Update in the Management of Upper GI Malignancy

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16th Annual Primary Care Symposium
December 3, 2016
Outline

• Esophageal Cancer
• Gastric Cancer
• Pancreatic Cancer
• Liver Cancer
• Head and Neck Cancer
Goals

• Review presentation, workup, and treatment for the most common upper GI malignancies
• Review some of the controversies and changes regarding treatments
• Review the role of medications to prevent liver cancer and head and neck cancer
Esophageal Cancer

- Over 16,000 people in the US diagnosed in 2015 with over 15,000 deaths (1)
- Distribution in the US has dramatically shifted from squamous cell carcinoma (SCC) to adenocarcinoma (AC)
- SCC risk factors are strongly EtOH and tobacco, but not as much for AC
- Obesity and long-standing GERD are risk factors for AC

Esophageal Cancer

- Presents with dysphagia, post-prandial chest pain, weight loss

- Workup includes endoscopy and endoscopic ultrasound

- Whole body imaging with both CT C/A/P and PET/CT (1)

Esophageal Cancer

Treatment

• Early stage (in situ, T1a, some T1b) – endoscopic resection

Esophageal Cancer

T1b and greater requires multimodality therapy

CROSS Trial

- 75% AC of esophagus and GE junction
- Randomized to surgery alone or neoadjuvant therapy
- 50 vs. 24 months median survival in the multimodality group

Esophageal Cancer

T1b and greater requires multimodality therapy

Improved 5 – year overall survival with multimodality therapy regardless of histology

Gastric Cancer

• Over 26,000 people in the US will be diagnosed in 2016 with over 10,000 deaths (1)
• Vastly larger incidence in Asia and in Asians
• H. Pylori infection, smoking, EtOH intake, high salt intake are all risk factors
• Cancers are more proximal in US

Gastric Cancer

- Presentation is variable from dysphagia to bleeding from tumors.
- Weight loss, anemia, abdominal pain
Gastric Cancer

- Similar workup to esophageal
- Endoscopy and EUS for initial staging
- CT C/A/P, PET/CT
- For early lesions, endoscopic therapy is appropriate
Gastric Cancer

- For all but the earliest cancers, multimodality therapy is critical.
Gastric Cancer

- Type of surgery – limited (D1) vs. extended (D2)
• Equivalent survival in D1 vs. D2 surgery in Italy but suggestion of improved survival if LN +
• MAGIC trial is widely but not univerally considered the standard.

• Those undergoing curative resection should have chemotherapy or chemoradiation depending on extent of lymphadenectomy
• So many variables make this a confusing landscape
• Recently, the harvest of 15LN was announced as a quality measure through the ACS Commission on Cancer.
Looking at the SEER Medicare database, ethnicity and place of birth are searchable demonstrating that Asian patients born in Asia, Asians born in the US, and non-Asians have different tumors and survival.

Statistical analysis shows the difference is not related only to location or LN harvest.

Pancreatic Cancer

- In 2016, over 53,000 people will be diagnosed and over 41,000 people will die with pancreatic cancer (1)
- Risk factors include pancreatitis, EtOH, tobacco
- Presentation commonly painless jaundice, vague abdominal pain, weight loss

Pancreatic Cancer

- Workup includes labs to evaluate jaundice
- Tumor markers – CA 19-9
- Imaging with pancreatic protocol CT (arterial, portal venous, and delayed venous phases), or MRI/MRCP
- Chest CT to complete staging, EUS/ERCP for diagnosis and often relief of jaundice

Pancreatic Cancer

- Imaging findings determine type of surgery and timing of surgery
- Resectable
- Borderline resectable
- Unresectable
- Determined by vascular relationships

Pancreatic Cancer

• Do we need a tissue diagnosis before treatment?

• Does everyone need chemotherapy?

Pancreatic Cancer

- Do we need a tissue diagnosis before treatment?
- Does everyone need chemotherapy?

Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline


Yes
Pancreatic Cancer

- Benefits of surgery upfront
  - Less post-operative morbidity
  - Option if difficulty making diagnosis
  - Can avoid a biliary stent

- Benefits of chemotherapy first
  - Avoiding surgery for biologically aggressive disease
  - Higher rate of R0 resection
  - More likely to receive chemotherapy

Pancreatic Cancer

• Resectable cancers

• Borderline resectable
  • These are tumors with very high rates of R1 resection
  • Phase II trial looked at neoadjuvant therapy for resectable (23) and borderline resectable (39) patients led to over 80% rates of R0 resection for patients who made it to resection

Pancreatic Cancer

- Technical aspects of surgery
Pancreatic Cystic Lesions

- Often V.O.M.I.T.
- Workup

# Pancreatic Cystic Lesions

<table>
<thead>
<tr>
<th></th>
<th>Age - Gender</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCN</strong> Benign</td>
<td>75% women 60-70 y</td>
<td>Lobulated microcystic 18% central scar with Ca++</td>
</tr>
<tr>
<td></td>
<td>Grandma</td>
<td></td>
</tr>
<tr>
<td><strong>MCN</strong> Malignant potential</td>
<td>99% women 40-50 y</td>
<td>Macrocystic Usually 1 cyst 25% peripheral Ca++</td>
</tr>
<tr>
<td></td>
<td>Mother</td>
<td>95% in tail and body</td>
</tr>
<tr>
<td><strong>Main-duct IPMN</strong></td>
<td>M=W 60-80 y</td>
<td>Dilated Pancreatic duct Protruding papil of Vater</td>
</tr>
<tr>
<td>Malignant potential</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side-branch IPMN</strong></td>
<td>M=W 60-80 y</td>
<td>Bunch of grapes connection to PD</td>
</tr>
<tr>
<td>Malignant potential</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Liver and Bile Duct Cancers

- Bile duct cancers (gallbladder CA and cholangiocarcinoma) were diagnosed in over 10,600 patients in the US in 2015 with close to 4,000 deaths (1)
- Risk factors include chronic inflammation, primary sclerosing cholangitis and inflammatory bowel disease
- Presentation commonly painless jaundice, vague abdominal pain, weight loss

Cholangiocarcinoma

- Diagnosis includes labs and LFTs, and imaging, often with ultrasound demonstrating biliary ductal dilatation
- Tumor marker – CEA, CA 19-9
- Imaging – CT w contrast, MRI/MRCP
- Staging – PET/CT especially important due to the high likelihood of occult metastatic disease

Cholangiocarcinoma

- Treatment depends on location
- Intrahepatic
- Extrahepatic
  - Hilar (Kaltskin’s tumor)
  - Distal bile duct
- Gallbladder

Cholangiocarcinoma

- Treatment
- Surgery
  - GB – radical cholecystectomy
  - GB, lymph nodes, segment 4B and 5

Cholangiocarcinoma

- Treatment
- Surgery
  - Cholangiocarcinoma
  - Extrahepatic
  - Extrahepatic bile ducts and lymph nodes

Cholangiocarcinoma

• Treatment

• Surgery
  • Cholangiocarcinoma
  • Extrahepatic
  • Extrahepatic bile ducts and lymph nodes
  • Biliary reconstruction

Cholangiocarcinoma

- Treatment
- Surgery
  - **Intrahepatic** – segmental resection
  - Involved segment sparing parenchyma as much as possible
  - No lymph nodes
Cholangiocarcinoma

• Treatment

• Surgery
  • **Hilar** – Extended resection
  • Resection depends on involvement of blood vessels, ERCP results and amount of liver left behind
Hepatocellular Carcinoma

- Liver cancer (HCC) was diagnosed in an estimated 35,000 patients in 2015 with over 24,000 deaths (1)
- Risk factors are very well-defined and include hepatitis and cirrhosis – including non-alcoholic steatohepatitis (NASH), along with EtOH abuse, aflatoxin exposure
- Presentation often non-specific including pain, jaundice, malaise, and weight loss
- Screening patients at high risk plays an important role

Screening

- Based on large RCT from China demonstrating Q6 month U/S and alpha fetoprotein (AFP) level in Hep B or chronic hepatitis patients led to 37% decrease in mortality from HCC
- In the US, the AASLD doesn’t recommend use of AFP but it is still commonly used
- High risk population: viral or non-viral cirrhosis (including NASH), and Hep B carriers without cirrhosis
- US screening q 6 months (commonly w AFP)
- A liver nodule will prompt contrasted CT or MRI
- Lesions <1cm can be followed q 3 months

HCC

Treatment and workup

- Diagnosis can be made with classic enhancement pattern on imaging or needle biopsy
- Chest imaging and bone scan (only for symptoms) for staging
- Assessment of liver remnant volume and portal hypertension

Multidisciplinary care
  - Surgery, Embolization, Ablation, radiotherapy, transplant
Multidisciplinary treatment options

- A lot of our experience comes from colorectal liver mets and retrospective data

SIRFLOX: Randomized Phase III Trial Comparing First-Line mFOLFOX6 (Plus or Minus Bevacizumab) Versus mFOLFOX6 (Plus or Minus Bevacizumab) Plus Selective Internal Radiation Therapy in Patients With Metastatic Colorectal Cancer


Published Ahead of Print on February 22, 2016 as 10.1200/JCO.2015.66.1181

- No change in OS, but delayed progression in the liver

Multidisciplinary treatment options

- Y-90 radioembolization utilized the tumor’s arterial blood supply as opposed to healthy liver’s portal system blood supply.

Multidisciplinary treatment options

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Multidisciplinary treatment options

- JH is an 87yo man presented in 9/2015 with metastatic sigmoid colon CA
Multidisciplinary treatment options

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Multidisciplinary treatment options

- He underwent “gentle” chemotherapy and Y-90 embolization x 2
Multidisciplinary treatment options

- Sigmoid colectomy to deal with primary 3/2016, followed by “real” chemotherapy and re-imaging
Vaccines and Cancer

- Can vaccines really prevent or treat cancer?
Vaccines and Cancer

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- Hepatitis C is the leading cause of HCC
- Previous treatment was tedious and led to 40-45% cure rates
- Harvoni is a combination ledipasvir/sofosbuvir pill

### Vaccines and Cancer

- Can vaccines really prevent or treat cancer?
- Hepatitis C is the leading cause of HCC
- Previous treatment was tedious and led to 40-45% cure rates
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#### Table: Patients With Genotype 4, 5, or 6

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Weeks of Treatment</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>12</td>
<td>93%*</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>93%*</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>96%†</td>
</tr>
</tbody>
</table>

Vaccines and Cancer

• Can vaccines really prevent or treat cancer?
• HPV is a very common virus, certain strains of which have long been known to lead to cervical cancer
• HPV 6,11,16, 18 are the virulent forms and now have been increasingly implicated in head and neck squamous cell cancer.
• According to the CDC:
  • 11-12 year olds should get 2 doses of HPV vaccine 6-12 months apart (as of 10/19/2016).
  • Women up to 26 should be vaccinated
  • Men to age 21 and high risk populations to age 26

Vaccines and Cancer

• This vaccine has proven to decrease rates of cervical, genital, anal, and oropharyngeal infection with HPV.
• Will this lead to decreased incidence of cancer?

Vaccines and Cancer

- This vaccine has proven to decrease rates of cervical, genital, anal, and oropharyngeal infection with HPV.
- Will this lead to decreased incidence of cancer?

Figure 2.

Conclusion

• Review of incidence, workup, and treatment of upper GI malignancies
• Multidisciplinary treatment strategies are expanding the pool of candidates for successful treatments
• Surveillance can help diagnose more early cancers for some diseases (HCC mainly)
• Vaccination will make a major difference in the next decade for HPV and HCV related cancers
Thank You