Modern Management of Locally Advanced Rectal Cancer: Case-based discussion

W. Forrest Johnston, M.D.
Christophe Marques, M.D., Ph.D.
Jonathan Mizrahi, M.D.

Ochsner™ Health System

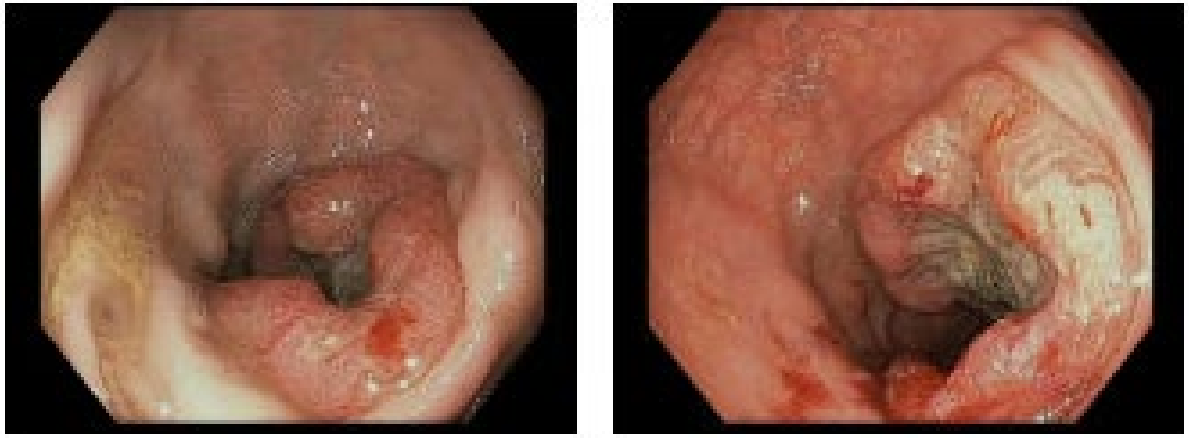
Case 1

- 58 year-old male presented to gastroenterologist via his PCP with complaint of bright red blood per rectum and pain with bowel movements. Worsened over the past 3 weeks.
- PMH: Essential HTN – on amlodipine 5mg daily. No prior CRC screening to date.
- PSH: No prior surgeries
- Family History: No known family history of cancer

Ochsner™ Health System

Case 1

- Colonoscopy Findings:
  - Ulcerated, partially obstructing mass in the rectum at 9 cm from the anal verge
  - Partially circumferential
  - Mass was biopsied
- Pathology:
  - Moderately differentiated invasive adenocarcinoma
  - pMMR by IHC



Ochsner™ Health System

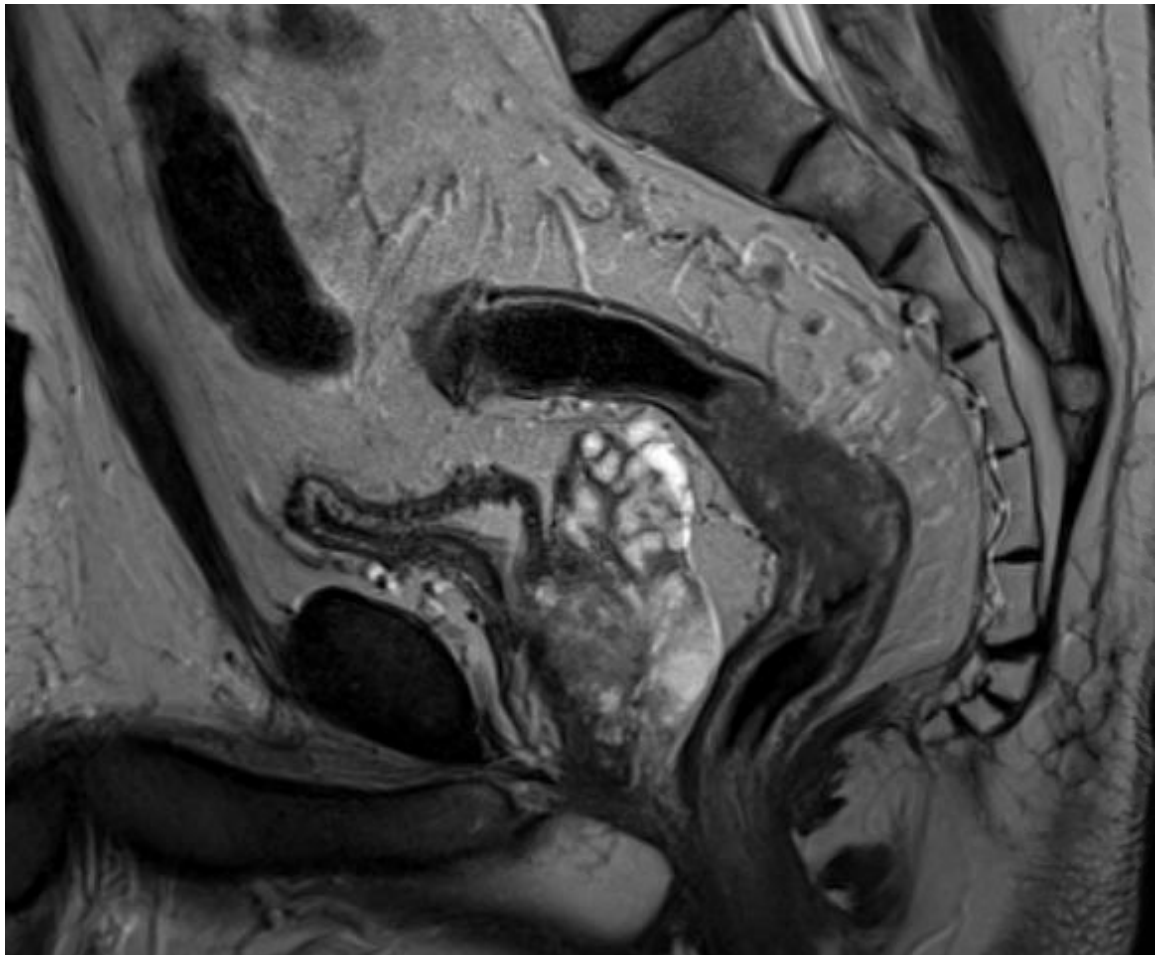
Case 1

- What imaging and labs are most helpful at this point?
  - CEA 1.0 ng/mL (normal < 5.0)
  - CBC without abnormalities
  - CMP without abnormalities
  - CT chest & abdomen showed no evidence of distant metastatic disease

Ochsner™ Health System

Case 1

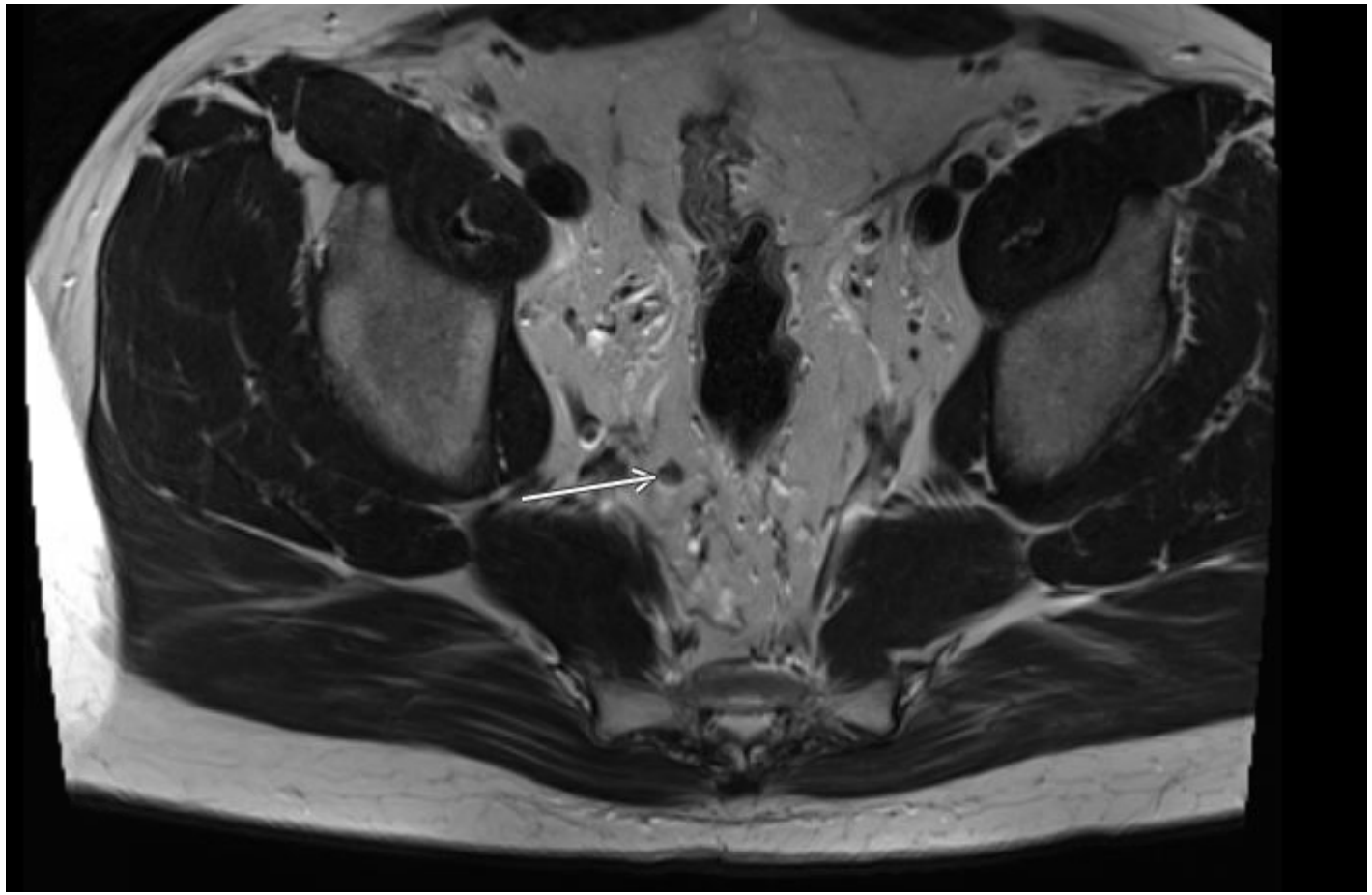
- MRI Pelvis – Rectal Ca Protocol
  - 4 cm posterior semi-annular mass that is 10 cm from the anal verge, straddling anterior peritoneal reflection
  - Tumor penetrates 1-5 mm beyond muscularis propria (T3b)
  - No sphincter involvement
  - MRF clear (> 2mm margin)



Ochsner™ Health System

Case 1

- MRI Pelvis – Rectal Cancer Protocol
  - 4 mesorectal lymph nodes, largest of which is 6.5 mm and heterogeneous.
  - No suspicious extramesorectal nodes



Ochsner™ Health System

Case 1

- What are his treatment options?

Ochsner™ Health System

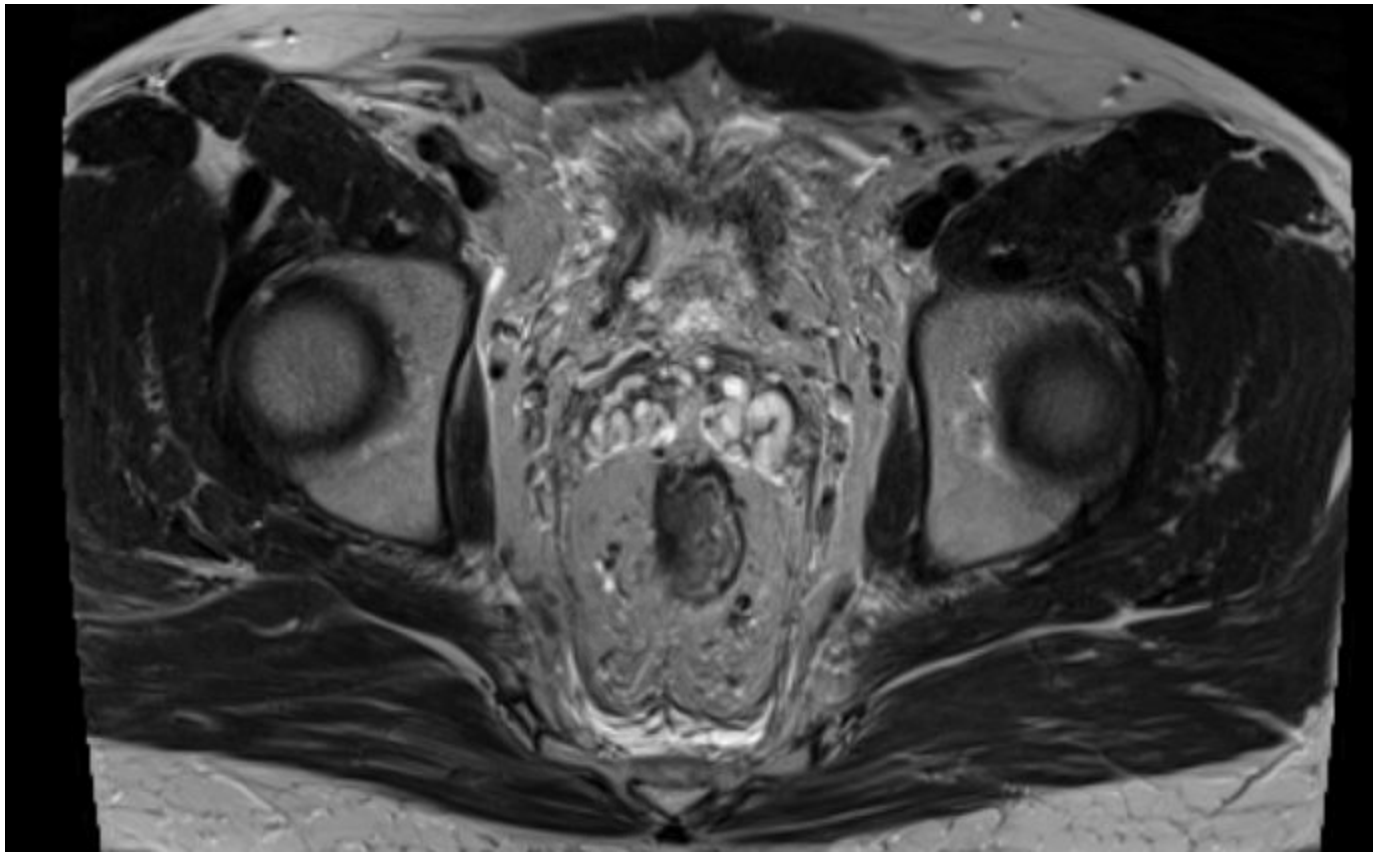
Case 1

- He was treated with short course radiation followed by 8 cycles of FOLFOX as part of total neoadjuvant therapy.

Ochsner™ Health System

Case 1

- Post-TNT MRI Pelvis – Rectal Ca Protocol
  - Residual mucosal and intramural diffusion restriction at site of treated tumor.
  - Tumor measures 2cm compared to 4cm with wall thickness 1.1 cm compared to 1.5 cm.
  - No suspicious lymph nodes
  - “Probable incomplete response”



Ochsner™ Health System

Case 1

- Post-TNT Flexible Sigmoidoscopy
  - Residual tumor beginning at 10 cm from anal verge, extending proximally by 5-7 cm.
  - Friable and smaller than initial presentation

Ochsner™ Health System

Case 1

- What is the next best step in management?

Ochsner™ Health System

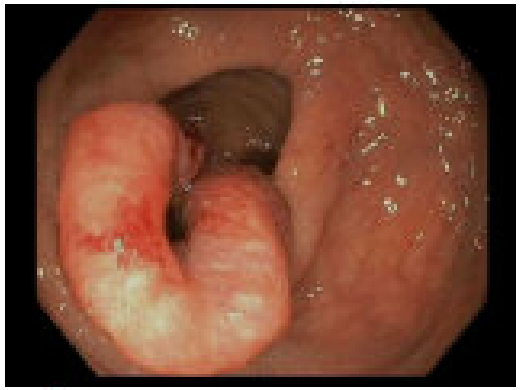
Case 2

- 40 year-old male presented to ER with BRBPR, weight loss.
- PMH: Essential HTN – on HCTZ 25mg daily. Obesity. No prior CRC screening to date.
- PSH: No prior surgeries
- Family History: No known family history of cancer

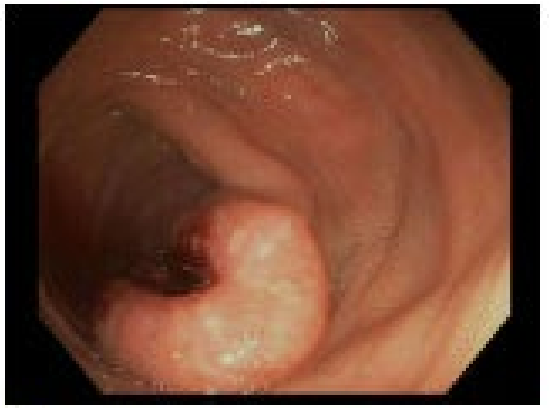
Ochsner™ Health System

Case 2

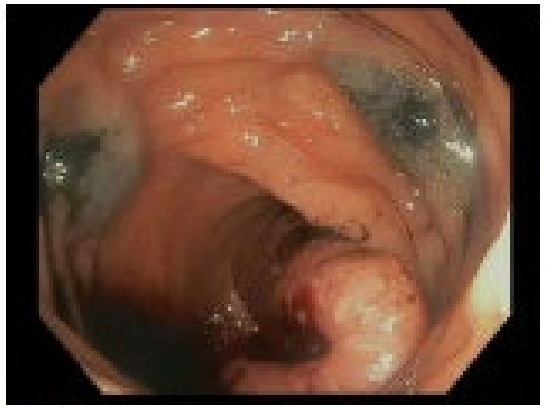
- Colonoscopy Findings:
  - Likely malignant tumor in recto-sigmoid colon at 15 cm
- Pathology:
  - Moderately differentiated invasive adenocarcinoma
  - pMMR by IHC



7 Rectosigmoid Junction Mass (15cm at distal aspect)



10 Rectosigmoid Junction Mass

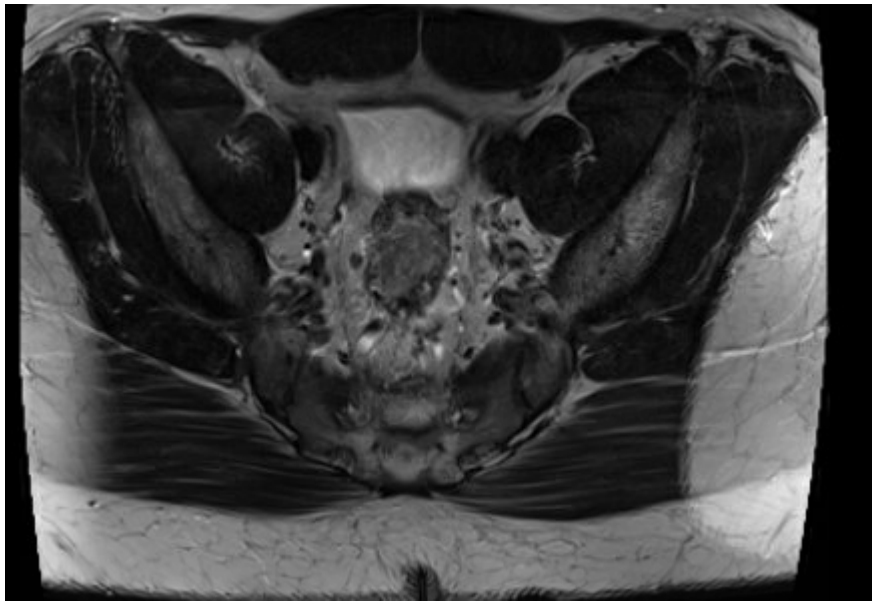


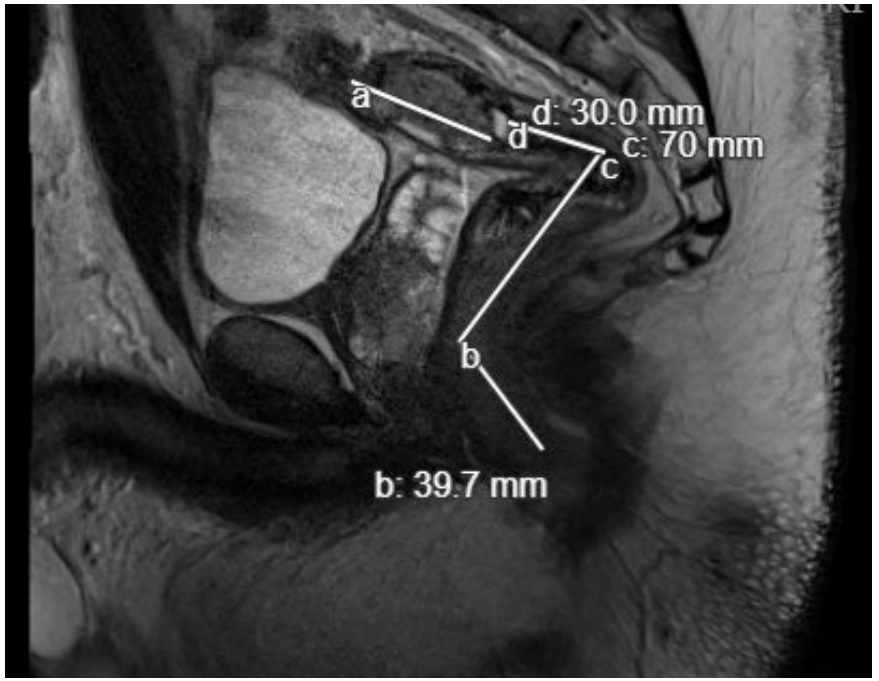
11 Rectosigmoid Junction

Ochsner Health System

Case 2

- MRI Pelvis – Rectal Ca Protocol
  - High (14 cm) anterior rectal tumor with invasion through muscularis and abutment of anterior peritoneal reflection and mesorectal fascia
  - Tumor is 4.5 cm in length
  - One suspicious lymph node





Ochsner Health System

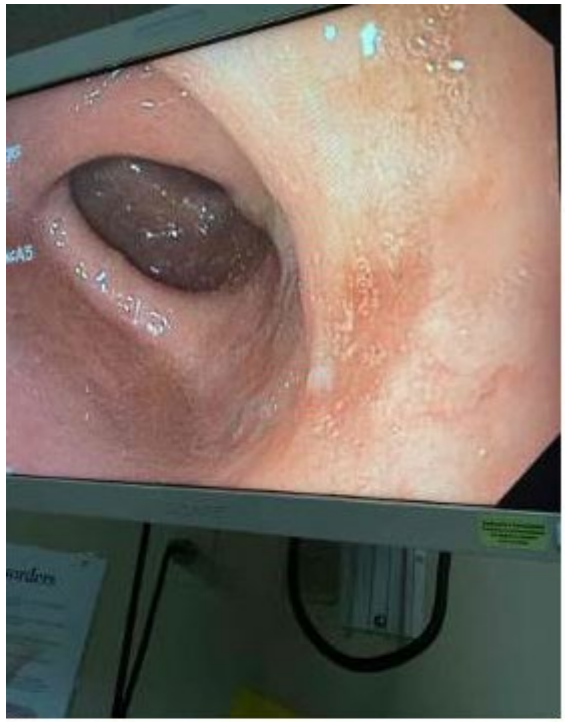
Case 2

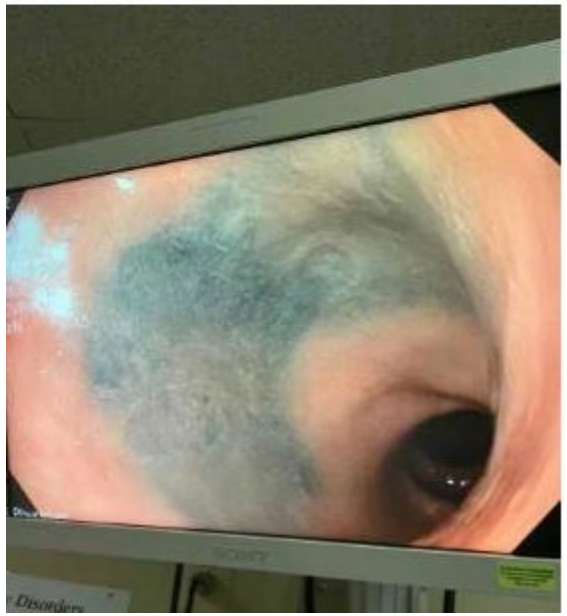
- He was treated with short course radiation followed by 8 cycles of FOLFOX as part of total neoadjuvant therapy.

Ochsner™ Health System

Case 2

- Post-TNT Flex Sig
  - Tattoo seen in upper rectum, small scar was appreciated at prior tumor site without any nodularity or mucosal abnormalities

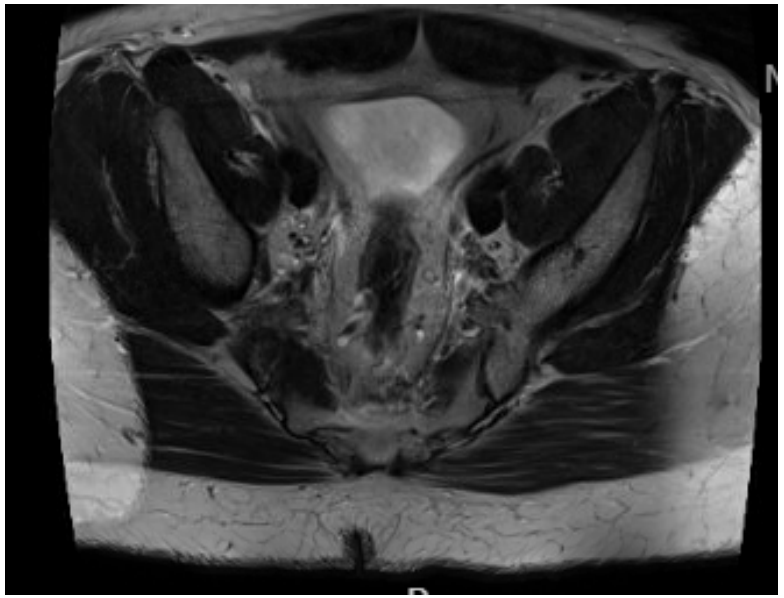


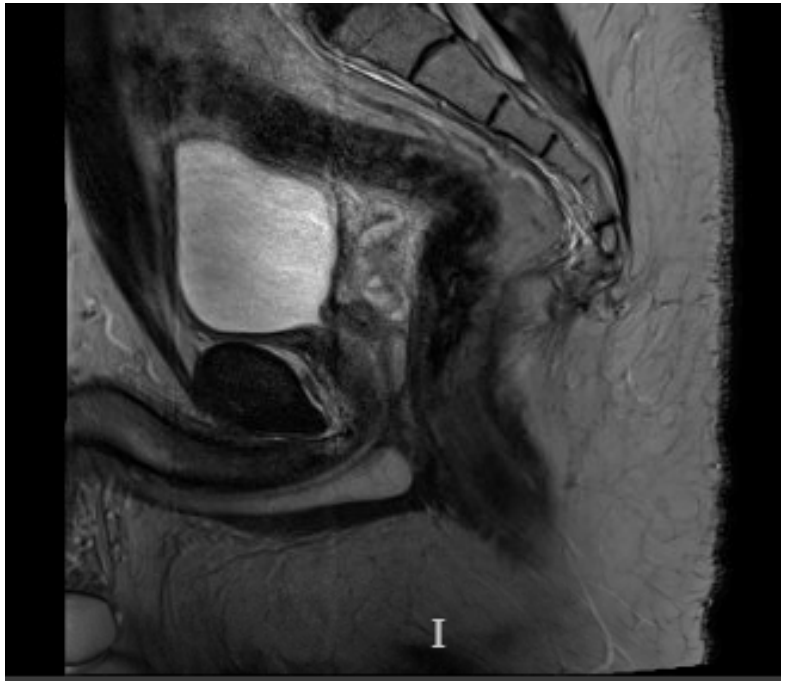


Ochsner Health System

Case 2

- Post-TNT MRI Pelvis – Rectal Ca Protocol
  - Dark T2 signal at site of prior tumor without measurable lesions or diffusion restriction
  - No suspicious lymphnodes





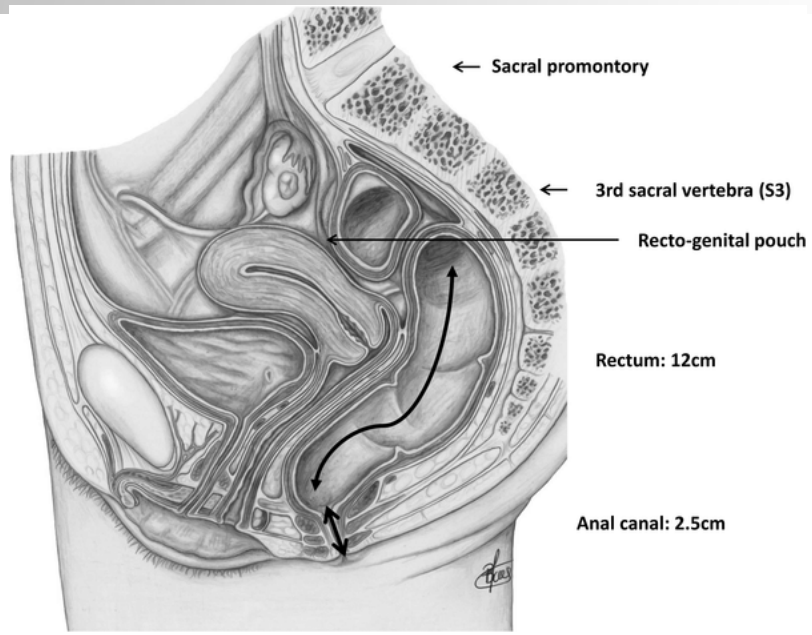
Ochsner™ Health System

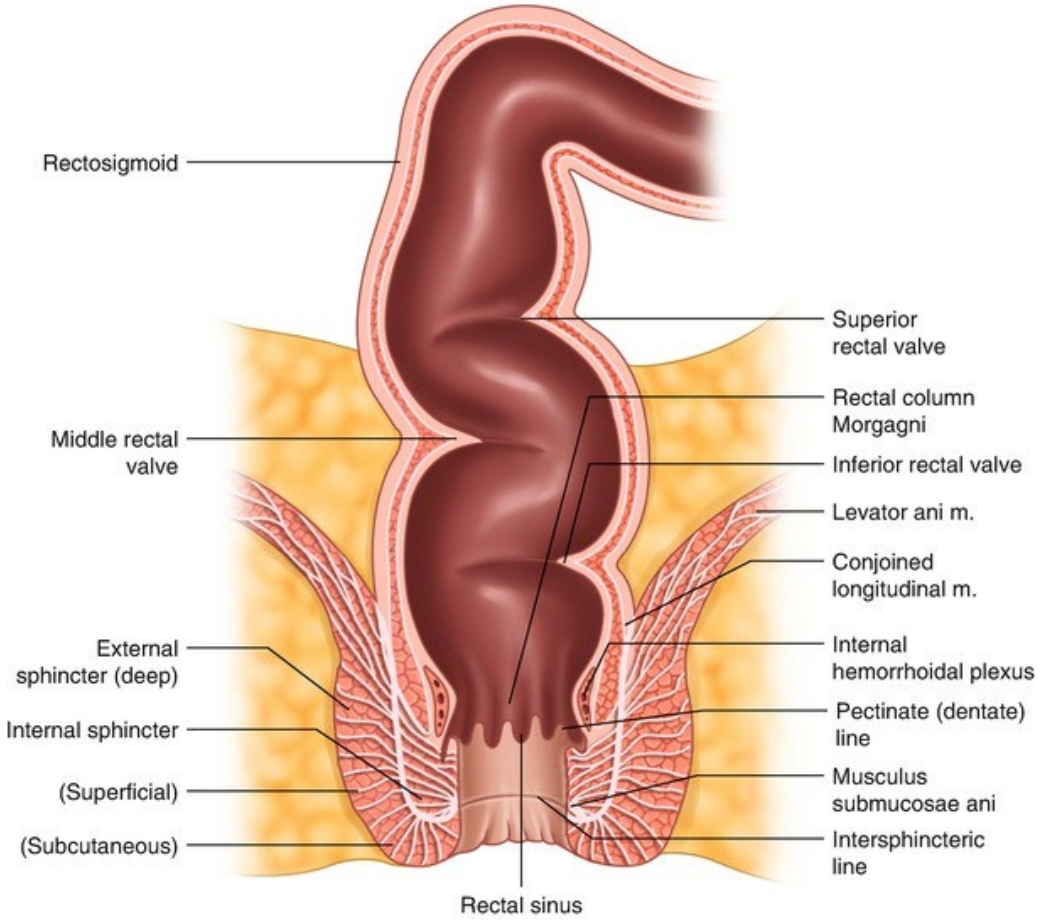
Case 2

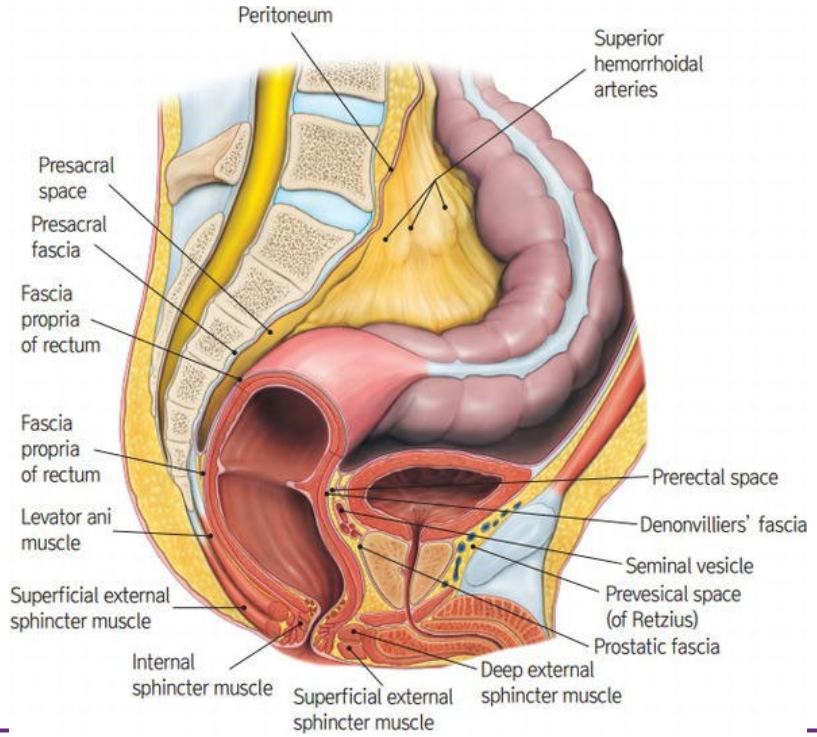
- What are the possible next steps in management?

Ochsner™ Health System

Anorectal anatomy



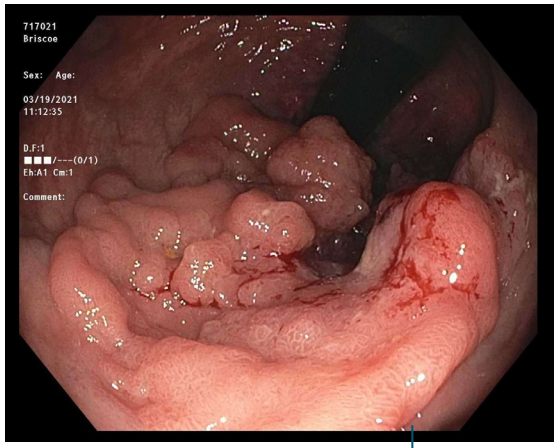




Rectal Cancer Treatment Options

- Surgery:
  - Local excision
  - Major resection
  - Sphincter preservation?
- Radiation
  - Short course (5 days)
  - Long course (25 days with chemosensitizer)
- Chemotherapy

Rectal Cancer Treatment Paradigm c. 2018



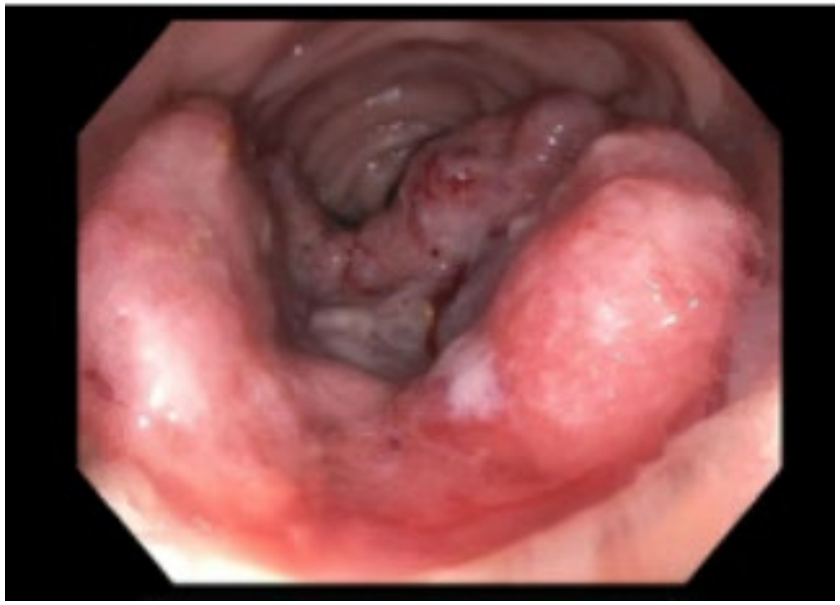
Benefits of TNT

- Increase compliance with chemotherapy
  - With postoperative adjuvant chemotherapy
    - 73% of patients started chemotherapy
      - (EORTC Radiotherapy Group Trial 22921, N Engl J Med. 2006;355:1114–1123)
    - 43% of patients received 95% of their planned chemotherapy
  - With neoadjuvant radiation and systemic chemotherapy
    - 82-100% completion rates
      - TNT metanalysis. Ann Surg 2020;271:440–448
- Increase rate of pathologic complete response
  - TNT increased the odds of pCR by 39% (1.39, 95% CI 1.08–1.81, P . 0.01)
    - TNT metanalysis. Ann Surg 2020;271:440–448
- Earlier reversal of ostomy
  - 2-3 months vs. 6-7 months

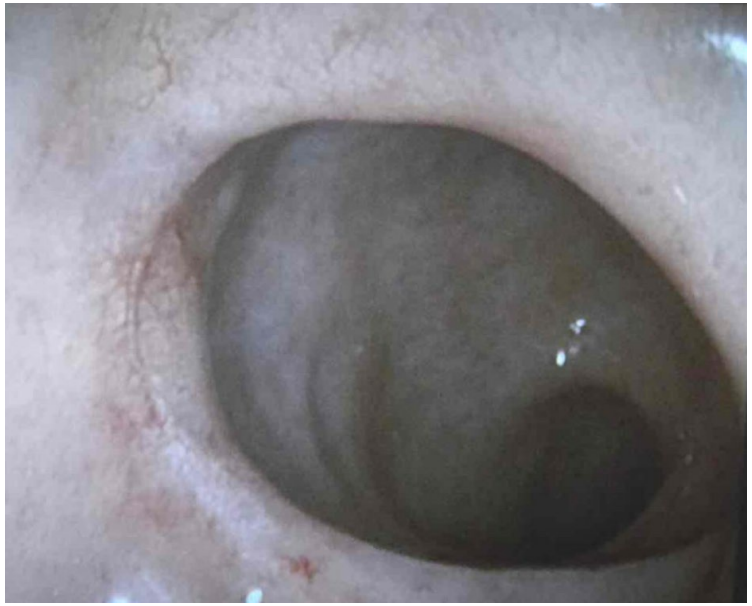
Complete Clinical Response (cCR)

- Received TNT:
  - Long course chemoradiation with 5FU (3/23/20-4/28/20) → 8 cycles of FOLFOX
- Re-staged

Pre-treatment



Post-treatment



- MRI: Tumor not visualized

Expectations

Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

Lancet 2018; 391: 2537–45

*Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium**

- IWWD study
  - 1000+ patients followed median 3.3 years
  - Most had long course chemo only (84%)
- Local regrowth
  - 25.2% at 2 years (95% CI 22.2-28.5%)
  - 64% in the first year
  - 88% in first 2 years
  - 97% located at bowel wall
  - 3% with isolated LN disease
  - Regrowth treated with resection with 6% positive margins

Thank you!

Jonathan.Mizrahi@Ochsner.org

904-333-3775

ochsner.org/podcast-cancer