

Case History:

A 74-year-old woman presents with symptoms of gastroesophageal reflux disease (GERD). Her past medical history is significant for chronic obstructive pulmonary disease and hyperlipidemia. Her current medications include omeprazole and pravastatin.

On endoscopy, there is a single, 3 mm, cardia-based polyp (Figure A). The remaining stomach, duodenum and esophagus is within normal limits.

The photos provided below are representative of the polyp. The biopsies from background stomach (not shown) are normal. A repeat upper GI endoscopy is performed one month later and shows no evidence of residual lesion. Upon follow-up twelve months later, the patient is doing well with no further clinical findings.



Figure A: Endoscopic image: a single 3 mm cardia-based polyp



Figure B: H&E, 4X

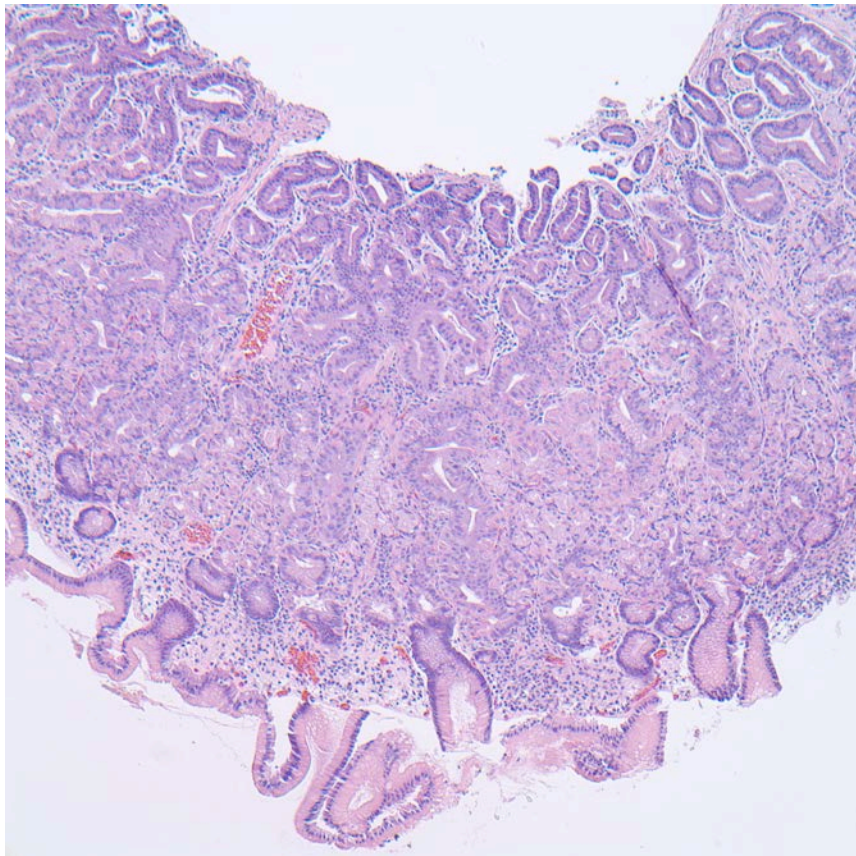
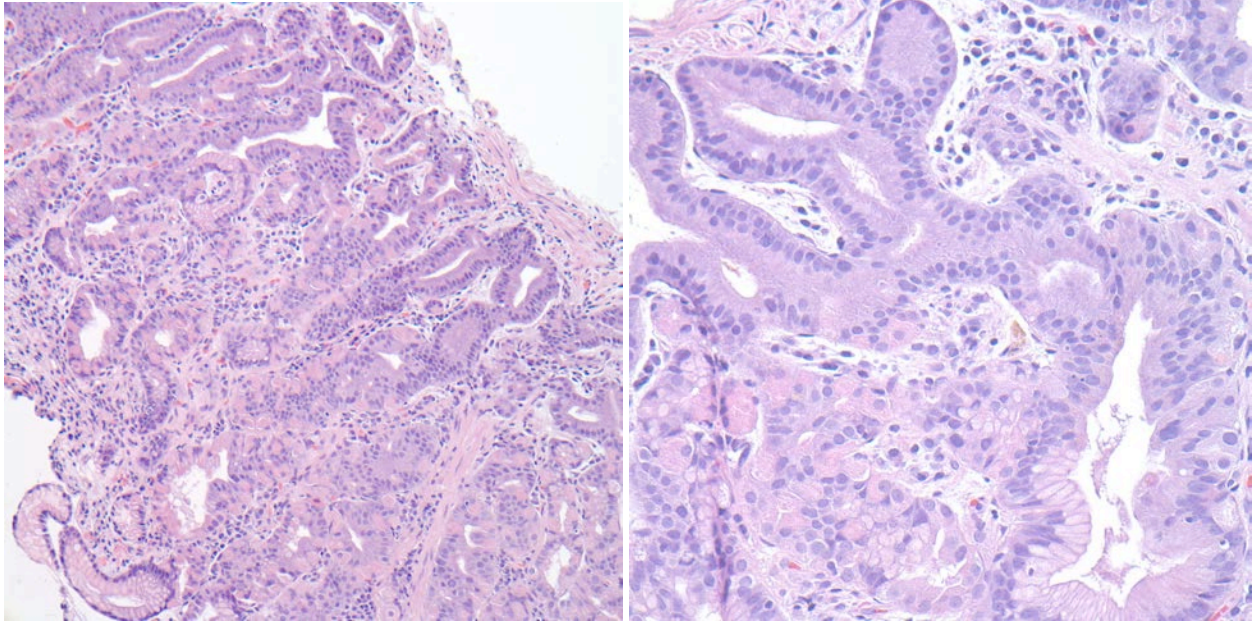


Figure C: H&E, 10X



Figures D: H&E, 20X (left), 40X (right)

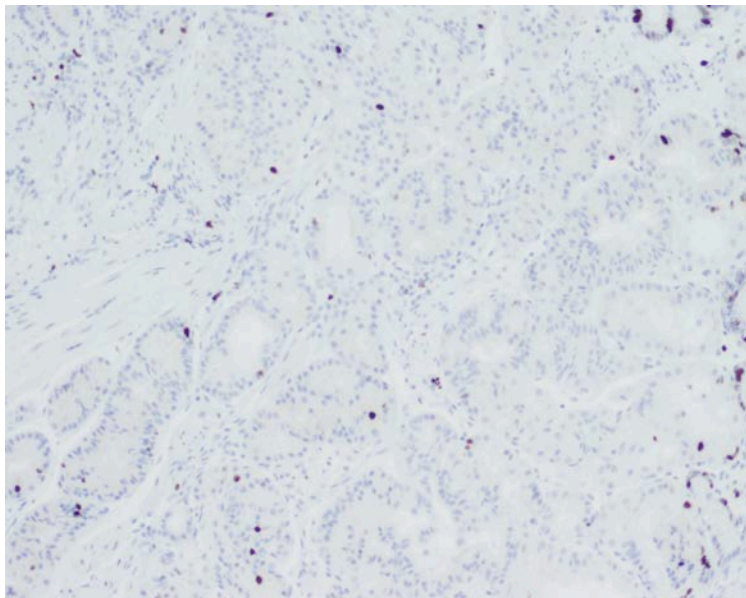


Figure E: Immunohistochemical staining for MIB-1 (20X)

What is your diagnosis?

- A. Fundic gland polyp (FGP)
- B. Oxyntic gland adenoma/polyp
- C. Gastric adenocarcinoma
- D. Pyloric gland adenoma
- E. Well-differentiated neuroendocrine tumor (NET)

Answer: (B) Oxyntic gland adenoma/polyp

Discussion:

Oxyntic gland adenoma is an uncommon polyp arising in the stomach and is characterized by a unique set of clinicopathologic features. Clinically, oxyntic gland adenoma is most often encountered in patients undergoing endoscopy for GERD-related symptoms. The lesion appears as a single polypoid growth, usually in the fundus (70%) or, less often, the cardia (30%) (1). It is considered a benign growth with no risk for recurrence if completely excised according to one study.

Histologically, as pictured in this case (Figures B-D), oxyntic gland adenoma is characterized by a proliferation of oxyntic-type glands in clusters and cords, generally contained in the deeper mucosa. Many cells have basophilic/amphophilic cytoplasm (chief cell component); there are also interspersed eosinophilic cells (parietal cell component) and clear cells (mucus cells). The proliferation has bland cytologic features. There are thin wisps of smooth muscle in between the glands, but no desmoplastic response. In areas, the cells extend superficially in between the overlying foveolar glands. Figures C and D demonstrate higher magnifications of the cellular component with relatively monotonous, medium-sized cells. There is no necrosis or mitotic figures. Immunohistochemistry for Ki-67 shows positive staining in less than 2% of cells (Figure E).

In the majority of cases, chief cells are the predominant cell type, although in a small minority of reported cases the mucus neck cells predominate. Parietal cells are interspersed in small numbers. A potentially worrisome feature can be disruption of normal glandular architecture by the proliferation of oxyntic cells. Yet the cells of oxyntic gland adenoma lack overt cytologic atypia, mitotic activity, necrosis, or desmoplasia. Immunostaining for Ki-67 demonstrates a low proliferation index. Upon review of the literature, the same entity is recognized under several designations including: “chief cell hamartoma” and “chief cell hyperplasia”, in addition to the aforementioned oxyntic gland adenoma/ polyp (1- 3).

Oxyntic gland adenoma was initially described as an unusual variant of fundic gland polyp (FGP) (choice A) (3, 4), associated with oxyntic-lined microcysts at the periphery of the lesion. However, microcyst formation has subsequently not been recognized as a characteristic histologic finding in most oxyntic gland adenomas (1).

The usual FGPs are body/ fundus-based lesions and are the most commonly evaluated type of gastric polyps. In contrast to oxyntic gland adenomas, they are typically multiple and measure less than 1.0 cm. Microscopically, they exhibit a predominant population of cystically dilated glandular spaces lined by attenuated parietal or mucus cells (5, 6).

Due to the disruption of the surrounding normal glandular architecture, oxyntic gland adenomas been categorized by some authors as rare variants of invasive gastric adenocarcinoma (choice C) (2). The so-called “gastric adenocarcinoma of fundic gland type/chief cell predominant type” or “gastric adenocarcinoma with chief cell differentiation” (GA-CCD) was proposed as a new type of invasive cancer by several authors (2). However, the bland cytologic features of the lesion, in combination with their benign clinical course, have prompted the proposal for re-designation of “GA-CCD” as oxyntic gland adenoma (1).

Classic gastric adenocarcinoma would feature more severe cytologic atypia, increased mitotic and/or proliferative activity, and a definite stromal/desmoplastic response. In addition to the histologic features, the clinical features of a true invasive adenocarcinoma would be expected to encompass the potential for recurrence and/or metastasis, features which have not been proven in any case of oxyntic gland adenoma (1).

Well-differentiated neuroendocrine tumor (NET) (choice E), like oxyntic gland adenoma may show a proliferation of monotonous cells arranged in nests and/or cords. In both monotony and tinctorial qualities, a NET may come into the differential diagnoses of an oxyntic gland adenoma/ polyp. However, NET cells contain nuclei with speckled salt and peppery chromatin and occasionally display endocrine granularity of the cytoplasm. Additionally, NETs stain for chromogranin and synaptophysin while oxyntic cells are negative (7).

Pyloric gland adenoma (choice D) is an uncommon lesion that may arise at various sites in the gastrointestinal tract. The stomach, particularly the gastric body, is the most common location. Outside the stomach, they are found at any site prone to pyloric gland metaplasia, such as the gallbladder or duodenum. Clinically, pyloric gland adenoma tends to occur in women and more likely in the setting of autoimmune gastritis (8). On microscopy, pyloric gland adenomas are composed of tightly packed pyloric gland-like cuboidal epithelium showing pale or eosinophilic cytoplasm. The nuclei are round without prominent nucleoli. Microscopic foci of dysplasia or carcinoma are commonly encountered in association with the pyloric gland adenoma (8).

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