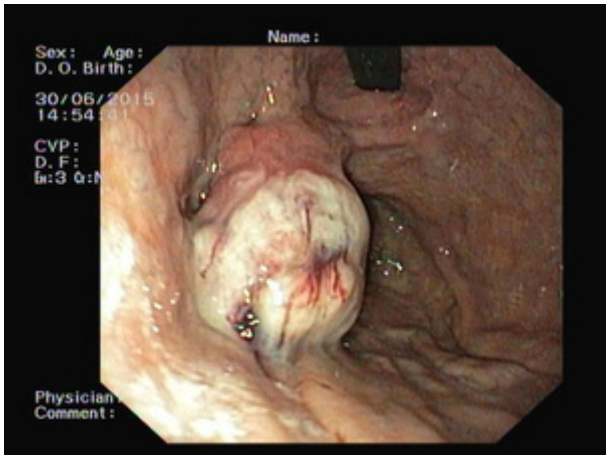
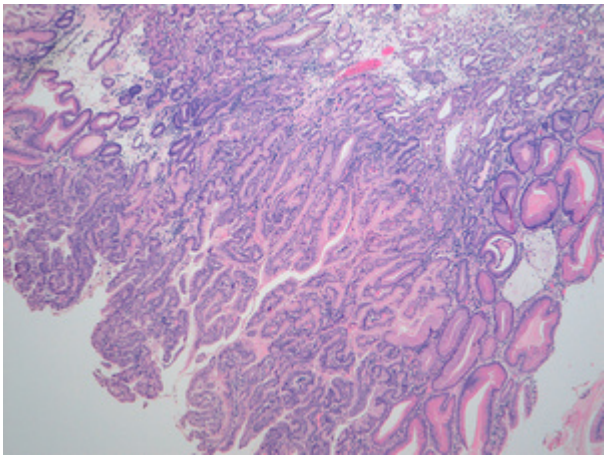
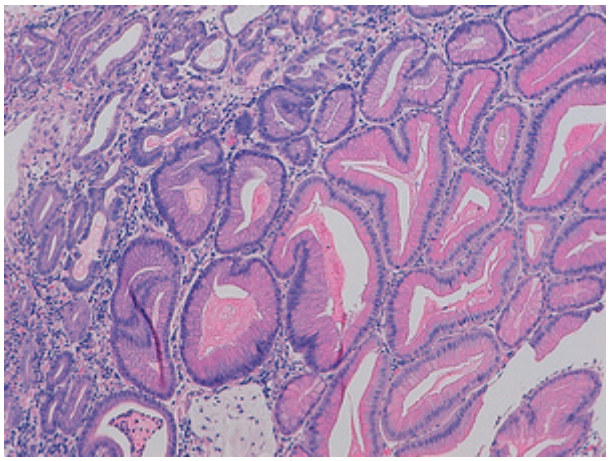
July 2016

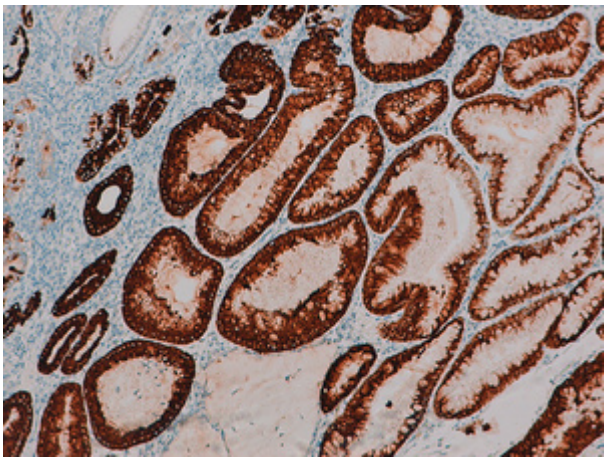
78 years-old Caucasian male who underwent upper-GI endoscopy for iron deficiency anaemia.

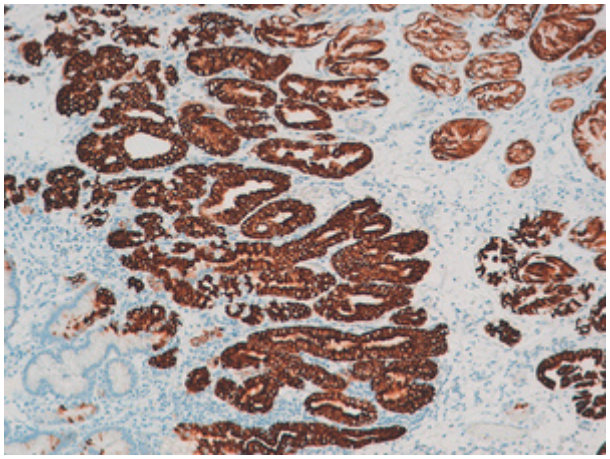
What is your diagnosis?

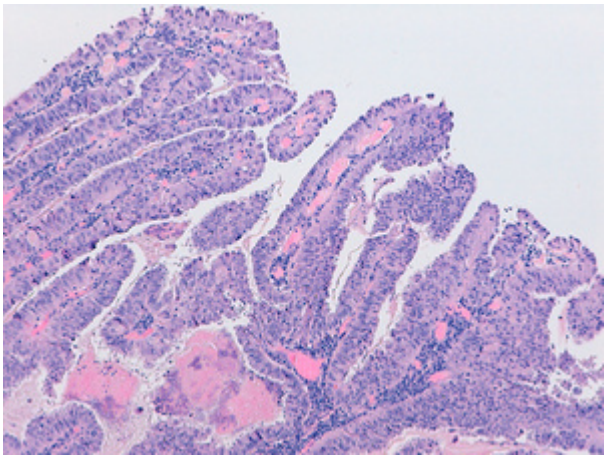


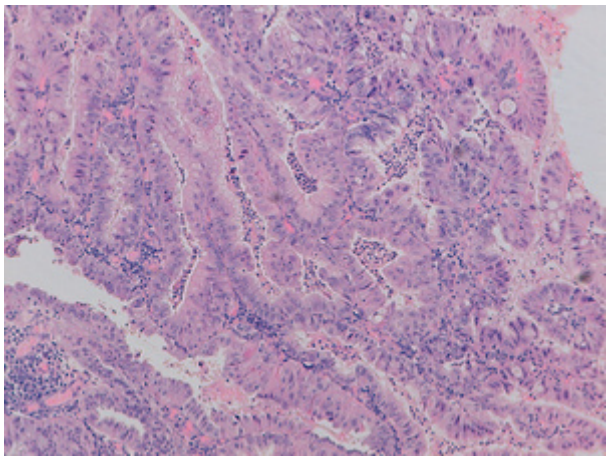
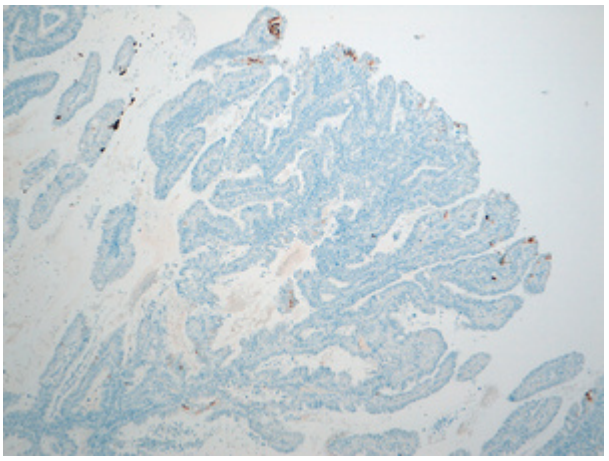
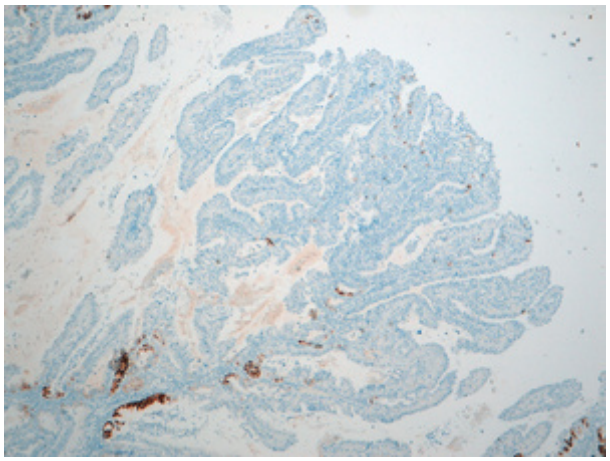










Diagnosis:

Pyloric gland adenoma with high-grade dysplasia (intraepithelial neoplasia).

Comment:

A 78 years-old caucasian male underwent an upper-GI endoscopy for iron deficiency anaemia. During the procedure, at the fundus, a semi-pedunculated polyp was seen, measuring 2.9 cm in largest diameter (A). Histology revealed an adenoma with villous projections and closely packed tubular pyloric-like glands with mucus-secreting cells (B, C) that co-expressed MUC5AC (D) and MUC6 (E). An area of high-grade dysplasia (intraepithelial neoplasia) covering nearly 20% of the polyp (F, G) with loss of mucins' expression (H, I) was identified. No goblet cells or squamous morules were seen.

Pyloric gland adenomas (PGAs) are uncommon lesions that account for 2.7% of all gastric polyps. They have a female predominance (60%), with a median age of 75 years. They are most frequent in the gastric body, but may encounter also at extragastric site, in the context of gastric heterotopia. They are associated with conditions that result in pyloric metaplasia, the prototype of which is autoimmune gastritis.

The endoscopic appearance of PGAs is of a polypoid, dome-shaped or fungating mass, with a median diameter of 1.7cm. Patients with PGA present with a range of signs and symptoms that may be related to the polyp or the underlying disease.

Histologically, PGAs are composed of tightly packed tubular pyloric-like glands lined by cuboidal or columnar mucus-secreting cells with pale to eosinophilic cytoplasm and small round nuclei with inconspicuous nucleoli; they lack well-formed apical mucin caps, which helps to differentiate them from foveolar-type adenomas (FAs). PGAs co-express MUC5AC and MUC6, while FAs only express MUC5AC. They rarely have intestinal areas; squamous morules may be observed. The extent of dysplasia increases with the lesions' size and cytological features are similar to those observed in classical adenomas. So PGAs should be recognized as having a high risk for progression to invasive adenocarcinoma (12-30%).

Gastric PGAs have less frequent nuclear expression of p53 (22%) when compared with intestinal-type adenomas (86%), and the expression of p53 may correlate with higher risk. Molecular analyses have identified mutations in KRAS, GNAS and less commonly in beta-catenin gene (CTNNB1) and SMAD4. Additionally, gastric PGAs have infrequent loss of mismatch repair (MMR) proteins, similar to intestinal-type adenomas, but in contrast to foveolar-type adenomas; however, in Lynch syndrome context, PGA may represent a precursor lesion of the MMR deficient pathway of carcinogenesis. A possible association between PGAs and familiar adenomatous polyposis (FAP) has been described.

Considering the significant risk of progression to invasive carcinoma, PGAs should be completely removed.

For further reading:

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- Chlumská A, Waloscheck T, Mukenšnable P, et al. Pyloric Gland Adenoma: a histologic, immunohistochemical and molecular genetic study of 23 cases. Cesk Patol 51(3): 137-140, 2015.
- Lee SE, Kang SY, Cho J, et al. Pyloric Gland Adenoma in Lynch Syndrome. Am J Surg Pathol 38: 784-792, 2014.
- Wood LD, Salaria SN, Cruise MW, et al. Upper GI Tract Lesions in Familiar Adenomatous Polyposis (FAP): Enrichment of Pyloric Gland Adenomas and other Gastric and Duodenal Neoplasms. Am J Surg Pathol 38: 389-393, 2014.

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