GASTRIC CANCER, GASTROINTESTINAL STROMAL TUMOR, PEPTIC ULCER DISEASE
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GASTRIC CANCER
- About 25,000 new cases diagnosed in 2015
- Median age 69 years
- 15th most common cancer in the US
- 4th most common cancer worldwide

GASTRIC CANCER
- Most common in Asia, parts of South America
- Lowest rates of disease in North America
- Highest death rates in Chile, Japan, former Soviet Union

GASTRIC CANCER MORBIDITY
- 60% male, 40% female in the US
- Median age 69
- Worldwide epidemiologic data suggests race may influence incidence and biologic behavior of gastric cancer

GASTRIC CANCER ANATOMY
- Mucosa
- Submucosa
- Muscularis
- Subserosa
- Serosa

HISTOLOGY
GASTRIC CANCER LOCATIONS
- 40% lower stomach (pyloric area)
- 40% middle stomach (body)
- 15% upper stomach (cardia)
- 5-10% multiple locations

GASTRIC CANCER STAGE AT DIAGNOSIS
- 25% of patients have localized disease
- 30% of patients have regional disease
- 30% of patients have distant metastases

GASTRIC CANCER SIGNS AND SYMPTOMS
- Nausea or vomiting
- Dysphagia
- Dyspepsia
- Early Satiety
- Anorexia
- Melena or pallor
- Hematemesis
- Weight loss
- Palpable mass

GASTRIC CANCER LATE FINDINGS
- Malignant pleural or peritoneal effusions
- Gastric outlet obstruction
- Hemorrhage
- Jaundice

GASTRIC CANCER PHYSICAL FINDINGS
- Physical signs are late events
- Organomegaly
- Sister Mary Joseph nodule, Blumer shelf, Virchow nodes
GASTRIC CANCER CAUSES
- Diet
- Tobacco use
- H. pylori infection
- Prior gastric surgery
- Genetic factors
- Obesity
- Radiation exposure

GASTRIC CANCER DIAGNOSIS AND STAGING
- History and Physical
- EGD and biopsy
- CT chest/abdomen/pelvis
- PET
- EUS - particularly useful for institutions favoring neoadjuvant treatment approaches

ENDOSCOPIC APPEARANCE

GASTRIC CANCER HISTOLOGY
- 95% of gastric malignancies are adenocarcinomas
- Lymphomas, GIST's, carcinoids, squamous cell carcinomas

GASTRIC ADENOCARCINOMA
- Tubular
- Papillary
- Mucinous
- Signet-ring
- Undifferentiated
LAUREN CLASSIFICATIONS

- Type I (Intestinal): chronic gastritis, retained glandular structure, minimally invasive, distinct margins, environmental risk factors, better prognosis
- Type II (Diffuse): scattered poorly differentiated cells, large areas of invasion, deceptive margins, genetic factors

GASTRIC CANCER STAGING

- T2 invades muscularis propria
- T3 invades subserosal connective tissue
- T4 invades serosa or adjacent structures

GASTRIC CANCER SURVIVAL BY STAGE

- Stage I: 50-80%
- Stage II: 30-40%
- Stage III: 10-20%
- Stage IV: <5%
- Above are 5 year survival rates.

GASTRIC CANCER SITES OF SPREAD

- Direct: omentum, pancreas, spleen, colon, mesocolon, duodenum, peritoneum
- Lymphatic: foregut and para aortic nodes
- Hematogenous: liver

LABORATORY STUDIES

- Generally non-specific although anemia is common
- CA 19-9 is elevated in 20% of patients
- CEA is elevated in 45-50% of patients
GASTRIC CANCER TREATMENT APPROACHES
- NCCN and European guidelines roughly correlate
- EMR is appropriate for Tis or T1 tumors that are well differentiated, <2cm, not ulcerated
- Other T1 tumors can be excised with perigastric node harvest
- Ib to IIIc tumors are treated with gastrectomy. D2 lymph node dissection is preferred. Neoadjuvant chemotherapy or chemoradiotherapy is appropriate
- Unresectable disease treated with either chemotherapy or chemoradiotherapy if appropriate

GASTRIC CANCER SURGICAL APPROACHES
- Subtotal or total gastrectomy can both be considered as long as an adequate gross tumor margin is obtained.
- D1 LN dissection: perigastric nodes
- D2 LN dissection: hepatic, L gastric, celiac, splenic artery, splenic hilum
- Complication rates and mortality probably modestly increased with D2 resections

HEREDITARY SYNDROMES
- Hereditary diffuse gastric cancer
- Lynch syndrome
- Familial adenomatous polyposis
- Peutz-Jeghers syndrome

GASTROINTESTINAL STROMAL TUMORS
- GIST’s comprise <1% of GI tumors
- About 2% of gastric tumors
- Most common mesenchymal neoplasm of the GI tract
GASTROINTESTINAL STROMAL TUMORS
- Historically classified as leiomyomas or leiomyosarcomas
- Smooth muscle features under light microscopy but not electron microscopy
- Immunohistochemistry evolved in the 1980's and noted these tumors expressed antigens related to neural crest cells
- Schaldenbrand and Appelman (1984) amongst the first pathologists to use the term “stromal tumor” in describing these neoplasms

1998 Kindblom noted origin in mesenchymal stem cells programmed to become interstitial cells of Cajal (ICC)
- ICC’s are GI pacemaker cells located in the muscularis propria
- Express KIT
- C-KIT proto-oncogene mutations identified in these neoplasms in 1998 (Hirotta, et al)

SANTIAGO RAMON Y CAJAL

Activated KIT mutations present in 85-90% of GIST’s
- 3-5% will contain PDGFR-alpha mutations
- The TKI Imantinib was shown in 2000 to target KIT and PDGFR-alpha

GASTROINTESTINAL STROMAL TUMORS
- Typically solitary
- 50-70% located in the stomach
- 20-30% located in the small intestine
- 5-15% located in the colon/rectum
- <5% located in the esophagus

GASTROINTESTINAL STROMAL TUMORS
- Fairly slow to metastasize
- Spread to liver and peritoneum
- Lymph node involvement is rare in adults
- Morbidity is related to obstruction, hemorrhage, or perforation
GIST 5 YEAR SURVIVAL
- 80% with localized disease
- 65% with regional disease
- 40% with metastatic disease
- 50% of patients will develop recurrence after complete resection

GIST’S CLINICAL PRESENTATION
- Incidental finding (tumors typically<3cm)
- Upper GI hemorrhage in 40-60% of patients
- Pain, anorexia, nausea, vomiting, weight loss
- Pallor, malaise, shock
- Palpable mass
- Peritonitis

GIST ASSOCIATED SYNDROMES
- Carney’s triad: gastric GIST, paragangliomas, pulmonary chondromas
- Carney-Stratakis syndrome: GIST and paraganglioma
- Neurofibromatosis Type I: small bowel multicentric GIST

GIST EVALUATION
- Laboratory tests are typically unrevealing although anemia is common
- Often EGD
- Axial imaging is vital
- MRI and PET can be helpful, used less commonly than CT

GIST ENDOSCOPY
- EGD: often performed to evaluate anemia. Findings typically are firm, smooth, submucosal mass frequently with overlying ulceration
- EUS: Useful to characterize and when appropriate biopsy
- Biopsy frequently non-diagnostic without US guidance
- Biopsy should not be obtained unless it will impact treatment

ENDOSCOPIC APPEARANCE GIST
GIST CT SCANNING

- Size, location, density, relationship to adjacent structures, metastatic disease
- Small tumors demarcate sharply, homogeneous density
- Intermediate tumors are irregular, hazy borders, more heterogeneous in density
- Large tumors are irregular, heterogeneous, and often metastatic

CT SCAN SMALL GIST

CT SCAN INTERMEDIATE GIST

CT SCAN LARGE GIST

GIST HISTOLOGY AND STAGING

- Mitotic Index, cellularity, necrosis, and nuclear atypia
- CD 117 (a C-Kit protein) is a growth factor receptor with TK activity that is expressed in nearly all GIST’s
- Mitotic index <5 or >5 per 50 HPF
- Tumor size, nodal disease, metastatic lesions
- Wide consensus for usefulness of TMN staging does not exist

GIST MEDICAL CARE

- TKI’s (imatinib) are important for unresectable or metastatic tumors, neoadjuvant treatment, or adjuvant treatment of high risk lesions
- Guided by genotyping of KIT and PDGRF-alpha mutations
- Edema, rash, diarrhea, nausea, abdominal pain, hepatotoxicity
- Preoperative Imatinib is continued for 2 years after surgery
- Adjuvant duration is 3 years
- Treat metastatic disease until progression is noted
- Evaluation of response can be difficult, MRI/PET can help
GIST SURGICAL CARE
• Resection is definitive therapy for localized disease, it is the only chance for cure
• Goal is negative microscopic margins
• En bloc resection of adjacent structures is appropriate
• Lymphadenectomy is not routinely required
• Palliative resections can be considered

5 year survival rates following R0 resection are 50-60%
5 year survival is achieved in 10% of palliative resections
Influenced by mitotic index, size, location, tumor rupture, R1 resection

PEPTIC ULCER DISEASE
• Focal defects in gastric or duodenal mucosa extending to submucosal layers or deeper
• Generally due to an imbalance between peptic acid and mucosal defenses
• Affects over 4 million people annually
• 10% lifetime risk of duodenal ulcer
• 20% risk in the presence of H. pylori
• Increased prevalence in the elderly

Helicobacter pylori infection
Drugs (NSAIDS)
Lifestyle factors
Physiologic stress
Hypersecretory states (uncommon)
Genetic factors

HELICOBACTER PYLORI
• Gram negative spirochete linked to gastritis in 1983
• Produces urease which alkalinizes its microenvironment
• H. pylori colonization leads to increased gastrin, pepsinogen, and decreased somatostatin and bicarbonate secretion
• pH is lowered with subsequent gastritis and/or duodenitis
H. PYLORI TESTING
- Carbon 13 urea breath test
- H. pylori fecal antigen testing
- H. pylori antibody serology
- EGD and biopsy

HELICOBACTER PYLORI

HELICOBACTER PYLORI TREATMENT
- PPI, amoxicillin, clarithromycin or metronidazole
- Bismuth, metronidazole, tetracycline
- PPI, bismuth, metronidazole, tetracycline

NSAIDS
- 25-30% of chronic users experience adverse GI events
- Disruptive to gastric/duodenal mucosal via COX-1 inhibition and subsequent impact on prostaglandin production
- Likely synergy with H. pylori infection
- Risk increased with advanced age, concomitant use of corticosteroids or anticoagulants, and COPD

LIFESTYLE FACTORS
- ETOH and tobacco use are not conclusively linked to peptic ulcer disease although both can cause gastroduodenal mucosal injury
- Likely potentiate the adverse effects of H. pylori infection or NSAID use.

PHYSIOLOGIC STRESS
- Burns, CNS injury, sepsis, and critical illness have been associated with gastritis and ulcers
- Cushing ulcers: CNS injury (gastric)
- Curling ulcers: Burns (duodenal)
PROGNOSIS
• Mortality risk is 1 per 100,000 cases
• Mortality from hemorrhage is 5%
• Surgical mortality risk for perforation 5-30%, increased with shock, renal failure, co-morbid conditions (COPD), advanced age, immunocompromised, gastric location

DUODENAL ULCERS
• Most common location, male predominance
• Typically in first portion of the duodenum
• Associated with elevated acid production
• Pain, perforation, bleeding, obstruction

DUODENAL ULCER TREATMENT
• PPI
• Diagnose and treat H. pylori infection
• Avoid NSAIDS
• EGD to treat hemorrhage (clips, energy, epinephrine)
• Angiography in high risk patients with ongoing hemorrhage

DUODENAL ULCER SURGICAL OPTIONS
• Patch/suture with medical therapy
• Truncal vagotomy and pyloroplasty
  - 3-10% recurrence
  - 1% mortality
• Truncal vagotomy and antrectomy
  - 1-2% recurrence
  - <2% mortality
• Highly selective vagotomy
  - 10-15% recurrence
  - <1% mortality

ENDOSCOPIC ULCER APPEARANCE

Surgical Indications
• Intractable bleeding
• Perforation
• Obstruction
• Neoplasm
**GASTRIC ULCERS**
- Elderly, male gender, NSAIDS, H. pylori, ETOH, tobacco, corticosteroids
- Can be associated with hemorrhage or perforation
- EGD, BIOPSIIES, treat hemorrhage, H. pylori, PPI

**DUODENAL ULCER SURGICAL OPTIONS**

**GASTRIC ULCER TYPES**
- Type I: lesser curve, distal, normal acid levels
- Type II: lesser curve with duodenal ulcer, elevated acid levels
- Type III: pyloric channel, think duodenal physiology
- Type IV: near GE junction, normal or low acid levels
- Type V: any (multiple) locations in setting of NSAID use

**ENDOSCOPIC ULCER APPEARANCE**

**GASTRIC ULCER CLASSIFICATION**

**GASTRIC ULCER SURGICAL INDICATIONS**
- Uncontrolled hemorrhage
- Perforation
- Concern for malignancy
GASTRIC ULCER SURGICAL OPTIONS

- Think excise ulcer when possible
- Oversew and biopsy for bleeding, shock
- Excision or biopsy/patch for perforation, shock
- Distal gastrectomy with or without vagotomy preferred in appropriate risk patients