

Gastric Neuroendocrine Tumor of Indeterminate Type

Introduction

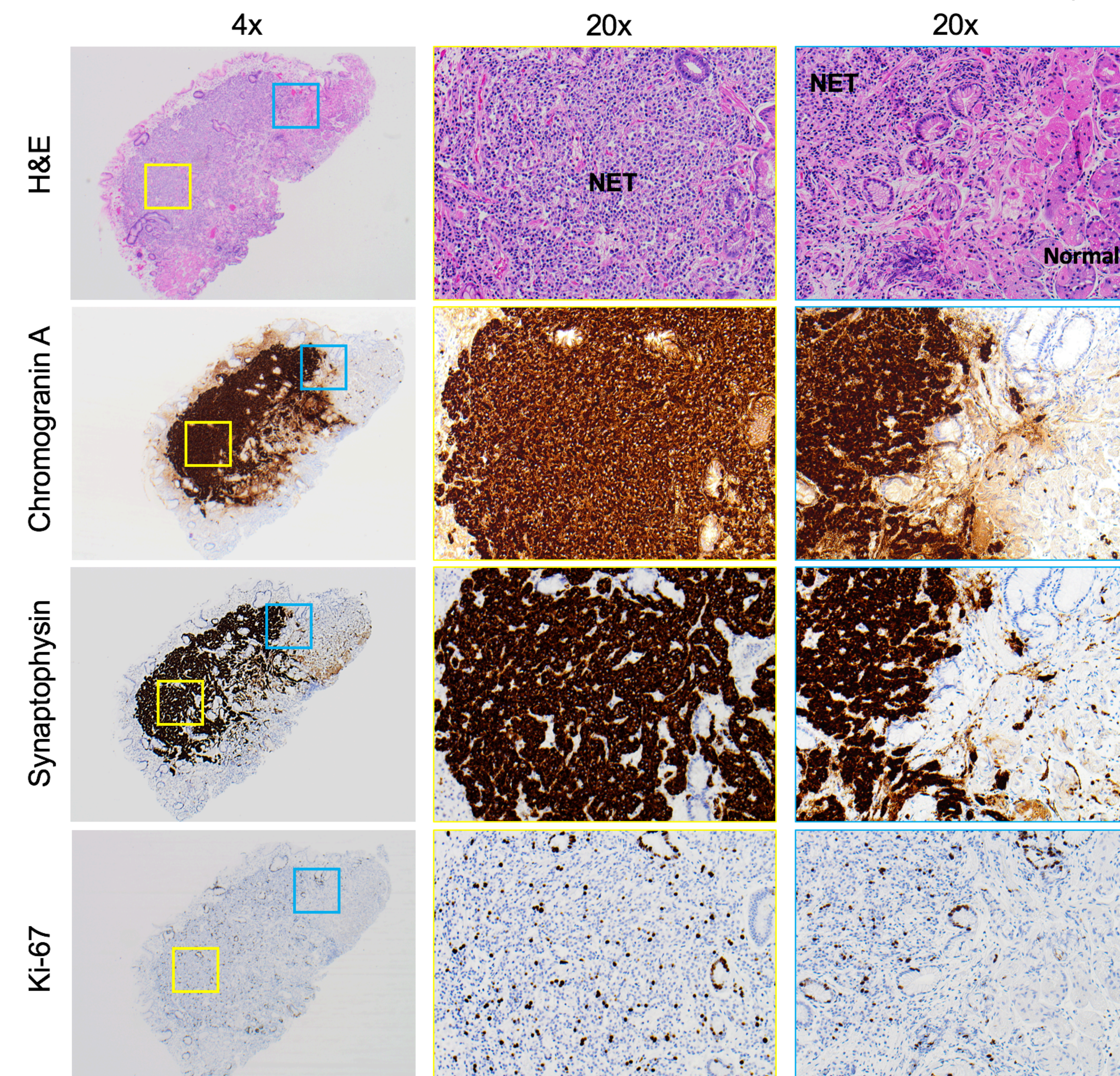
- Gastric neuroendocrine tumors (GNETs) are rare tumors making up less than 2% of gastric polyps.
- Type I GNETs are most common (70-80%) and are associated with atrophic gastritis, pernicious anemia, iron deficiency, elevated gastrin, and high gastric pH. These are typically small, low-grade, and may be multifocal.
- Type II tumors are also associated with elevated gastrin levels but a low pH, as seen in Zollinger-Ellison syndrome.
- Type III tumors are larger and more aggressive and occur sporadically in the setting of normal gastric mucosa, normal gastrin levels, and normal pH.

Objectives

- To bring awareness of the difficulty of categorizing certain GNETs based on classic criteria
- Demonstrate how proton pump inhibitors (PPIs) can affect the identification of certain GNETs

Case Report

- 70-year-old white male with history of gastroesophageal reflux disease (GERD) on chronic proton pump inhibitor (PPI) presented for esophagogastroduodenoscopy (EGD) for worsening GERD symptoms.
- EGD revealed 2 polyps in the body – each was 4-5 mm and was removed with hot snare. A few smaller polyps were removed with biopsy forceps.
- The gastric mucosa was grossly normal. Sydney protocol biopsies were obtained.
- The 2 larger polyps returned as well-differentiated GNETs, grade 1 (Ki-67 index 2.5%). The smaller polyps returned as areas of intestinal metaplasia (IM), but Sydney protocol biopsies did not reveal *H. pylori*, atrophic gastritis, or IM.
- EGD was repeated off PPI for 1 week and fasting labs were obtained. Gastric pH was 1, serum gastrin was 78 pg/mL (normal), vitamin B12 and ferritin were normal, and intrinsic factor and parietal cell antibodies were negative.



Well differentiated neuroendocrine tumor:

- Monotonous cells with round or oval nuclei with salt and pepper chromatin
- Tumor cells arranged in nests, trabecular or organoid architecture. No necrosis was observed
- Low grade or grade 1 (G1): mitoses $\leq 2/2 \text{ mm}^2$ and Ki67 index $< 3\%$
- Positive stains: (brown color shows positive staining)

Chromogranin
Synaptophysin



Gastric polyp

Conclusions

- This case highlights a scenario in which a GNET is difficult to categorize based on classic criteria.
- As type III lesions are very aggressive with high risk of metastasis, distinguishing between type I and type III lesions is paramount.
- While grossly and histologically resembling a type I GNET (multifocal, small, low-grade), the GNETs in this case were present in the absence of atrophic gastritis, and the patient had a normal gastrin and low gastric pH off PPI.
- The lack of atrophic gastritis and normal gastrin levels are more suggestive of a type III tumor, but one would expect a single, large, high-grade GNET in that case.
- As PPI use has increased in the past 30 years, so has incidence of GNETs; it is possible that a chronic, PPI-induced "hyper-gastrin" state was responsible for this patient's GNETs and that gastrin normalized once PPI was discontinued. More studies are needed to further categorize GNETs with indeterminate features.