there appeared to be no gross residual tumor”

• Pathology - pCR
  – Benign colonic mucosa with acute hemorrhage and fibrosis of submucosa
  – Seventeen benign lymph nodes (0/17)
Surveillance

<table>
<thead>
<tr>
<th></th>
<th>First 2 years</th>
<th>Years 3-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>H&amp;P</td>
<td>Q 3-6 mo</td>
<td>Q 6 mo</td>
</tr>
<tr>
<td>CEA</td>
<td>Q 3-6 mo</td>
<td>Q 6 mo</td>
</tr>
<tr>
<td>CT Chest/Abd/Pelvis</td>
<td>Q 3-6 mo</td>
<td>Q 6-12 mo</td>
</tr>
</tbody>
</table>

- Colonoscopy in 1 y
  - Except if no preoperative colonoscopy due to obstructing lesion, then colonoscopy in 3-6 mo

- PET/CT not routinely recommended

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May 16, 2016
References


