Pancreatic Cancer Basics

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Case Study

- Mr. T is a 36 yo male who presented in the fall of 2003, at the age of 33, with complaints of abdominal discomfort and “generally feeling ill”
- Seen by PCP, symptoms thought to be secondary to irritable bowel syndrome or GERD, and was started on Prilosec
Case Study

- Symptoms persisted despite Prilosec, and the patient ultimately developed jaundice with markedly elevated LFTs
- An abdominal ultrasound was performed at Lawrence & Memorial hospital confirming biliary dilatation
- ERCP was performed and a biliary stent was placed – pt was d/c’d home with presumed gallbladder disease
Case Study

- Patient subsequently presented to YNHH ED with severe abdominal pain in Jan 2004, repeat abdominal ultrasound revealed enlargement in HOP.
- Follow up CT scan confirmed mass in HOP, 4.5x2.5cm, with dilation of the intrahepatic and pancreatic ducts.
- EUS with FNA of pancreas was performed.
Case Study

- Diagnosis was made as adenocarcinoma arising from the head of the pancreas
- Staging CT scans revealed no evidence for metastatic disease, therefore, patient was referred to surgical oncology for consideration of Whipple procedure
Epidemiology

- 33,730 cases of pancreatic cancer are anticipated in 2006, with 32,200 expected deaths

- 4th leading cause of cancer-related death in the U.S.; second only to CRC as a cause of digestive cancer-related death

- Mortality rates closely follow incidence rates due to poor prognosis
Epidemiology

- Incidence rare before the age of 45, however, sharply rises thereafter
- Incidence higher in men than women
- Increased incidence in blacks compared to the general population
Pancreatic/Biliary Anatomy

- The pancreas = retroperitoneal organ located deep within the abdominal cavity that serves both exocrine and endocrine function
  - Exocrine – secretes digestive enzymes including amylase and lipase
  - Endocrine – secretes metabolic mediators including insulin, glucagon, and somatostatin
Pancreatic/Biliary Anatomy
Pancreatic tumors can arise from both the exocrine and endocrine portions of the pancreas, however, of pancreatic tumors, 95% develop in the exocrine portion. These include: ductal epithelium, acinar cells, connective tissue, and lymphatic tissue.
Histology

- Of all pancreatic cancers, 80% are adenocarcinomas of the ductal epithelium
- Only 2% of tumors from the exocrine pancreas are benign
- Less common types of exocrine pancreatic tumors include: giant cell carcinoma, adenosquamous carcinoma, cystadenocarcinoma, papillary cystic carcinoma
- The most common types of endocrine pancreatic tumors include: insulinoma, gastrinoma, VIPoma
Genetic Factors

- Up to 5-10% of patients with pancreatic carcinoma have some genetic predisposition to developing the disease.
- Inherited disorders that increase the risk of developing the disease include: hereditary pancreatitis, hereditary breast/ovarian cancer, multiple endocrine neoplasia, familial atypical multiple mole melanoma syndrome (FAMM), HNPCC, FAP/Gardner syndrome, Peutz-Jeghers syndrome.
Risk Factors

- Age
- Chronic pancreatitis
- Tobacco
- DM
- Hereditary predisposition
- Obesity/Diet
Screening

- USPSTF (United States Task Force) – recommends against routine screening in asymptomatic individuals
- Consideration may be given to screening with EUS and/or CT scan in the high-risk population
Clinical Features

- Signs and symptoms vary depending on the anatomic location of the tumor (head vs. body/tail)

- If head of pancreas is involved, symptoms may include:
  - Obstruction of the bile duct to the small intestine or stomach may occur, associated with jaundice, pruritis, and/or vomiting
Clinical Features

- Conversely, if the body/tail of the pancreas is involved, symptoms may include: upper abdominal/back pain, weight loss (usually substantial, 30-50lb), and fatigue
  - In general, 90% of the time, the tumor has already metastasized outside the region of the pancreas
  - The pain may be intermittent, worse with eating, and usually associated with a poor prognosis
Clinical Features
Clinical Features

- Other symptoms include the following:
  - Anorexia
  - Early satiety
  - Diarrhea
  - Steatorrhea
Diagnosis/Staging

- Diagnosis is made based upon one or more of the following:
  - Routine labs tests – may suggest a rise in the serum bilirubin or alk phos, or the presence of mild anemia, however the dx is typically made radiographically and histologically
  - Ultrasound/EUS
  - CT scan
  - MRI/MRCP
  - Serum tumor markers – elevated CA 19-9, CEA
Diagnosis/Staging

- Laparoscopy is emerging as a new staging modality for periampullary tumors to detect small occult mets, not seen on CT scan
- Can potentially reduce the number of apparent operable cases that are found unresectable at laparotomy
Staging

*TNM staging:*

**T (Tumor)**
- TX – primary tumor cannot be assessed
- TO – No evidence of primary tumor
- Tis – In situ carcinoma
- T1 – Tumor limited to pancreas, 2cm or less
- T2 – Tumor limited to pancreas, more than 2cm
- T3 – Tumor extends beyond pancreas, but without involvement of celiac axis or SMA
- T4 – Tumor involves the celiac axis or the SMA (unresectable)

**N (Nodes)**
- NX – Regional lymph nodes cannot be assessed
- NO – No regional lymph node metastasis
- N1 – Regional lymph node metastasis

**M (Metastasis)**
- MX – Distant metastasis cannot be assessed
- MO – No distant metastasis
- M1 – Distant metastasis
Staging

- Stage 0 – Tis N0M0
- Stage IA – T1N0M0
- Stage IB – T2N0M0
- Stage IIA – T3N0M0
- Stage IIB – T1-3N1M0
- Stage III – T4Any NM0
- Stage IV – Any T Any NM1
Treatment

- Resectable vs. Locally-Advanced vs. Metastatic disease
- Adjuvant vs. Neoadjuvant treatment
- Surgery vs. Chemotherapy vs. Radiation therapy
Surgery

- Surgical resection is the only potentially curable treatment option, however, even then, the 5 yr survival rate is only about 25-30% for node-negative disease and <10% for node-positive disease.
- Due to the late presentation, only approx. 15-20% of cases are resectable at the time of diagnosis.
Determining Resectability

- Absolute contraindications include: mets to liver, peritoneum, omentum, or any extrabdominal site
- Most surgeons require that the tumor does not involve sites that would not be encompassed within the resection, and does not involve the adjacent critical structures such as SMA/SMV, portal vein, celiac axis, or hepatic artery
Potentially Resectable on CT scan
Unresectable on CT scan
Liver Mets
Surgical Resection

- The standard operation for pancreas cancer is pancreaticoduodenectomy, or Whipple procedure.
- The outcome of resection depends mainly on surgical margins, nodal status, and extent of local invasion.
Mr. T met with the surgeon, and planned for Whipple procedure on 1/23/04

Intraoperatively, he was found to have hepatic arterial involvement, and deemed unresectable

The surgery was aborted, and the patient was referred to Medical Oncology for consideration of alternate treatment options
Chemotherapy regimens typically include:

- Gemcitabine
- 5-FU
- Tarceva
- Xeloda
- Oxaliplatin
- CPT-11
- Taxotere
- Bevacizumab
- Cetuximab
Radiation therapy

- Radiation is a useful modality, however, there is no clear consensus on the role of radiation, and optimal timing for its use
  - Side effects include fatigue, diarrhea, abdominal pain, myelosuppression
Advanced Disease

- Clinical benefit response – early studies suggested that patients who lacked an objective response often had improvement in their symptoms (i.e., pain, weight loss) and performance status

- If patient is hesitant about considering chemotherapy, the above should be discussed at length
Complications/Palliation of Symptoms

- Jaundice – biliary stent vs. bypass procedure
- Duodenal obstruction – duodenal stent vs. bypass procedure
- Delayed gastric emptying – prokinetic agents may be helpful
- Pain – celiac plexus block, narcotics, palliative radiation
- Depression – adequate tx with antidepressants and emotional support
- Malabsorption/Cachexia – consider pancreatic enzyme replacement
- Ascites – palliative paracentesis, gentle diuresis
Celiac Plexus Nerve Block

Celiac plexus nerve block Schematic view of a retrocrural approach to a celiac plexus block during CT vision (panel A), and spread of contrast medium during fluoroscopy (AP view, panel B). (Redrawn from Mercadente, S, Nicosia, F, Reg Anesth Pain Med 1998; 23:37.)
Case study

- Mr. T initially started therapy on ECOG 1200 with weekly Gemcitabine and concomitant radiation therapy with the potential to achieve surgical resection.
- This was followed by Gemcitabine in combination with Oxaliplatin.
- His CT scan did not suggest a marked response, so Cetuximab was added.
Case study

- He ultimately required cessation of Oxaliplatin therapy related to peripheral neuropathy, and continued Gemcitabine and Cetuximab
- Finally, in November 2004, surgical resection was again attempted with Whipple procedure
Case study

PANCREATIC HEAD, DUODENUM, PANCREATICODUODENECTOMY:

- PANCREAS WITH CHRONIC PANCREATITIS, FIBROSIS AND REACTIVE CHANGES, SEE NOTE
  - NO RESIDUAL TUMOR IDENTIFIED
  - STROMAL RADIATION CHANGES ARE NOTED
  - SURGICAL RESECTION MARGINS ARE NEGATIVE FOR TUMOR
  - DUODENUM AND ANTRUM WITH REACTIVE EPITHELIAL CHANGES
  - EIGHTEEN BENIGN LYMPH NODES (0/18)
  - POST CHEMOTHERAPY AND RADIATION HISTOPATHOLOGIC STAGE AND GRADE (AJCC 2002): T0 NO MX, STAGE 0

NOTE: No residual tumor is identified. In the head of the pancreas close to the distal bile duct, an areas of dense fibrous tissue is identified (1.5 cm in maximum dimension) and possibly represents site of prior tumor. There is extensive intersitial fibrosis in and around the pancreas with acinar atrophy.
Clinical Trials at Yale for Pancreatic Cancer

1. **HIC 0602001069** Wasif Saif M.D. A Phase II Clinical Trial of Genexol-PM in Patients with Advanced Pancreatic Cancer (closed to enrollment)

Phase I studies including:

1. **HIC 0509000642** Wasif Saif M.D. A Phase I, Open-Label Study Evaluating the Pharmacokinetics of Components of S-1 in Patients with Impaired Hepatic Function

2. **HIC 0509000643** Wasif Saif M.D. A Phase I, Open-Label Study Evaluating the Pharmacokinetics of Components of S-1 in Patients with Varying Degrees of Renal Function

3. **HIC 0604001305** Wm. Kevin Kelly M.D. Open Label, Dose Escalation Trial of Oral PXD101 in patients with Advanced Solid Tumors
Final Points

- Pancreatic cancer is the 4th leading cause of cancer-related death in the U.S.; second only to CRC as a cause of digestive cancer-related death
- Surgical resection is the only potentially curable treatment option
- Palliation of symptoms in advanced disease is key
- Clinical trials should always be considered given the poor prognosis, and an additional potential benefit to the patient
THANK YOU

QUESTIONS???:  370-7617, 785-2341