PANCREATIC ADENOCARCINOMA

Georgetown University Medical Center CyberKnife Team:

Radiation Oncologist: Gregory J. Gagnon, M.D.
Medical Oncologist: John Marshall, M.D.
Medical Physicist: Michael S. Lundsten, M.Sc.
Sonja Dieterich, Ph.D.
Radiation Therapist: Sosena Asrat, R.T.(T.)
Gerard Elie, R.T.(T.)

CyberKnife Center:

Georgetown University Hospital
Washington, DC
Case History:
The patient, a registered pharmacist, was in good health until 7/13/03 when he developed generalized pruritis and jaundice with a bilirubin level in the 5-7 mg/dl range. On 7/29, an elevated gastrointestinal cancer antigen (CA19-9) serum level of 189 units/ml was obtained. On 8/6, a CT scan with 3D reconstruction of the pancreas revealed a 2.5 cm mass AP within the uncinate process abutting the superior mesenteric artery (SMA) medially and the common bile duct (CBD) laterally. A 2 x 1 cm lymph node was identified within the portacaval space. On 9/10 an ultrasound-guided fine needle aspiration (FNA) revealed adenocarcinoma. A cholecystectomy was performed. Another 3D scan on 9/14 revealed involvement of the superior mesenteric vein (SMV) with occlusive thrombus and tumor involving approximately 180 degrees of the SMA, although the vessel remained patent.

CyberKnife Treatment Rationale:
The patient was not felt to be a resection candidate due to the involvement of the SMA and the SMV. He was treated with chemotherapy – continuous-infusion 5-FU, cisplatin (30 mg/m²) and interferon alpha throughout radiotherapy (see previous RT treatment above). Radiotherapy was followed by postoperative chemotherapy – gemcitabine, Taxotere and Xeloda – which caused bone marrow suppression issues. Post standard RT treatment, the pancreatic mass increased in size to 2.8 cm AP (compared to the previous 2.5 cm).

CyberKnife® Radiosurgery was felt to be a reasonable treatment which might render the disease inactive or perhaps allow for subsequent surgery.

Pretreatment CT (8/6/03) showing the pancreatic mass, which measured 2.5 cm AP. A biliary stent is seen in place. The tumor was deemed unresectable because of involvement of the SMA and SMV.

Pretreatment PET showing a positive FDG uptake in the pancreas.
TREATMENT DETAILS:

<table>
<thead>
<tr>
<th>Tumor Volume:</th>
<th>33.31 cc</th>
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<tbody>
<tr>
<td>Imaging Technique(s):</td>
<td>CT</td>
</tr>
<tr>
<td>Rx Dose &amp; Isodose:</td>
<td>24 Gy to 81%</td>
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<tr>
<td>Conformality Index:</td>
<td>1.56</td>
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<tr>
<td>Tumor Coverage:</td>
<td>97.2% of PTV</td>
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<tr>
<td>Fractions / Treatment Time:</td>
<td>3 / 115 minutes average</td>
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<tr>
<td>Path Template:</td>
<td>3 path 900_1000 mm</td>
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<tr>
<td>Tracking Method:</td>
<td>6D fiducial tracking</td>
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<tr>
<td>Collimator(s):</td>
<td>15 mm</td>
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<tr>
<td>Number of Beams:</td>
<td>278</td>
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Planning Process and Goals:
The 81% isodose line represents the prescribed dose of 24 Gy to the tumor. The treatment plan provided a 1.56 conformality index. Tumor coverage was 97.2% of the planning treatment volume. The tumor and the critical structures (duodenum, stomach, bowel, aorta and inferior vena cava (IVC)) were contoured for dose calculation purposes. An optimized inverse treatment plan was created such that the 81% isodose contour provided a conformal index of 1.56 while minimizing dose to the critical structures.

Treatment Delivery:
The patient was treated with 24 Gy to the 81% isodose line in three stages from 4/14 - 4/16/04. This treatment was five months after completion of initial radiation therapy and chemotherapy and seven months after initial symptoms. The planning CT for CyberKnife revealed that the prior standard RT and chemotherapy had not reduced the size of the tumor, though the size appeared to have stabilized.

The patient tolerated his treatment with no morbidity other than some fatigue.

Rendering of the CyberKnife's beam positions for the treatment of the pancreas from an anterior view point.

Axial and sagittal planning images obtained on 3/26/04 with the tumor, isodose curves, and critical structures reconstructed from 1 mm sections. Note the highly conformal dose distribution to the pancreas avoids the aorta (violet), IVC (blue), duodenum (green), stomach (light blue) and bowel (pink and coral).

Dose volume histogram (DVH) for tumor and critical structures.
Outcome and Follow-Up:
- Follow-up PET scan is negative in the pancreatic bed and the mass is not clearly identified.
- Tumor demonstrated an impressive shrinkage on CT scan on March 2005, acquired 11 months post CyberKnife radiosurgery.
- Patient is doing exceedingly well with no pain, 13 months post CyberKnife, 22 months post initial symptoms.
- Patient is far exceeding survival expectations, 10 - 12 months for locally advanced disease.

Conclusion and CyberKnife Advantages:
- Pancreatic cancer presents many problems, including significant nutritional problems, chronic pain, difficulties with local control, frequent systemic metastases, especially to liver, intraperitoneal metastatic spread, and a dismal survival rate. An improvement in local control will be a necessary but not sufficient step to improve on the current therapeutic outcomes.
- The CyberKnife is well-poised to improve the local control rates. This is accomplished with high dose fraction dose-escalation delivered via a highly conformal approach. Improvements in systemic therapy are also necessary, which can easily be sequenced into the treatment as the CyberKnife treatment is of short duration.
- Therapeutic expectations of this disease are largely palliative, but systemic improvements could lead to survival improvements.
- CyberKnife radiosurgery alone may produce survival gain in a small number of patients as suggested by this case.

Post CyberKnife radiosurgery CT in March 2005 shows an impressive reduction in the tumor size compared to both the initial CT (p. 2) and the planning CyberKnife CT (p. 3) scans. No tumor recurrence has been observed.

Follow-up FDG PET-CT scan in March 2005 is negative in the pancreatic bed. The mass has significantly reduced in size since the CyberKnife radiosurgical procedure.

CYBERKNIFE AT GEORGETOWN UNIVERSITY HOSPITAL (www.georgetownuniversityhospital.org)

Georgetown's CyberKnife was the first system on the East Coast, which was installed in the Spring of 2002. The CyberKnife, an image-guided robotic radiosurgery system, allows Georgetown physicians to provide a targeted, painless alternative to open surgery and a treatment option for certain tumors that are otherwise untreatable. Georgetown's Neurosurgery and Radiation Oncology Departments have created an interdisciplinary approach to provide patients with the most comprehensive diagnosis and treatment process possible. Over 250 patients were treated in 2004 with a clinical workload of 49% intracranial, 16% spine and 35% extracranial non-CNS lesions. Since initial installation, Georgetown has treated over 850 patients.

References: