ZOLLINGER-ELLISON SYNDROME

FLAME LECTURE: 76

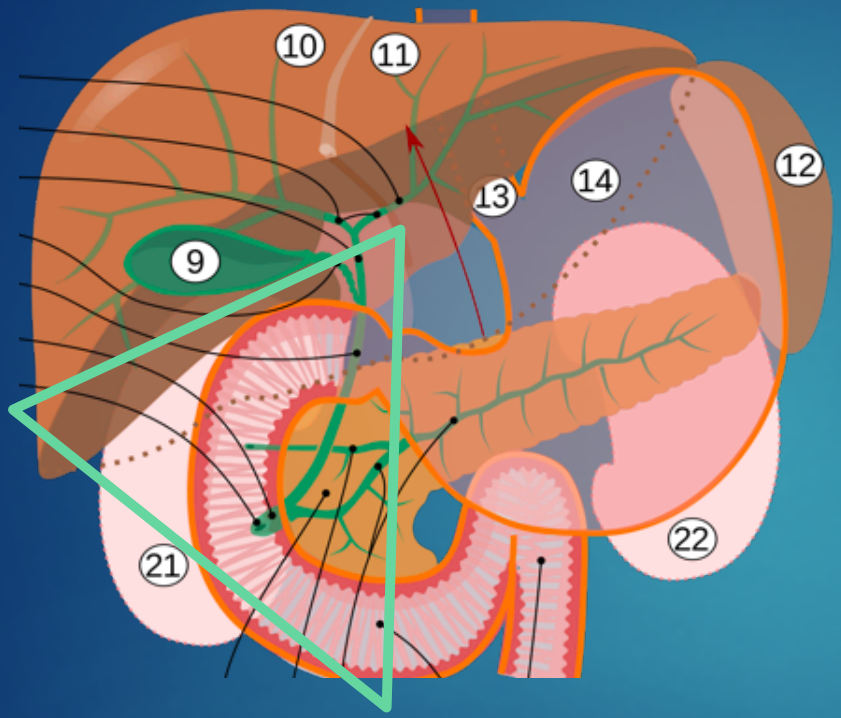
ANSAR & THAKER 3.6.20

LEARNING OBJECTIVES

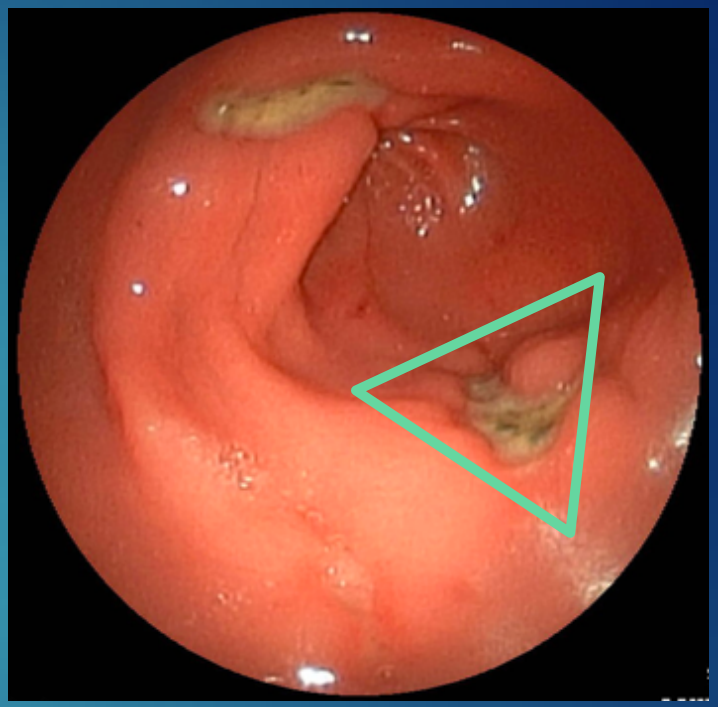
- Characterize Zollinger-Ellison syndrome (ZES)
- Describe the symptoms of ZES
- Specify common diagnostic methods
- Outline common treatment options
- See also – for closely related topics
  - FLAME LECTURES on Peptic Ulcer disease

OVERVIEW

- In 1955, Drs. Zollinger and Ellison discovered that ulcers in the small intestine which were refractory to both medical and surgical therapy we caused by gastrin-secreting tumors (gastrinomas) in the "gastrinoma triangle"[2]
- ZES is constellation of PUD, GERD, and diarrhea[2]



Gastrinoma Triangle - Outlined by the hepatic portal vein, neck and body of the pancreas, and latter two-thirds of the duodenum



Ulcers located in the distal duodenum in a patient with ZES

EPIDEMIOLOGY

- ~80% of ZES cases occur in isolation and 20% are associated with MEN1[2]
  - Approximately 50% of patients with MEN1 have ZES[2]
- Annual incidence of ZES is 1-3 cases per million per year[2]
- Most common between the ages of 20-60[2,3]

HISTORY / PHYSICAL EXAM

- Symptoms:
  - Abdominal pain and diarrhea occur >70% of cases[3]
  - Heart burn (44%), nausea (33%), vomiting (25%), weight loss (17%)[3]
  - Only 11% of patients had only one symptom[3]
- Physical exam does not typically reveal any findings

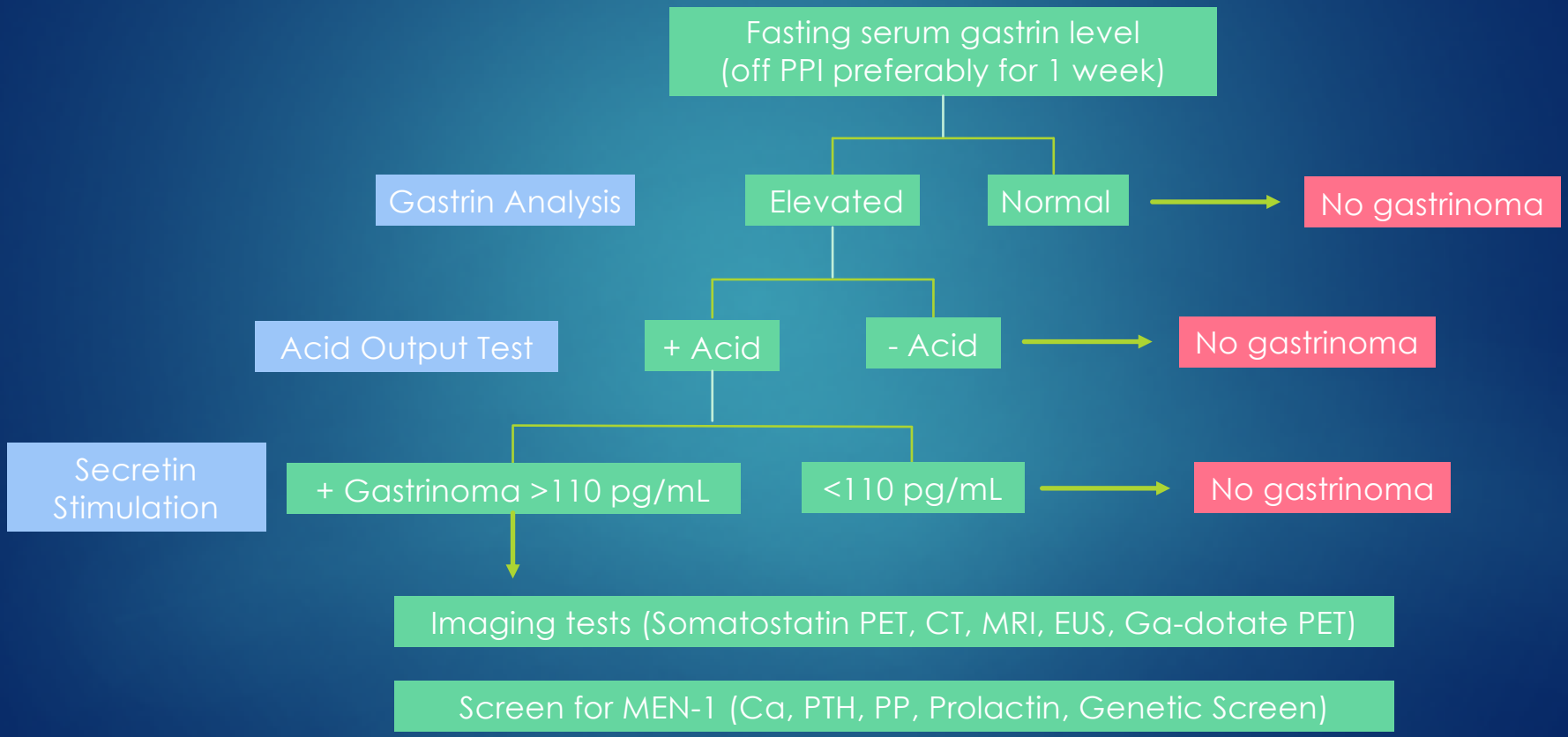
DIAGNOSIS

- Fasting serum gastrin level – initial test, 99% sensitivity
  - Positive if >100 pg/ml
  - Diagnostic if >1000 pg/ml with a pH < 2[1]
- Basal acid output test – 98% sensitivity
  - Positive if >15 mEq/hour[1]
- Secretin stimulation test – measures serum fasting gastrin levels after admin. of IV secretin
  - Positive when ≥ 200 pg/ml[1]
- False positives / False negatives
  - Unreliable gastrin assays, frequent PPI/H2 blocker use, and primary hyperparathyroidism[1]
  - False positive secretin stimulation tests can due to hypercalcemia and PPIs

ADDITIONAL EVALUATION

- Suspicion of ZES requires screening for MEN 1
- Imaging studies to localize tumors and evaluate for metastases
  - CT or MRI
- Somatostatin Receptor Scintography (SRS) or ^{68}Ga-dotate PET scan
- Invasive modalities if other studies are negative
  - Endoscopic ultrasound
  - EGD

DIAGNOSTIC ALGORITHM



MANAGEMENT/TREATMENT

- Medical management of symptoms with PPIs/H2 blockers/octreotride and evaluation for potentially curative surgery
  - Mainstay is high dose PPI therapy[2]
- The goal of surgery is tumor control to minimize acid secretion[1]
  - Surgery highly debated and patient selection is critical
- 60-90% malignant with mets to lymph nodes, liver, or distant organs at diagnosis[2]
- Long term follow up with repeat lab testing and systematic re-imaging based on size, location, staging and association with MEN 1

IMPORTANT LINKS / REFERENCES

- Albers MB, Manoharan J, Bartsch DK. Contemporary surgical management of the Zollinger-Ellison syndrome in multiple endocrine neoplasia type 1. Best Pract Res Clin Endocrinol Metab. 2019 Oct;33(5):101318. doi: 10.1016/j.beem.2019.101318. Epub 2019 Aug 31.
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