Pancreas Cancer: Updates for the Primary Care Physician

Disclosures

- I am a speaker for Janseen Pharmaceuticals
- I will not be speaking on any off label uses
Outline

- Pancreas Anatomy
- Neuroendocrine pancreas cancer
- Pancreatic adenocarcinoma
- Diagnosis
- Treatment
- Future therapies and targets

Anatomy of the Pancreas

- Remember - a “hidden” organ in the body, virtually impossible to palpate
- Detection of pancreas disease remains a source of frustration in modern medicine as often life-threatening lesions are only noted by their impact on other organs
Anatomy (cont)

- Important structures
  - The tail of the pancreas and spleen are in the LUQ and the head of the pancreas is in the RUQ (right of the midline).
  - Place your right hand over your upper abdomen with fingers extending to the left over the lower portion of your rib cage and the tip of your thumb extended up over the lower portion of the sternum, then your pancreas lies behind your hand in the back (retroperitoneal) portion of the abdomen.

Anatomy

- The head of the pancreas lies in the loop of the duodenum as it exits the stomach.
- The tail of the pancreas lies near the hilum of the spleen.
- The common bile duct passes through the head of the pancreas to join the main duct of the pancreas near the duodenum.
Pancreatic Cancer

- Majority pancreatic cancers arise from the exocrine pancreas
- Pancreatic adenocarcinoma comprises 90% of pancreatic cancers
- Other subtypes of exocrine pancreas such as acinar cell carcinoma are rare
- Pancreatic neuroendocrine tumors that arise from endocrine islet cells form a small minority of pancreas cancers

Neuroendocrine Pancreas Cancer

- Account for around 7% of all pancreas tumors
- They develop from islet cells
- Can be divided into functional or non-functional
- Many different types of tumors
- Include Glucagonoma, Insulinoma, VIPoma, amongst others
2017 → 53,670 patients were diagnosed with pancreas cancer, and 43,090 died of pancreas cancer in the United States
Comprises 3.1% of all new cancer diagnosis
HOWEVER, is the 4th leading cause of cancer related deaths
Around 90% diagnosed after the age of 55
Median age is 70
Males have a slightly increased incidence compared to females

African Americans have a higher incidence (15.5 vs 12.4 per 100,000 years) and have a higher mortality rate
Modest increase in 5 year survival
1975 → 3%
2008 → 7.6%
Clinical Presentation

- Most common presentation → pain, jaundice, weight loss
- Symptoms at diagnosis → weight loss, anorexia, abdominal pain, epigastric pain, dark urine, jaundice
- Signs at presentation: jaundice, hepatomegaly, right upper quadrant mass, cachexia

Presentation

- Varies by tumor location
- ~60-70% are pancreas head tumors, ~20-25% are body/tail
- Head more likely to present with jaundice
- Pain is also a frequently reported symptom; typically insidious in nature, present for 1-2 months about presentation
- Severe back pain often seen as sign/symptom
Presentation

- Recent onset of DM II can be noted
- Unexplained superficial thrombophlebitis (migratory)
- Higher association of unexplained thrombotic events
- Rarely, skin findings such as erythematous subcutaneous areas of nodular fat necrosis

Metastatic Disease at Presentation

- Abdominal mass
- Virchow’s node (left supraclavicular adenopathy)
- Palpable periumbical mass (Sister Mary Joseph)
- Routine lab tests typically abnormal, however not diagnostic
Differential

- Often a difficult diagnosis to "pin down" as differential is large
- PPV is low for pancreas cancer
- Differential for Jaundice- again, large
- Epigastric pain
- Weight loss
- Rarely found incidentally

Diagnosis

- Signs/Symptoms clearly not enough alone
- Risk factor evaluation (genetics, age, smoking, DM II) consider early and more aggressive evaluation
- Imaging with liver function tests including AST/ALT, Alk Phos, Bili, lipase
- CA 19-9, while not used for screening, can be beneficial
Imaging

- CT is preferred imaging modality
- US good for large tumors (over 3 cm) however difficult to see tumors smaller than that size
- CT should be ordered WITH contrast in patients with epigastric pain and other symptoms
- Some institutions use MRI (none locally)

Tumor Markers

- CA 19-9 “gold” standard
- Sensitivity ~70-92%
- Specificity ~68-92%
- Not good for small cancers
- Frequently elevated in other cancers; not good for a presumptive diagnosis in patients with widespread disease
Tumor Markers

- Baseline tumor markers can predict probability of resectable disease; values > 130 typically non-resectable
- Values > 130 had 11% resection rate, while those under are at 26%
- Serial monitoring is a reasonable approach for patients who have received potentially curable treatment, and for those undergoing treatment with metastatic disease
- Rising markers often a sign of recurrent disease
Initial Staging/Resection

- Resection determined by multiple factors including age, performance status, health, respiratory status
- Reasons for a non-resectable tumor often include distant metastatic disease
- Local “unresectable” disease often due to vascular invasion if encasement of the SMA/SMV, or celiac artery

Pancreatic Cancer

- Whipple- large surgery, needs to be healthy
- Even after curative whipple surgery, many, many will still relapse
- If postoperative shows no evidence of recurrent or metastatic disease, standard of care is adjuvant chemotherapy
Pancreatic Cancer- Adjuvant treatment

- ESPAC-4
- Phase III Trial randomized Patients 1:1 to adjuvant Gem alone
  Gem with Capectabine
- Primary Endpoint was overall survival
- 732 patients enrolled, 73- final analysis

ESPAC-4

- Median OS Gem/Capectabine group 28 months compared to
  25.5 months in Gem alone
- Slightly more Grade ¾ events in the combination arm
- Now one of the Standards of care in adjuvant treatment for
  resected pancreas cancer
- Data points to “completing” chemotherapy as important
  prognostic indicator, starting within 12 weeks
Local disease/locally advanced

- GI consultation
- Consider ERCP, MRCP, EUS
- Surgical consultation
- If noted to be resectable

Risk Factors

- Family History and Hereditary Syndromes
- Firmly linked to cigarette smoking (increase in risk is small)
- Increased BMI
- Exposure to chemicals and heavy metals, as well as heavy alcohol consumption
  - Early Screening program at Honor Health (next slide)
Early Detection Program @ HonorHealth

- The Early Detection Program launched in November 2015
- The first individual at risk for pancreatic cancer was consented on 12/1/2015
- The first individual at risk for breast/ovarian cancer was consented on 4/5/2017
- Colorectal cohort- opened

EDP Scientific Objectives

- Contribute to evidence-based
  - National guidelines (for PC, Ovarian, Breast cancer detection)
- Identify risk factors
- EDP Data collection & Analysis
- Screen Biomarkers for earlier detection
  - Create novel blood, urine, and imaging tests
Risk Stratification

**Average Risk**
- 1 Family member with PDAC > 55 y/o

**Moderate Risk**
- ≥ 2 first-, second-, or third-degree family members with PDAC
- 1 first degree family member with PDAC

**High Risk**
- ≥ 3 first-, second-, or third-degree family members with PDAC
- ≥ 2 first-degree family members with PDAC:
  - 1 first- and 1 second-degrees with PDAC,
  - 1 at < 55 y/o
- Genetic syndrome with PDAC (HBOC, Lynch, etc)

**Blood Tests**: CBC, CMP, CA 19-9, CEA, Uric Acid, TSH, Mg, Vitamin D 25OH, Lipid panel, Hgba1C

**Imaging**: MRI/MRCP, CT

**Procedures**: Endoscopic Ultrasound, Whipple, Distal Pancreatectomy

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Pancreatic Cancer- Metastatic Disease

- Pancreas metastatic disease incurable, difficult to treat
- Standard of care is chemotherapy alone, and typically in combination with multiple different drugs
- Treatment can include radiation therapy for local control
- Slow advances in primary treatment
Pancreatic Cancer

- **1997**: Gemcitabine (Median OS 5.65 months ¹)
- **2011**: FOLFIRINOX (Median OS 11.1 months, RR 31.6% ²)
- **2013**: Nab-paclitaxel + Gemcitabine (Median OS 8.5 months, RR 23% ³)
- **2015**: 5-FU + Nal-irinotecan – First time FDA approved 2nd line therapy! (Median OS 6.2 months, 1 year survival 24% ⁴)

Pancreatic Cancer

- Metastatic Disease
- If patients have jaundice, placement of stent to be considered with interventional GI
- Germline testing
- Gene profiling of tumor
- MSI and/or MMR testing
Pancreatic Cancer Treatment

- Treat those with good performance status with chemotherapy, either FOLFIRINOX, Gem/Nab-Paclitaxel, or Gem alone
- Consider olaparib for those with BRCA1/2 mutations
- "Chemotherapy holidays" are often given to these patients
- Almost all will progress- goal is for quality and quantity

Pancreatic Cancer

- Poor performance status patients will benefit from palliative and best supportive care
- Can consider targeted therapy (olaparib, immunotherapy)
- Can also consider palliative RT
Pancreatic Cancer - Future?

- Addition of more chemotherapy agents with immunotherapy?
- Earlier detection?
- Identifying genes/targeted therapy
- Remains a difficult to diagnosis early, treat effectively with surgery and/or chemotherapy
- One of the largest challenges we face in the oncology community

Stay safe!

- Contact information:
  - Brendan Curley, DO, MPH
  - Office: 20745 N Scottsdale Road #115
  - Scottsdale AZ 85255
  - Office #: (623) 238-7570
  - Twitter @Dr_Curley