Case History

A 33-year-old female with history of gastroesophageal reflux disease and H. pylori gastritis presented with epigastric pain and dysphagia. Endoscopic ultrasound demonstrated a 2.5 cm mass located on the lesser curvature and originating from within the muscularis propria (Figure 1A). CT scan showed an enhancing submucosal lesion without gastric outlet obstruction (Figure 1B). A laparoscopic partial gastrectomy was performed.

Gross examination revealed a well demarcated tan-pink firm submucosal lesion, 2.5 x 2.5 x 2.2 cm (Figure 2). Histologic sections (Figure 3A-C) and immunohistochemical stains for smooth muscle actin (SMA), caldesmon, and synaptophysin (Figure 3D-F) are presented below. In addition, immunostaining for calponin was positive and for pancytokeratin, DOG-1, and chromogranin was negative (not shown),

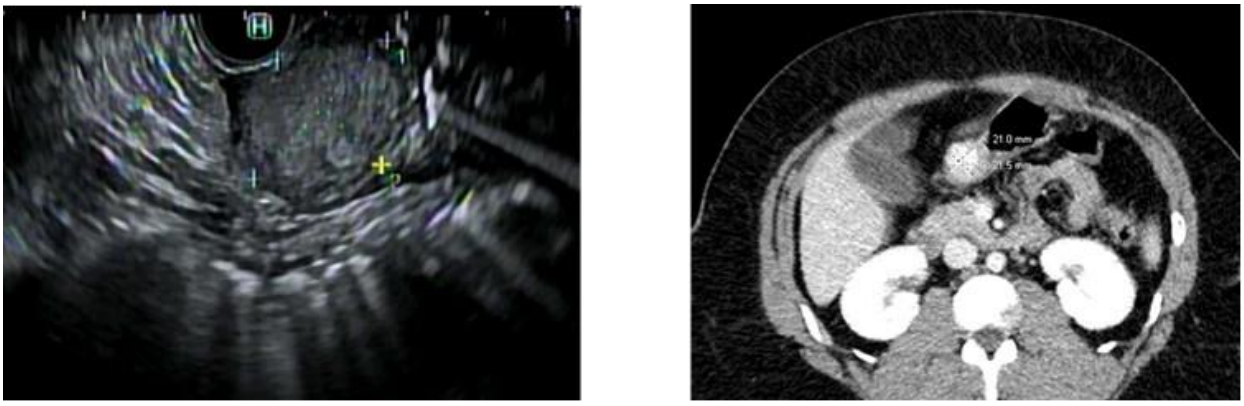

Figure 1. Endoscopic images show an intramural (subepithelial) mass in the lesser curve of the stomach, which appeared to originate from within the muscularis propria (A). Abdominal CT scan with contrast show avidly enhancing submucosal mass arising from the inferior aspect of the antrum of the stomach (B).

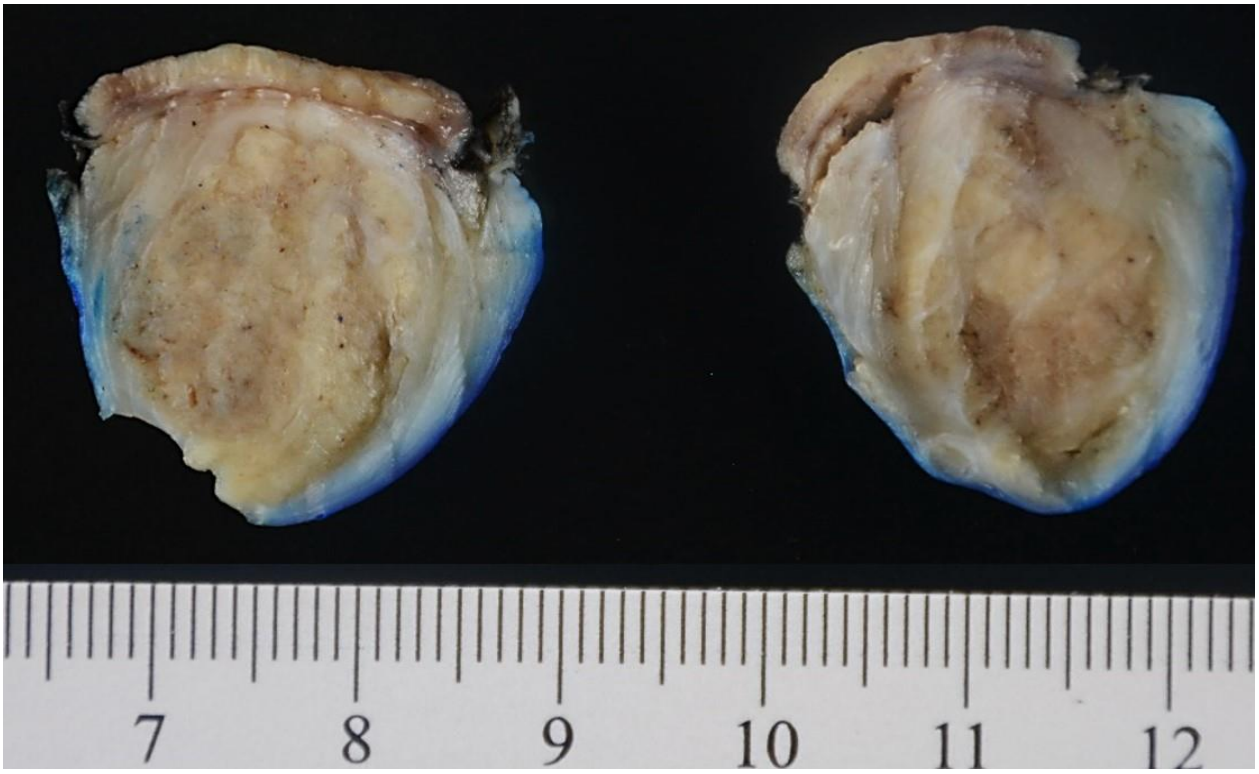

Figure 2. Gross examination shows a submucosal lesion. The serosa is inked blue.

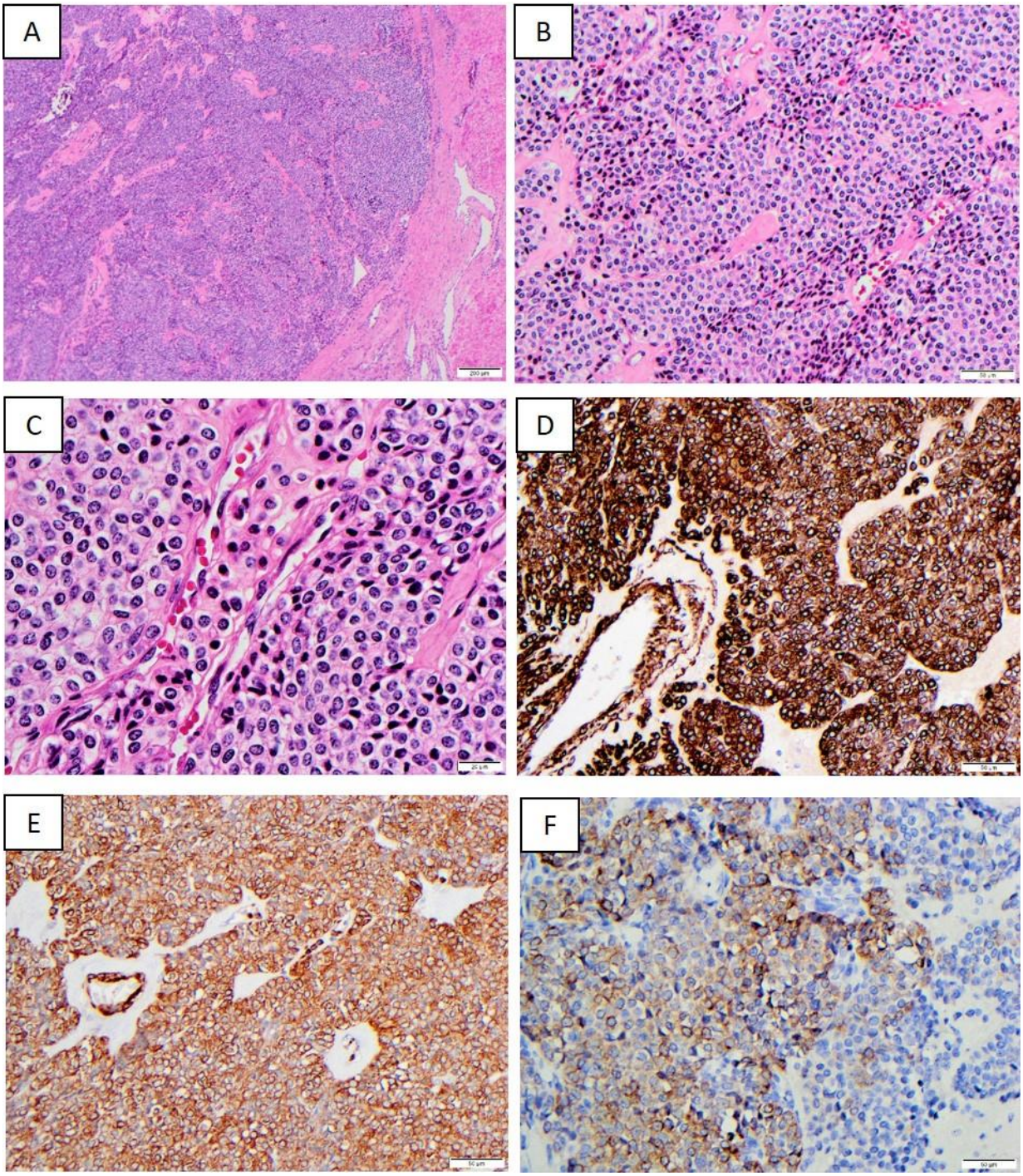

Figure 3. H&E sections show a well-demarcated intramural tumor (A, x 4) composed of nests and trabeculae (B, x 20) of monomorphic cells with round nuclei and well-defined cell membrane (C, x 40). Immunohistochemical stains show that tumor cells are positive for SMA (D, x 20), caldesmon (E, x 20), and synaptophysin (F, x 20).

What is the most likely diagnosis?

A) Gastric Neuroendocrine Tumor

B) Gastrointestinal Stromal Tumor (GIST)

C) Gastric Glomus Tumor

D) Gastric Leiomyoma

The correct answer is C

Histologically, sections show a well circumscribed neoplastic proliferation located intramurally and composed of nests and trabeculae. The cells are monomorphic and demonstrate cytoplasmic clearing, round nuclei and well-defined cell membrane. Immunohistochemically the tumor cells are positive for SMA, caldesmon, and synaptophysin. These features support the diagnosis of glomus tumor.

Discussion:

Glomus tumor is a mesenchymal neoplasm of modified smooth muscle cells that originates from the perivascular glomus body cells. Glomus tumors typically arise in the periungual sites, but may be found in other locations such as the bone, mediastinum, and gastrointestinal tract. Gastrointestinal glomus tumor is a rare neoplasm that most commonly is found in the stomach. In a study of 32 cases, the median age at presentation was 55 years and there was female predominance (11). Typically, gastric glomus tumor presents clinically with chronic pain with or without chronic upper gastrointestinal bleeding. On rare occasion, gastrointestinal perforation may occur. Most glomus tumors are sporadic; however, a small subset of tumors is associated with Neurofibromatosis type 1.

Histologically, gastrointestinal glomus tumors show identical features to glomus tumors of the periungual sites. They are typically multinodular and are composed of monomorphic cells with sharply defined cell borders. Clear cytoplasm is seen frequently. The nuclei are uniform with delicate chromatin. Although occasional mitoses might be seen, frequent mitoses, especially atypical mitotic figures, spindle cells or marked nuclear atypia if present should raise the possibility of a malignant form of glomus tumor.

Immunohistochemically, glomus tumor cells are positive for SMA, caldesmon, and synaptophysin. The latter shows positive expression in a subset of tumors and leads to a mistaken diagnosis of neuroendocrine tumor. Glomus tumor is negative for desmin, S100,

keratin, and more specific neuroendocrine markers such as chromogranin. At the molecular level, glomus tumors show *NOTCH* gene rearrangements (*NOTCH1, NOTCH2*, or *NOTCH3*), *BRAF* (p.V600E) and *KRAS* (p.G12A) mutations with variable detection rate (6). They are treated with surgical excision and typically have excellent prognosis.

Differential diagnosis

A) Gastric Neuroendocrine Tumor (GNET)

GNETs are quite common in the stomach and can be sporadic, or associated with autoimmune gastritis and multiple endocrine neoplasia 1 syndrome (MEN1). In contrast to glomus tumors that are centered in the muscularis propria, GNETs are usually centered in the mucosa/submucosa and often show extension deeper into the wall of the stomach. The tumor cells have round nuclei with inconspicuous nucleoli and typical "salt and pepper" chromatin quality. By immunohistochemistry, they are positive for cytokeratin, synaptophysin, and chromogranin but are negative for SMA and caldesmon.

B) Gastrointestinal Stromal Tumor (GIST)

Gastrointestinal stromal tumors arise in the muscularis propria, most commonly of the stomach, but also of the gut. Microscopically they show well-demarcated tumor nodules composed of spindle cell and/or epithelioid cells. Typically, GISTs are positive for CD117, DOG1, CD34. Although GISTs may show SMA expression, they are negative for caldesmon. Neuroendocrine markers are also negative.

D) Gastric Leiomyoma

The esophagus and colon are the most common sites for gastrointestinal leiomyomas. Tumor cells typically show eosinophilic cytoplasm arranged in long fascicles and are positive for SMA, and desmin, while negative for cytokeratins, synaptophysin, chromogranin, CD117, and DOG-1.

Reference:

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