Gastric Neuroendocrine Tumors

Johanna Basa M.D.
Kings County Medical Center
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No disclosures
Outline

- Case
- Classification
- Pathophysiology
- Diagnosis
- Management
Case

• 35 year old male with PMH of GERD not on proton pump inhibitors presented to an outside hospital with complaints of abdominal pain. His work up at that time revealed multiple gastric polyps and hypercalcemia.

• On review of systems he denied flushing, headache, nausea, vomiting, new stretch marks, or kidney stones.

• Family history was negative for endocrine malignancy/pathology.
Case

- EGD performed at the outside hospital showed multiple polyps, and biopsy was consistent with neuroendocrine tumor, favor type 1 gastric carcinoid.

- An octreoscan showed uptake in the right peri-aortic region and right upper abdominal area.

- A sestamibi scan done at the outside hospital was positive for uptake in the right lower lobe.
Case

- Gastrin level 542
- Calcium 11.9
- PTH 221.3
- On physical exam he was well appearing
- CV: reg rate
- Resp: clear bilaterally
- Abd: soft, NT, ND
Case

- Procedure performed: Exploratory laparotomy, subtotal gastrectomy, billroth II reconstruction, intra operative ultrasound

- Findings: Multiple polyps in the antrum, no lesions seen in the duodenum or pancreas on US
Case

- POD#0-4 Pt was kept NPO with NGT
- POD# 5 NGT and JP drains were removed
- POD#7 Pt was advanced to clears
- POD#9 Pt was discharged home
- POD#12 He was re-admitted with diagnosis of hypercalcemia Ca 12.5 and delayed gastric emptying
Case

- POD#12-20 Hypercalcemia was corrected, he was started on TPN and erythromycin and treated with NGT decompression
- POD#21-22 NJT was placed endoscopically, he was started on NJ tube feeds
- POD#24 NJT was removed
- POD#29 Pt was discharge home, tolerating soft diet.
Case

• Pathology: Neuroendocrine tumor well differentiated <2-10 per high power field invading into the submucosa. T2N1pMx. Stains positive for chromgranin A, synaptophysin, negative ki-67.

• Gastric adenocarcinoma, poorly differentiated with signet ring features, one lymph node positive T1N1pMx

• 2 Hepatic artery lymph nodes positive for neuroendocrine tumors
Should this patient with diagnosis of type 1 carcinoid have endoscopic resection or antrectomy?
Gastric Carcinoids

- 4% of all GI NET, 1% of gastric neoplastic
- 4 subtypes
- Types 1-3 originate from enterochromaffin cells
- Types 1,2 are gastrin dependant, small <2cm, multifocal
- Type 3 is not associated with hypergastrinemia, usually large and solitary
- Type 4 is usually large, ulcerated, poor prognosis.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
</tr>
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<tbody>
<tr>
<td>Associated disease</td>
<td>Chronic atrophic gastritis, Pernicious anemia</td>
<td>Zollinger-Ellison, and MEN I</td>
<td>None</td>
<td>Non ECL carcinoids</td>
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<tr>
<td>Proportion of tumors</td>
<td>80%</td>
<td>5%</td>
<td>10-15%</td>
<td>&lt;5%</td>
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<tr>
<td>Site of tumor</td>
<td>Fundus</td>
<td>Fundus</td>
<td>Antrum or Fundus</td>
<td>Antrum or Fundus</td>
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<tr>
<td># of tumors</td>
<td>Multiple</td>
<td>Multiple</td>
<td>Single</td>
<td>Single</td>
</tr>
<tr>
<td>Size of tumor</td>
<td>&lt;1cm</td>
<td>&lt;1 cm</td>
<td>2-5cm</td>
<td>&gt;2cm</td>
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<tr>
<td>Plasma gastrin level</td>
<td>High</td>
<td>High</td>
<td>Normal</td>
<td>High</td>
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<tr>
<td>Gastric acid output</td>
<td>Low</td>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Good</td>
<td>Good</td>
<td>Poor</td>
<td>Poor</td>
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</table>
Figure 1: Pathophysiologic mechanisms of normal acid secretion from parietal cells after a meal (a) and ECL-cell hyperplasia in patients with achlorhydria and loss of somatostatin negative feedback (b).
**Figure 2:** Factors contributing to type 1 GCs development.
Diagnosis

- History
- EGD
- CT scan of the abdomen and pelvis
- Octreotide scan
- Endoscopic ultra sound
Figure 4: Management flow chart of GCs according to ENETS guidelines. ¹Consider SSAs.
Does this patient have Multiple neuroendocrine neoplasia syndrome? MEN??
MEN1

- Think 3 P’s
- Autosomal dominant
- Multiglandular Parathyroid disease
- Benign and malignant neuroendocrine tumors of the pancreas and duodenum
- Adenomas of the anterior pituitary
- Tumor suppressor gene located on chromosome 11 and encodes for MENIN.
MEN2A

- Autosomal dominant
- Think PMP
- Parathyroid (either adenoma or multigland hyperplasia)
- Medullary thyroid cancer
- Pheochromacytoma
MEN 2B

- Autosomal dominant
- Think **PMM**
- **Pheochromocytoma**
- **Medullary thyroid cancer**
- **Mucosal neuromas**
- Mutations on the RET proto-oncogene
<table>
<thead>
<tr>
<th>Benign diseases</th>
<th>n</th>
<th>Percentage (%)</th>
<th>Tumor-related diseases</th>
<th>n</th>
<th>Percentage (%)</th>
<th>Current study</th>
<th>European community</th>
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<tbody>
<tr>
<td>Medical comorbidities</td>
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<td></td>
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<td></td>
<td></td>
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<td>Anemia (B12 deficiency)</td>
<td>47</td>
<td>42.3</td>
<td>Parathyroid adenoma</td>
<td>6</td>
<td>5.4</td>
<td>853.9</td>
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<td>Hashimoto's thyroiditis</td>
<td>41</td>
<td>36.9</td>
<td>Papillary thyroid carcinoma</td>
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<td>426.9</td>
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<td>Hypertension</td>
<td>22</td>
<td>19.8</td>
<td>Colon cancer</td>
<td>2</td>
<td>1.8</td>
<td>284.6</td>
<td>75</td>
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<tr>
<td>Hyperlipidemia</td>
<td>12</td>
<td>10.8</td>
<td>Breast cancer</td>
<td></td>
<td></td>
<td>287.8</td>
<td>110.3</td>
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<td>Diabetes mellitus type 2</td>
<td>11</td>
<td>9.9</td>
<td>Lung cancer</td>
<td></td>
<td></td>
<td>284.6</td>
<td>23.9</td>
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<tr>
<td>Anemia (iron deficiency) and osteoporosis</td>
<td>10</td>
<td>9</td>
<td>Prolactinoma</td>
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<td>143.9</td>
<td>30</td>
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<tr>
<td>Diabetes mellitus type 1</td>
<td>7</td>
<td>6.3</td>
<td>Endometrial carcinoma</td>
<td>1</td>
<td>0.9</td>
<td>142.3</td>
<td>5</td>
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<tr>
<td>Multinodular goiter</td>
<td>6</td>
<td>5.4</td>
<td>Acute myelogenic leukemia</td>
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<td></td>
<td>142.3</td>
<td>8</td>
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<td>Obesity, rheumatoid arthritis, and coronary heart disease</td>
<td>4</td>
<td>3.6</td>
<td>Prostate cancer</td>
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<td>137.7</td>
<td>78.9</td>
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<td>Ischemic attack, Sjögren's syndrome, and systemic lupus erythematos</td>
<td>3</td>
<td>2.7</td>
<td>Medullary thyroid carcinoma</td>
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<td></td>
<td>142.3</td>
<td>1</td>
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<tr>
<td>Premature ovarian failure, impaired fasting glucose, renal transplantation, and psoriasis</td>
<td>2</td>
<td>1.8</td>
<td>Hepatocellular carcinoma</td>
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<td></td>
<td></td>
<td>8.9</td>
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<tr>
<td>Addison's disease, Graves' disease, vitiligo, depression, chronic autoimmune hepatitis, and lymphocytic colitis</td>
<td>1</td>
<td>0.9</td>
<td>Midgut carcinoid</td>
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<td></td>
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<td>0.9</td>
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Data retrieved from reference 2 and European Society of Medical Oncology (references 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29).
What are our plans for his hyperparathyroidism?
Criteria for surgical referral and parathyroidectomy

- All symptomatic patients
- All asymptomatic patients with the following
  - Serum Ca >1mg/dl (>0.25mM/Liter) above the upper limits of normal
  - Bone density at the hip, lumbar spine, distal radius that is >2 SD below the peak bone mass
  - All individuals less than 50 yrs of age
  - Patients whom medical surveillance is undesirable or impossible
An important stimulant of gastin release from endocrine cells in the antrum is:

- A. small peptide fragments and amino acids
- B. locally released somatostatin
- C. Dietary fat
- D. Acidification of the antral lumen.
Question

- A 30 yr old man presents to his primary care physician with fatigue and weakness. During workup, he is found to be hypercaclemic. Further evaluation reveals that he has family history of pancreatic and pituitary tumors. Which of the following is true regarding patients with MEN syndromes?
A. All three types of MEN syndromes are characterized by hyperparathyroidism.

B. 90% of patients with MEN IIa will have hyperparathyroidism.

C. Hypercalcemia can exacerbate the symptoms of neuroendocrine tumors.

D. Single parathyroid adenomas are the cause of hyperparathyroidism in patients with MEN.

E. Hyperparathyroidism should be first managed in patients with MEN I and MEN IIa.