PEDGIHEP ,VOL12, 2010.ZOLLINGER ELLISON SYNDROME.
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Zollinger-Ellison Syndrome:

ITS a rare syndrome is characterized by refractory, severe peptic ulcer disease caused by gastric hypersecretion due to the autonomous secretion of gastrin by a neuroendocrine tumor, a gastrinoma.

The syndrome was originally described by Zollinger and Ellison in 1955.In 1960, Cawkwell described the first childhood case of Zollinger-Ellison syndrome in *The New Zealand Medical Journal.*

Epidemiology:
Prior to the introduction of acid-suppressing drugs, including histamine H2-receptor antagonists and, more recently, proton pump inhibitors (PPIs), Zollinger-Ellison syndrome carried high mortality rates. Because safe control of gastric acid hypersecretion can be achieved with PPIs in virtually all patients, mortality and morbidity are now attributed to advanced disease with metastases to liver and bones.
10-year survival rate was 94% in the overall Zollinger-Ellison syndrome population. The survival rate at 10 years was slightly lower (89%) when Zollinger-Ellison syndrome was associated with MEN-1. Gastrinomas may be malignant or benign but usually slowly grow. The male-to-female ratio in childhood Zollinger-Ellison syndrome (ZES) is 4:1. The youngest patient reported with Zollinger-Ellison syndrome was a boy aged 7 years.

History:

The typical presentation of Zollinger-Ellison syndrome (ZES) is severe abdominal pain with or without diarrhea. Most children present with complications of peptic ulcer disease (PUD), such as bleeding from an ulcer or duodenal perforation. Abdominal pain is the most common presenting symptom in Zollinger-Ellison syndrome. The second most common symptom of Zollinger-Ellison syndrome ulcers is diarrhea. The physical examination findings are often normal.

Etiology:

all patients who are under evaluation for Zollinger-Ellison syndrome should undergo genetic testing for MEN-1. MEN-1 is due to mutations in the tumor suppressor gene *MEN1*, located on chromosome 11q13. *MEN1* encodes a transcriptional regulator, menin.

Differential diagnosis:

Acid peptic disease.
GER
Esophagitis
H pylori.
MEN
MAS

Laboratory Studies:

STEP 1: fasting Gastrin levels higher than 100 pg/mL are highly suggestive of Zollinger-Ellison syndrome. If the gastric pH level is less than 2, a gastrin level of higher than 1000 pg/mL is diagnostic .FSG >10 times : DIAGNOSTIC.

STEP2: if the fasting gastrin is elevated while taking a PPI, the fasting gastrin level should be repeated after stopping the PPI for at least 1 week.

STEP 3: If the gastrin level is 100-1000 pg/mL and the pH level is less than 2, OR. FSG 1-1.9 times : secretin stimulation test :

- In the 24 hours prior to the test, the patient receives no antacids. A nasogastric tube is placed into the antrum, and the stomach is emptied
  - After blood to measure the basal gastrin level is obtained, 2 IU/kg of secretin is intravenously administered. Blood is obtained at 2.5 minutes, 5 minutes, 10 minutes, 15 minutes, and 30 minutes. An increase of serum gastrin levels to higher than 200 pg/mL is diagnostic of Zollinger-Ellison syndrome.

- Tumor size does not relate to serum gastrin levels or the severity of symptoms
  - In an unoperated stomach, a BAO of more than 15 mEq/h is diagnostic of Zollinger-Ellison syndrome. If the patient underwent gastric resection for acid reduction, a BAO of more than 5- 10 mEq/h is diagnostic for Zollinger-Ellison syndrome.

- If the patient has multiple endocrine neoplasia type 1 (MEN-1), other laboratory abnormalities may be suggestive of Zollinger-Ellison syndrome.
  - High plasma calcium levels
  - High parathyroid hormone (PTH) levels
  - High prolactin levels

Imaging Studies:

Somatostatin receptor scintigraphy (SRS) can reveal 57-78% of gastrinomas and has a sensitivity of 84-94%. It is currently the single most effective imaging modality for gastrinomas. SRS may not accurately reveal tumor size or location and is best used in conjunction with CT scanning with intravenous contrast. It is also useful because it allows for whole body scanning and measure of whole body tumor content during a single test.

Pathology:

Immunohistochemistry staining may be positive for chromogranin A, neuron-specific enolase, and synaptophysin, as well as for pancreatic peptide, somatostatin, adrenocorticotropic hormone (ACTH), and vasoactive intestinal polypeptide (VIP).

Medical Treatment of Gastric Acid Hypersecretion:

PPIs have become the first-line treatment in Zollinger-Ellison syndrome. PPIs are rapidly and almost completely absorbed. The peak plasma concentration is reached in 1-3 hours. The prodrug is quickly metabolized by the liver, primarily by cytochrome P-450 isoenzyme CYP2C19, resulting in a half-life of roughly 1 hour. H2-receptor antagonists are no longer indicated because PPIs provide more effective antisecretory effects and prolonged use of H2-receptor antagonists leads to tachyphylaxis.

Somatostatin analogues such as octreotide decrease gastrin and gastric acid secretion and can be used to treat the symptoms associated with gastrinoma. Small studies in adults using weekly subcutaneous octreotide acetate for 1-48 months led to a decrease in abdominal pain and diarrhea in most patients.

Surgical Care:

1. Surgery is now focused on staging (when gastrinomas are not revealed by imaging) and reducing tumor burden to decrease metastases and improve disease-free survival. Local tumor excision is currently the procedure of choice.

2. At the time of laparotomy for possible cure, a parietal cell vagotomy should be performed to decrease antisecretory drug requirements in the 70% of patients who are not cured long term.

3. Parathyroidectomy in patients with ZES and in patients with MEN-I with hyperparathyroidism decreases fasting gastrin levels; decreases serum gastrin increases following secretin injection, decreases BAO, and increases sensitivity to antisecretory drugs.

4. diffuse metastatic disease to the liver is not present and the patient does not have MEN-I, surgical exploration is indicated.

5. patients with MEN-I and ZES the role of surgery is controversial.

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