ARROCase:

Borderline Resectable Pancreatic Cancer

Resident: Jordan Kharofa, MD
Staff: Beth Erickson, MD
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Medical College of Wisconsin
Department of Radiation Oncology
Case Presentation:

- 60 year old previously healthy male
- Presentation: 6 week history of poorly localized abdominal pain with radiation to his back. No nausea or vomiting episodes.
- Approximately 15 lb weight loss despite normal intake.
- Self-referred to his PCP

Pertinent Exam Findings

- KPS:100
- GENERAL: The patient appears healthy in no distress.
- LYMPHATICS: He has no cervical or supraclavicular lymphadenopathy.
- ABDOMEN: Somewhat obese. He is tender in the right upper quadrant. There are no palpable masses. He has no enlargement of his liver or his spleen. He has no fluid wave.
- HEAD: Examination of his eyes reveals normal, symmetrically reactive to light. No scleral icterus. Oral cavity with no visible lesions.
Workup

• Labs:
  • CBC, LFTs, Basic Chem unremarkable
  • CA 19-9 → 49.1 (H)

• Imaging:
  • CT ABD(pancreas protocol): 4.3x 3.4 cm pancreatic head mass. The mass completely encases the SMV and the portal vein/SMV confluence. The mass abuts the SMA ~120°
  • CT chest, PET → No metastatic disease *Role of PET evolving

• EUS w FNA: No enlarged peripancreatic LN. Celiac axis normal. Bx shows adenocarcinoma

• If neoadjuvant therapy planned, place biliary stent for in cases of biliary obstruction. Also consider diagnostic laparoscopy if neoadjuvant therapy planned.

• Renal perfusion scan prior to radiation therapy

• The patients was considered **borderline resectable** due to SMA abutment <180° and SMV encasement.
# Definition of Resectability

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>SMA, Celiac,</td>
<td>No abutment</td>
</tr>
<tr>
<td>Hepatic Artery (HA)</td>
<td>No abutment</td>
</tr>
<tr>
<td>SMV/PV</td>
<td>No abutment, distortion, tumor thrombus or encasement</td>
</tr>
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</table>
## Definition of Resectability

### Borderline Resectable

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>&lt;180° abutment</td>
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<table>
<thead>
<tr>
<th>Hepatic Artery (HA)</th>
<th>NCCN Version 2.2012</th>
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<tbody>
<tr>
<td>1. Gastro-duodenal artery encasement up to the Hepatic artery or</td>
<td></td>
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<tr>
<td>2. Direct abutment of hepatic artery w/o extension to celiac axis</td>
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<thead>
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<tbody>
<tr>
<td>1. Impingement and narrowing of the lumen</td>
<td></td>
</tr>
<tr>
<td>2. Encasement or short segment venous occlusion *</td>
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</tbody>
</table>

* Many institutions that perform venous resections with reconstruction consider short segment occlusion of the SMV as technically resectable.
## Definition of Resectability

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<tbody>
<tr>
<td>SMA, Celiac</td>
<td>&gt;180°</td>
</tr>
<tr>
<td>SMV/PV</td>
<td>Unreconstructable SMV/PV</td>
</tr>
<tr>
<td>Other</td>
<td>1. Aortic invasion or encasement</td>
</tr>
<tr>
<td></td>
<td>2. LN metastases beyond the field of resection</td>
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</table>
Treatment Decision Point

- Consultation with Surgical Oncology, Medical Oncology, Radiation Oncology

- Potential treatment options
  - Surgery followed by adjuvant chemo-radiation
  - Induction chemotherapy, chemoradiation, followed by surgery
  - Induction chemotherapy followed by surgery

- Potential advantages to a neoadjuvant approach
  - Increased access to multimodality therapy
  - Identification of patients at high risk for early metastases who are not likely to benefit from surgical resection
  - Improved tumor oxygenation and free radical formation
  - Potential increased margin negative resection and downstaging of borderline resectable patients
  - Improved radiation target delineation
  - Decreased incidence of pancreaticeo-jejunal anastomotic leak postoperatively
The optimal treatment algorithm for borderline resectable pancreatic cancer is not defined.

Treatment often begins with two months of systemic therapy followed by restaging and chemo-radiation.

MCW treatment algorithm:

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**Borderline Resectable**

<table>
<thead>
<tr>
<th>Wk 0</th>
<th>Wk 1</th>
<th>Wk 2</th>
<th>Wk 3</th>
<th>Wk 4</th>
<th>Wk 5</th>
<th>Wk 6</th>
<th>Wk 7</th>
<th>Wk 8</th>
<th>Wk 9</th>
<th>Wk 10</th>
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<th>Wk 17</th>
<th>Wk 18</th>
<th>Wk 19</th>
<th>Wk 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>PreTx Staging</td>
<td>Induction Chemotherapy</td>
<td>14 day break</td>
<td>Chemoradiation</td>
<td>3-4 week break</td>
<td>Restaging 1</td>
<td>Restaging 2</td>
<td>SURGERY</td>
<td></td>
<td></td>
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Courtesy of MCW Pancreatic Cancer Research Group
Chemotherapy

- **Induction Chemotherapy**
  - Phase II trial for induction Gemcitabine/Cisplatin prior to Gem/XRT in resectable disease. (Varadhachary et al, JCO 2008)
  - Increasing use of FOLFIRINOX (Bolus 5-FU, Leucovorin, Irinotecan, oxaliplatin) induction in medically fit patients secondary to survival benefit observed in the metastatic setting over single agent gemcitabine (Conroy et al, N Engl J Med 2011)

- **Chemoradiation**
  - gemcitabine (400mg/m2 weekly) or
  - capecitabine (825 mg/m2 twice daily on radiation treatment days) frequently used
Radiation Planning- IMRT

**Simulation:**

- Supine with arms up in alpha cradle or other immobilization. PO and IV contrast if available.
- Consider 4D-CT to evaluate motion. Superior/inferior displacement may be >1.5 cm.

**Contours:** No consensus for preoperative treatment volumes.

- Some institutions treat primary tumor with a margin
  - MCW → CTV includes: Primary mass, SMA origin with ~ 7mm margin, SMA and SMV vessels adjacent to the pancreatic head, Enlarged lymph nodes, +/- Celiac axis depending on tumor location. Carve out bowel and bone. Do not routinely include porta hepatic or peri-aortic LN regions.

- PTV: CTV + 1cm depending on institutional protocol
  - MCW: Daily IGRT for all patients. Respiratory gating used if motion >1.0 cm (40-60% phase), ITV of primary mass created if motion < 1.0 cm.

- OAR: Small bowel, large bowel, duodenum, stomach, liver, kidneys (preferentially spared if renal perfusion scan reveals dominance), cord.
Case Treatment

• Induction Chemotherapy
  • 4 cycles of FOLFIRINOX → Restaging shows no evidence of progression with decline in CA19-9 from 49.1 to 21. CT Imaging revealed some decrease in size of primary mass with stable SMA/SMV relationship.

• Chemoradiation
  • 50.4 Gy at 1.8 Gy/ Fx to >95% PTV using IMRT with concurrent capecitabine (825 mg/m2 twice daily on radiation treatment days) Restaging showed no evidence of progression with stable SMA/SMV relationship

• Pancreatic duodenectomy (whipple) performed with SMV resection and Internal Jugular Vein interposition graft
  • Final path: ypT2N1b, 2.5 cm tumor with >50% tumor necrosis, 2/39 LN involved, margins negative. Tumor distance from SMA margin 5 mm.
On Treatment Issues

- Premedication
  - Ondansetron 8mg 30-60 minutes pretreatment then as needed
  - Daily proton pump inhibitor 30-60 minutes before breakfast

- Dyspepsia
  - Gaviscon liquid 15-30 ml QID between meals and before bed.
  - Simethicone prn

- Creon taken with meals and snacks

- Rule out cholangitis for RUQ pain, fever
Representative Target Volumes

- GTV
- SMV
- SMA CTV
- Duodenum
- PTV
Representative Target Volumes
# IMRT Constraints

## Table 2. Dose Constraints for IMRT Optimization

<table>
<thead>
<tr>
<th>Structure</th>
<th>Constraints</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>PTV</td>
<td>5040 cGy (1.8 Gy/Fx)</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>Liver</td>
<td>Volume at 3000 cGy</td>
<td>&lt; 30%</td>
</tr>
<tr>
<td>Liver mean dose</td>
<td>&lt;2800 cGy</td>
<td>-</td>
</tr>
<tr>
<td>L Kidney and R Kidney</td>
<td>1500 cGy</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>Stomach</td>
<td>4500 cGy</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>Stomach Max Dose</td>
<td>5300 cGy</td>
<td>-</td>
</tr>
<tr>
<td>Duodenum Max Dose</td>
<td>5300 cGy</td>
<td>-</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>4500 cGy</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>Small Bowel Max Dose</td>
<td>5300 cGy</td>
<td>-</td>
</tr>
<tr>
<td>Large Bowel</td>
<td>4500 cGy</td>
<td>&lt;50%</td>
</tr>
<tr>
<td>Large Bowel Max Dose</td>
<td>5300 cGy</td>
<td>-</td>
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Representative Isodose Distribution
Dose Volume Histogram
Case Specific Teaching Points

- Multidisciplinary management is essential for patients with borderline resectable pancreatic cancer.

- In the setting of SMA abutment or SMV encasement, a surgery first approach may risk an R1/R2 resection.

- In this case, the patient was able to achieve margin negative resection following neoadjuvant therapy despite initial vascular involvement.

- Katz et al reported on 160 patients with borderline resectable pancreatic cancer. Following neoadjuvant treatment, 66 (41%) of patients underwent surgical resection and 94% of resected patients had negative margins (1).
References

