GASTROINTESTINAL MALIGNANCIES

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Outline

• Colorectal Cancer
• Pancreas Cancer
• Gastric Cancer
• Hepatobiliary Cancer
• Anal Cancer

Introduction

• Epidemiology
• Screening
• Clinical Presentation
• Evaluation
• Treatment

Colorectal Cancer

Etiological Factors

• Hereditary causes
• Environmental factors (most important)
  • Dietary factors
  • Environmental chemicals
  • Geographical location
• Predisposing diseases
  • Inflammatory bowel disease
• Other factors (e.g., physical activity)
Hereditary Etiology of CRC

<table>
<thead>
<tr>
<th>Hereditary Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial</td>
<td>30%</td>
</tr>
<tr>
<td>NPCC</td>
<td>10%</td>
</tr>
<tr>
<td>FAP</td>
<td>1%</td>
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<tr>
<td>Sporadic</td>
<td>59%</td>
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</tbody>
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Presentation

- Right sided: Iron deficiency
- Left sided: Obstruction
- Bleeding
- Perforation

Case Study

- 62 year old male patient previously healthy presents with a 3 month history of:
  - Progressive fatigue
  - Shortness of breath with excretion
  - Family history negative for colon cancer
  - Physical exam: mild hepatomegally
  - Laboratory evaluation: Iron deficiency anemia

Case Study

- Next step in the work up
  a. FOBT
  b. Colonoscopy
  c. Upper Endoscopy
  d. Dietary consult for nutritional causes of iron deficiency
  e. CEA

Case Study

- Colonoscopy
  - Ascending colon, concentric mass
  - Scope readily passed through mass
  - No clinically evident bleeding
  - Biopsy: adenocarcinoma KRAS mutant
- Next Step:
  a. Refer to surgery for resection
  b. Start chemotherapy
  c. Complete staging with CT scan
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CT Scan of the abdomen:
- Multiple liver lesions

CEA: 150 ng/ml

Evaluation
- Colonoscopy + Biopsy
- CT Scan
- CEA
- PET Scan
- EUS (rectal cancer)

Case Study
- Next step
  a. Surgery
  b. Chemotherapy with Bevacizumab FOLFOX
  c. Chemotherapy with cetuximab FOLFIRI
  d. Liver biopsy

Case Study
- Next step
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Management
- Non metastatic:
  - Colon: resection + chemotherapy (Stage II and III)
  - Rectal: Chemoradiotherapy then surgery (stage II or III)
- Metastatic disease:
  - Chemotherapy: 5FU, oxaliplatin (FOLFOX) or 5FU, Irinotecan (FOLFIRI) plus a biologic agent (bevacizumab or EGFR inhibitor)
  - EGFR inhibitors (cetuximab or panitumumab) work only in KRAS wild-type tumors (50%)
  - Surgery: Palliative if obstruction/ perforation
Pancreatic Cancer

Epidemiology

- Annual new cases: 26,300
- Annual Mortality: 27,800
- #4 cancer-related mortality
- 5-year survival rate less than 5%
- Mortality is higher in African-Americans

Pancreatic Cancer - Risk Factors

- Cigarette smoking
- High intake of fat and animal protein (Meat)
- Diabetes (> 1 year before)
- Pancreatitis (Tropical, familial, chronic)
- Familial syndromes:
  - Familial Atypical Multiple Mole Melanoma (p16)
  - HNPCC
  - BRCA2
  - Peutz-Jeghers
  - Ataxia-telangiectasia

Presentation

- 95% arises from exocrine pancreas
  - Adenocarcinoma in histology
  - 5% are islet cell tumors (Carcinoid or neuroendocrine)
- 70% are in the head of pancreas
- 80-90% have KRAS mutation

Case Study

- 68 year old male patient presents with non-specific abdominal pain. Work up included a CT scan revealing a 1X1 cm hypo-enhancing mass in the head of the pancreas. Mass confined to pancreas
- Previous history significant for new onset diabetes diagnosed 3 months ago
- History of 20PKY smoking quit 10 years ago
Next Step:
- A. Repeat CT scan in 3 months
- B. Obtain CA19-9
- C. Obtain biopsy
- D. Refer to surgery for evaluation for resection

Presentation
- Jaundice
- Pain: back pain or midepigastric pain
- Constitutional Symptoms: weight loss, fatigue
- New onset diabetes: present 10% of cases
- Other: Pancreatitis, GI bleed, Obstruction

Evaluation
- Loco-regional staging:
  - Ultrasound
  - Thin cut CT scan
  - MRI
  - Endoscopy: ERCP/ultrasound
- Distant metastasis:
  - CT scan
  - Laparoscopy

Intra-op Assessment of Resectability

Study Case
Pancreaticoduodenectomy revealed adenocarcinoma of the pancreas. Patient is back for follow up in 1 month. He has recuperated nicely and is now at baseline level of functioning. Which of the following are you least likely to recommend:
A. Observation only
B. Refer for adjuvant chemotherapy
C. Refer for radiation therapy
D. Repeat endoscopy
Study Case

Pancreatectoduodenectomy revealed adenocarcinoma of the pancreas. Patient is back for follow up in 1 month. He has recuperated nicely and is now at baseline level of functioning. Which of the following are you least likely to recommend:

A. Observation only
B. Refer for adjuvant chemotherapy
C. Refer for radiation therapy
D. Repeat endoscopy

Management

- Early stage disease (T1-3, N0-2)
  - Surgery: Whipple procedure
  - Chemotherapy +/- radiation
- Locally advanced disease (T4)
  - Chemo-radiotherapy or chemotherapy
- Metastatic disease:
  - Chemotherapy: Gemcitabine- or 5FU-based
    - FOLFIRINOX or Gemcitabine and abraxane for good performance status
    - Gemcitabine or palliative care for poor performance status

The same patient also states that he has been feeling somewhat depressed as he has never fully regained his strength following the surgery. He continues to lose weight despite eating at least 2000 calories per day. He denies any nausea but does c/o of loose stools following meals. What would you do next?

A. Check Stool for C. diff
B. Refer to GI for repeat endoscopy
C. Start PPI
D. Empiric trial of pancreatic enzymes

Gastric/GEJ

Adenocarcinoma of the distal esophagus
Cancer of the cardia
Subcardial cancer

One Organ System, Three Cancers

Squamous cell carcinoma

Non-cardia cancer
Esophageal Cancer

Adenocarcinoma of GEJ

- Incidence rates increased >350% since the mid 1970s.
- Increasing 20% per year in U.S.
- Even higher in U.K., Australia, Holland.
- Rates for gastric cardia adenocarcinoma also increased.

Distal Gastric cancer

- Incidence: 22,000 cases/year
- Risk has fallen 10 folds over last century
- 2nd most common malignancy worldwide
- High prevalence in the Far East

Risk Factors

- GEJ/ Cardia
  - Chronic GE reflux (proximal GEJ)
- Distal Gastric
  - Diet: Smoked, salted, preserved foods; decreased intake of fruits & vegetables
  - Male gender
  - Chronic gastritis → metaplasia → dysplasia → cancer
    - Helicobacter pylori: 3-6 X increased risk
    - Pernicious anemia

Presentation

- Early satiety
- GI bleed
- Weight loss
- Lymph adenopathy
  - supraclavicular, peri-umbilical

Evaluation

- Endoscopy
- Endoscopic ultrasound for local staging
- CT scan
- PET scan
Management

- Early stage disease (CIS, T1)
  - Partial gastrectomy
- Intermediate Stage (T2-T4, N1 or N2)
  - Surgery
  - Adjuvant: Chemoradiation (5-FU)
  - Neoadjuvant: Chemotherapy followed by surgery
- Advanced stage disease
  - Chemotherapy: 5-FU, taxane, platinum, irinotecan
  - If the tumors are Her-2-neu positive (20%) then add trastuzumab

Hepatocellular Cancer

Epidemiology

- Male:female 3:1
- Risk factors:
  - Hepatitis B viral infection
  - Hepatitis C viral infection
  - NASH
  - Metabolic disorders: hemochromatosis
  - Toxin exposure: aflatoxin

Risk of HCC

- Identifiable population at risk:
  - Cirrhotic Hepatitis B 3-8%/year
  - Cirrhotic Hepatitis C 3-5%/year
  - Stage 4 primary biliary cirrhosis 3-5%/year

Study Case

A 44 y/o male with a history of HCV infection presents with RUQ pain. Physical exam hepatomegally. Imaging studies reveal a 12 cm mass in the liver which enhances on arterial phase and washes out on venous phase in addition to portal and para-aortic enlarged lymph nodes. What is the next step?

A. Liver biopsy
B. Alpha-fetoprotein
C. Refer to transplant surgery
D. Refer to Medical Oncology
**Presentation**

- Liver mass - enlarged liver
- Elevated AFP
- Pain RUQ
- Worsening LFT

**Evaluation**

- Biopsy
  - OR
- The presence of the following triad
  - >1cm + arterial enhancement + venous washout

**Therapeutic Options**

- Liver Transplant
- Liver Resection
- Local Ablation
  - Percutaneous ethanol injection
  - Radiofrequency ablation

**Management**

- Locally advanced unresectable and asymptomatic with no vascular involvement
  - Chemoembolization
  - Clinical trial
- Metastatic; vascular (portal) involvement or PS 1-2
  - Palliative care: Sorafenib
  - Clinical trials

**Transplant**

- Milan Criteria:
  - 1 nodule ≤ 5cm
  - 2-3 nodules ≤ 3 cm
- Transplant offers the best long term control (5-year DFS 60% vs. 30% resection)
- Main problem is limitation related to organ availability
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Biliary Cancer

Epidemiology

- 3% of all GI cancers worldwide
- 90% of biliary tract cancers are adenocarcinoma
- Gallbladder Cancer (GBC) is the most common BTC with 5000 new cases diagnosed every year in the US.
- Cholangiocarcinoma (CC) are classified either intrahepatic or extrahepatic (IHC and EHC)
  - EHC are more common

Biliary Tract Cancer - Risk Factors

- Gallbladder Cancer
  - Cholelithiasis
  - Calcified gallbladders
  - Typhoid carrier
- Cholangiocarcinoma
  - Ulcerative colitis 9 – 21X
  - Primary sclerosing cholangitis
    - 80% have UC concurrently

Treatment

- Surgery
  - Resection – Local recurrence common
  - Liver Transplant
    - Highly select patient population
    - Only at select centers
- Systemic chemotherapy
  - Gemcitabine & Cisplatin – proven survival advantage

Anal Cancer
**Epidemiology**

- Histology: Squamous cell cancer
- Risk factors:
  - HPV infection
  - Homosexual men with HIV infection

**Presentation**

- Anal mass
- Pain
- Bleeding

**Evaluation**

- Rectal exam
- Anoscopy + biopsy
- CT scan

**Management**

- Localized disease:
  - Chemoradiotherapy: 5-FU + Mitomycin-C
  - OR
  - 5FU + Cisplatin
- Advanced disease:
  - Chemotherapy

**Thank You**