Small Bowel: Carcinoid Tumors/Neuroendocrine Tumors

Resident Teaching Conference

Sept 5, 2012

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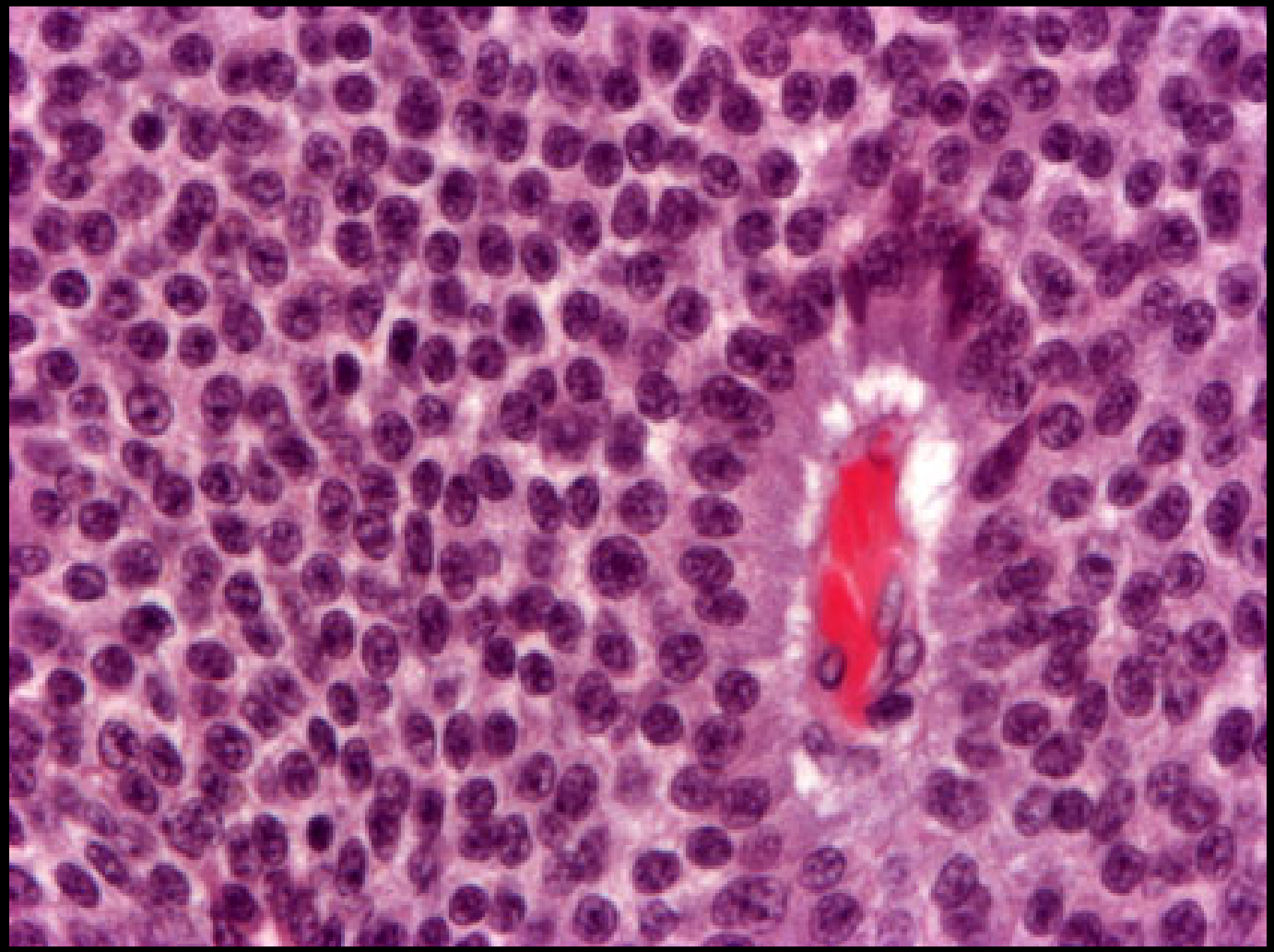
Carcinoid Tumors

- Arise from enterochromaffin cells (Kulchitsky cells)
- Histologically and biochemically diverse tumors
- Classification is based on anatomical location

Carcinoid Tumors



Carcinoid Tumors

- Most commonly found in GI tract
  - Appendix (45%)
  - Ileum (28%; almost always last 2 ft of ileum)
  - Rectum (16%)
  - Stomach
- 20-30% multicentric
- 10% associated with other malignancy (adenoca)
- 10% associated with MEN 1

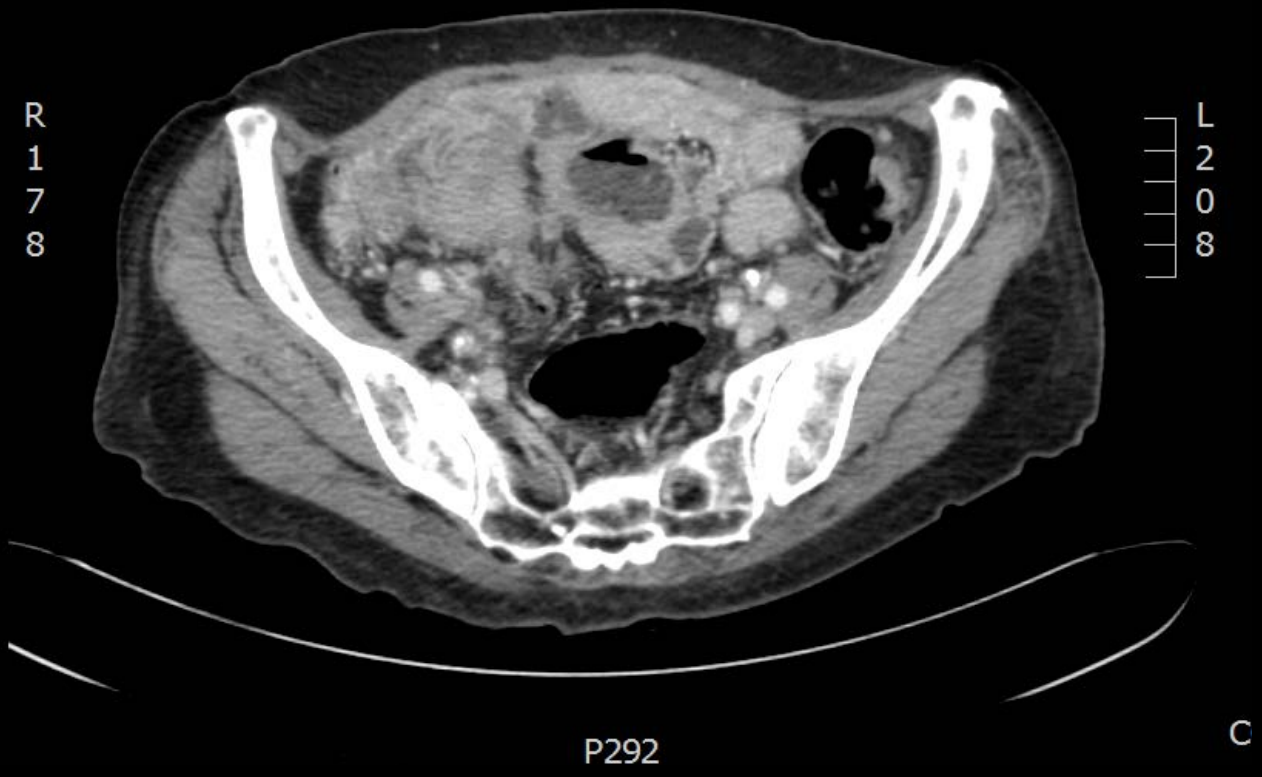
Epidemiology

- 5% of all GI tract malignancies
- Surveillance Epidemiology and End Results (SEER) data & NCDB:
  - Of 67, 843 patient's with SB malignancies
    - 37.4%: carcinoid
    - 36.9%: adenocarcinomas
    - 25.7%: stromal tumors or lymphomas
- Incidence has increased 4 fold from 1985 to 2005

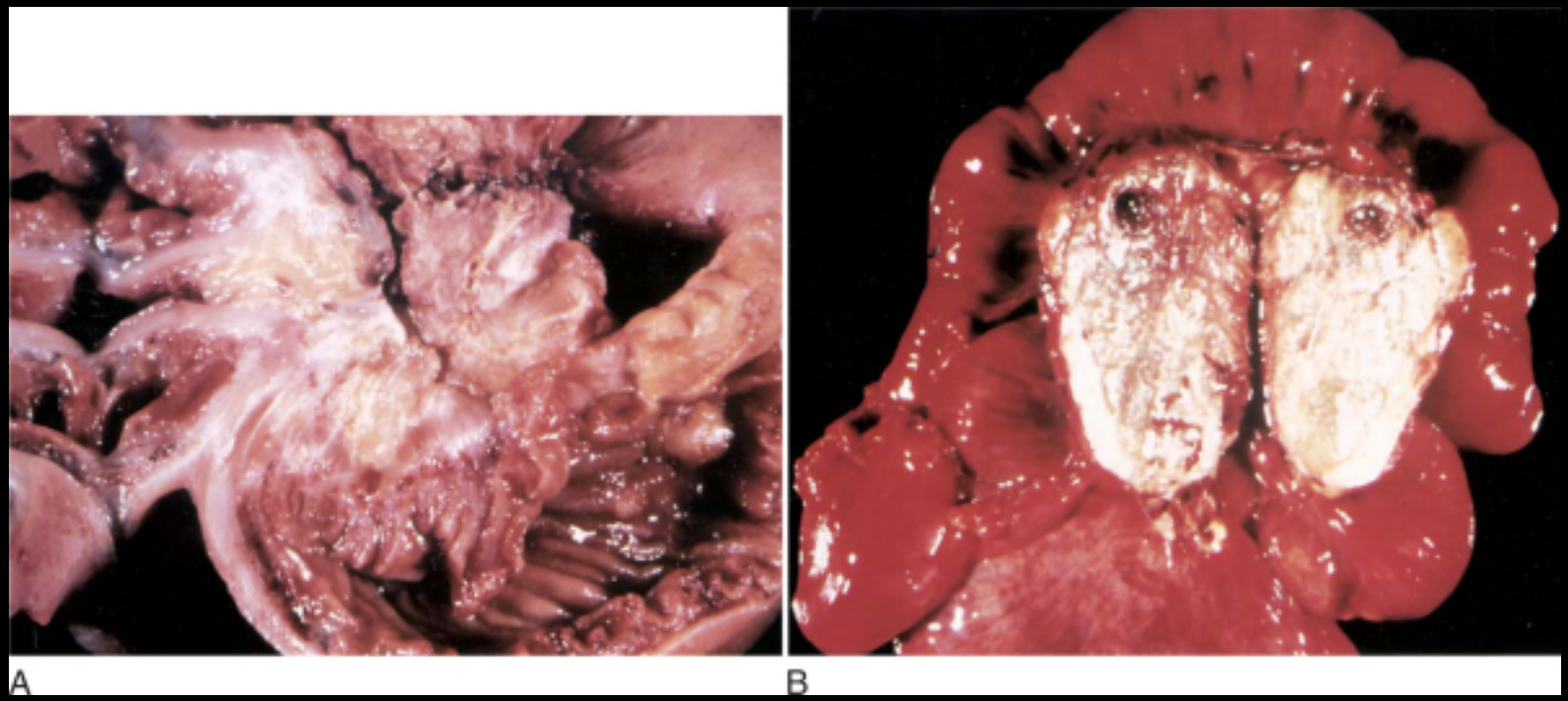
Pathologic characteristics

- Small, firm, submucosal tumors
- White, yellow, or gray
- Slow growing
- Overlying mucosa may be intact or ulcerated
- Cause intense desmoplastic reaction – mesenteric fibrosis

Desmoplastic reaction



Carcinoid Tumors



Clinical Presentation

- Asymptomatic 60-70%
- Vague, chronic symptomatology
  - Episodic abdominal pain, crampy pain, abdominal distension, nausea/vomiting
- Progress to SBO, ischemia and/or bleeding
- In 30-45% of patients, the diagnosis is made at the time of exploratory laparotomy for SBO, intussusception or mesenteric ischemia

Diagnosis

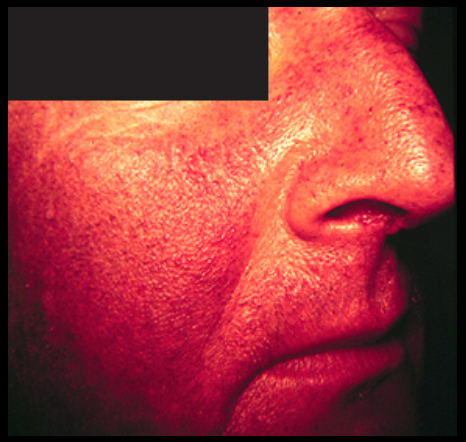
- Urine levels 5-hydroxyindoleacetic acid
- Plasma level chromogranin A
  - Elevated in 80%
  - More helpful for surveillance
- Imaging:
  - Barium swallow
  - CT contrast
  - Octreotide scan—used to access metastatic dx
    - Most tumors express somatostatin receptors
  - Endoscopy
    - EUS, capsule, double-ballon enteroscopy

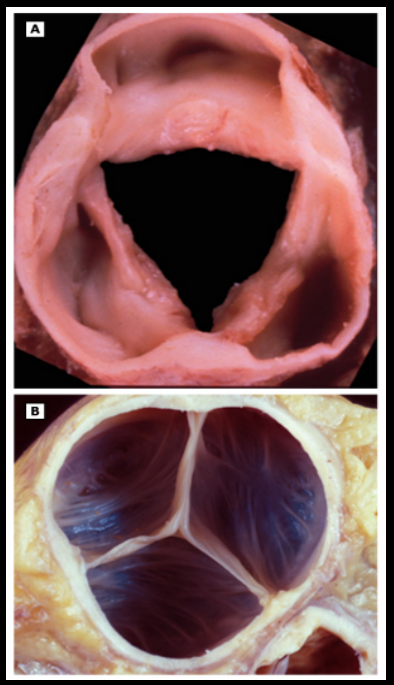
Malignant Carcinoid Syndrome

- Occurs in < 10% pts with carcinoid tumors
- Most often associated with SB carcinoid
- Due to hepatic replacement by metastatic disease or large retroperitoneal disease burden
  - Serotonin, 5-hydroxytryptophan, histamine, dopamine, kallikrein, substance P, prostaglandin, neuropeptide K

Malignant Carcinoid Syndrome

- Symptoms:
  - Cutaneous flushing
  - Palpitations
  - Diarrhea
  - Hepatomegaly
  - Neoplastic infiltrative cardiomyopathy
    - Pulmonic stenosis (90%)
    - Tricuspid insufficiency (47%)
    - Tricuspid stenosis (42%)
  - Bronchoconstriction





Pre-operative planning

- 1. Determination of the extent of disease burden
- 2. Identification of multifocal disease
  - Synchronous carcinoid and non-carcinoid tumors
- 3. Optimize fluid status and electrolytes
- 4. Pharmacologic treatment of carcinoid syndrome
- 5. Detection of cardiac pathology

Special Considerations

- Always explore abdomen for synchronous lesions
- Anesthesia can precipitate carcinoid crisis:
  - Hypotension
  - Flushing
  - Tachycardia → arrhythmias
- Treat with octreotide bolus, fluids, antihistamine, steroids, and albuterol

Gastric carcinoid

- Type I- associated with atrophic gastritis, chronic hypergastrinemia
  - Slow growing, very low rate of metastasis
  - Small (<1cm), multiple and polypoid
- Type 2- arise in setting of ZES, MEN-1
  - Small, slow growth, higer rate of metastasis
- Type 3- solitary, sporadic tumors
  - Large, more aggressive, highest rate metastasis

Treatment- gastric

- Type I
  - Observe, remove endoscopically if small
  - Antrectomy for large, recurrent, multiple tumors- removes gastrin secreting cells
- Type 2
  - If ZES- resect gastrinoma
  - Antrectomy if unable to identify gastrinoma
- Type 3
  - Gastrectomy with LN dissection

Duodenal Carcinoids

- <1cm may be treated with endoscopic resection
  - No evidence of LN involvement
- 1-2 cm and peri-ampullar lesions:
  - transduodenal excision
- >2cm and lesions with LN involvement:
  - Pancreaticoduodenectomy

Jejunum/Ileum

- Segmental resection for tumors < 1 cm with no evidence of nodal disease
- Wide excision of bowel and mesentery for tumors > 1 cm, multiple tumors, or + nodes
- Terminal ileum: R hemicolectomy

Appendiceal

- Usually well-differentiated
- Appendiceal carcinoid- metastatic risk related to size
  - < 1 cm: 2% metastatic
  - 1-2 cm: 50% metastatic
  - > 2 cm: 80-90% metastatic

Treatment- appendiceal

- Appendiceal carcinoid
  - < 1 cm- appendectomy
  - 1-2 cm debatable
  - > 2 cm, involving mesoappendix- R hemicolectomy
- Adenocarcinoid/goblet cell variant
  - More aggressive, often peritoneal disease
  - Right hemicolectomy, poss systemic therapy

Rectal carcinoid

- Usually incidental finding on colonoscopy
- Likelihood metastasis depends on size
- Do not usually produce serotonin or carcinoid syndrome

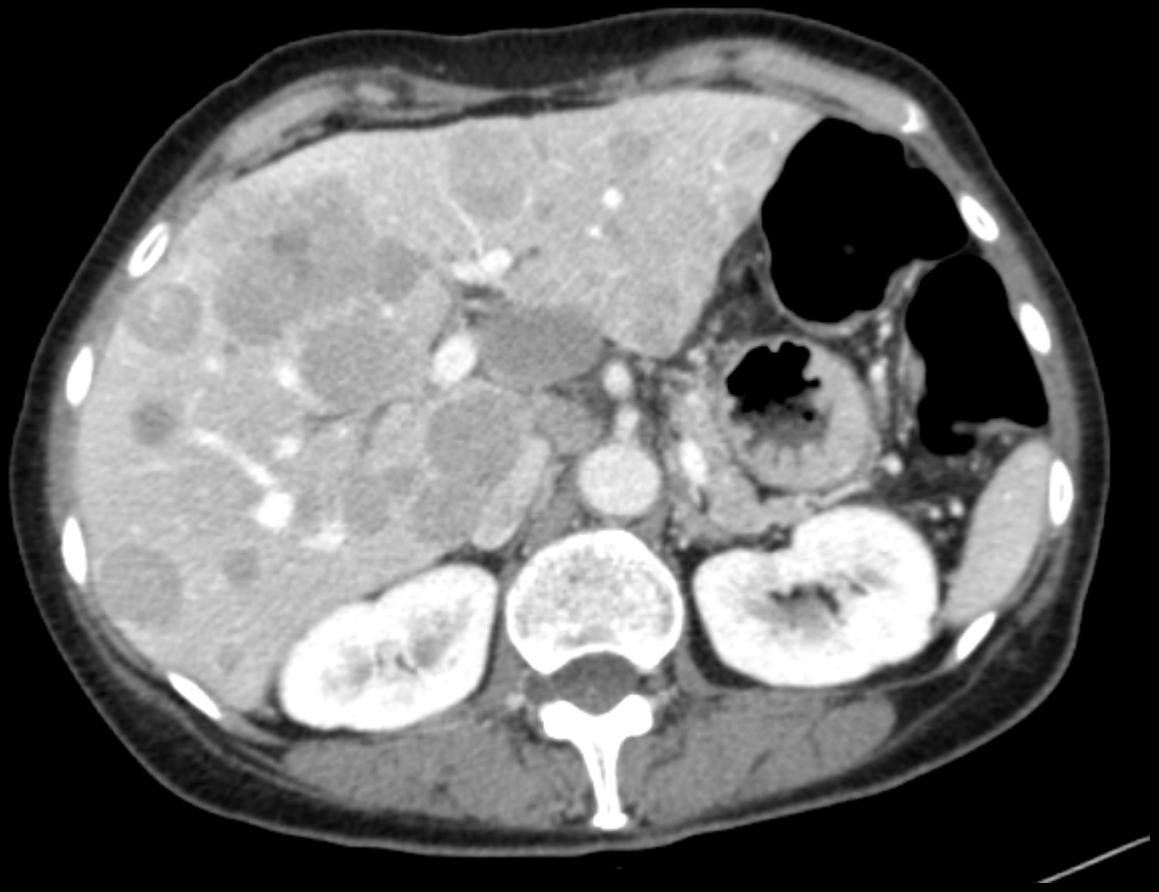
Treatment- rectal

- Rectal
  - <1 cm- endoscopic excision
  - 1-2 cm- evaluate with endorectal US or CT to look for regional disease
  - >2 cm- LAR/APR with total mesorectal excision

Prognosis

- Variable malignant potential
  - Ileal much more likely to metastasize than appendiceal
- 5 yr survival:
  - 65% if locoregional
  - 35-50% if distant disease
- Worst prognostic factors:
  - Presence of liver mets and carcinoid heart disease

Metastatic carcinoid

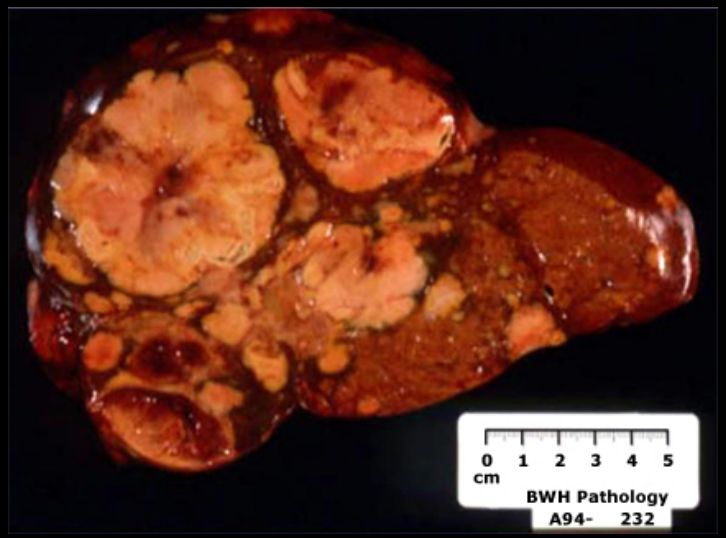


Metastatic disease

- Over 60% of patients will have nonlocalized disease at diagnosis
  - 50% will have liver metastases
- Surgical resection remains gold standard
- Patient's resected for cure have a survival rate of 60-80% at 5 years

Metastatic Disease

- Surgical debulking-
  - Hepatic resection: wedge or lobe
- Hepatic chemoembolization, RFA
- Transplantation



- Medical therapy:
  - Long-acting Somatostatin Analogs/Octreotide
    - Reduces hypersecretion-related symptoms
      - symptoms diarrhea and flushing (NOT R heart valvular disease)
    - Reduces biochemical markers by 60-80%
    - Can cause tumor regression in some cases
      - <10% of patients of partial or complete response
      - 24-57% of patients have stabilization of tumor growth
  - Peptide-Receptor Radionuclide Therapy
    - ^{177}Lu-octreotide: survival benefit of several years

Medical Therapy

- IFN-alpha
  - Second line for functioning tumors
  - Symptom control in up to 50% of patients
  - 10-15% have partial tumor size response
- Chemotherapy
  - Limited success (regression in 1/3 pts)
  - Used only for symptomatic pts unresponsive to other therapy
    - More effective for tumors with high proliferative rate (Ki67)
    - Streptozocin, 5-FU, doxorubicin

SESAP Question

- Which of the following statements about malignant tumors of the appendix is true?

A) R hemicolectomy is the recommended treatment for all appendiceal carcinoid tumors

B) Carcinoid is the second most frequent appendiceal malignancy

C) Hepatic metastases can be demonstrated in most patients with even small appendiceal carcinoids

D) Appendiceal carcinoids have a lower 5-yr survival than noncarcinoid malignancies of the appendix

E) Appendiceal goblet cell carcinoids < 1 cm can be safely treated with simple appendectomy

SESAP Question

- A 66 yo healthy man with epigastric abdominal pain and anemia is evaluated with upper endoscopy. Four 1 cm submucosal tumors are identified in the body of the stomach. Biopsies show carcinoid tumor. Fasting serum gastrin is 950 pg/ml (nl < 100). W/u shows carcinoid assoc with gastric achlorhydria, pernicious anemia, and hypergastrinemia. Best management would be:

A) Total gastrectomy

B) PPI

C) Antrectomy with gastroduodenostomy

D) Proximal gastrectomy with esophagogastrostomy

E) Enucleation of all 4 tumors

SESAP Question

A) Gastric carcinoid

B) SB carcinoid

C) Colon carcinoid

D) Appendiceal carcinoid

E) Rectal carcinoid

- 1. Associated with MEN 1
- 2. Atypical carcinoid syndrome
- 3. Urinary 5-HIAA sensitive for diagnosis