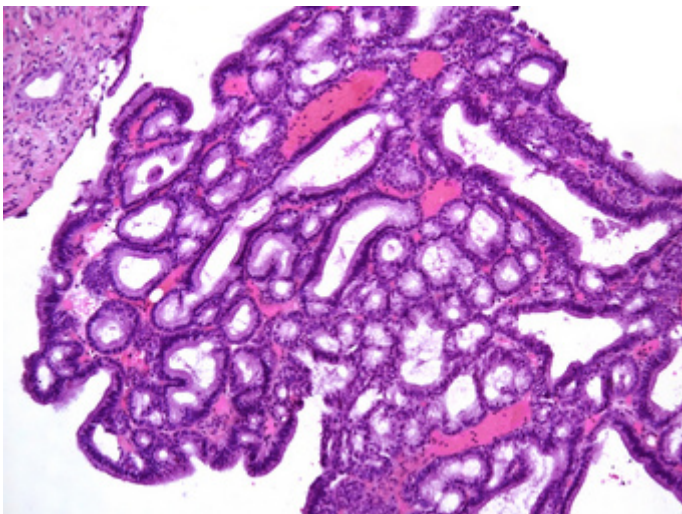
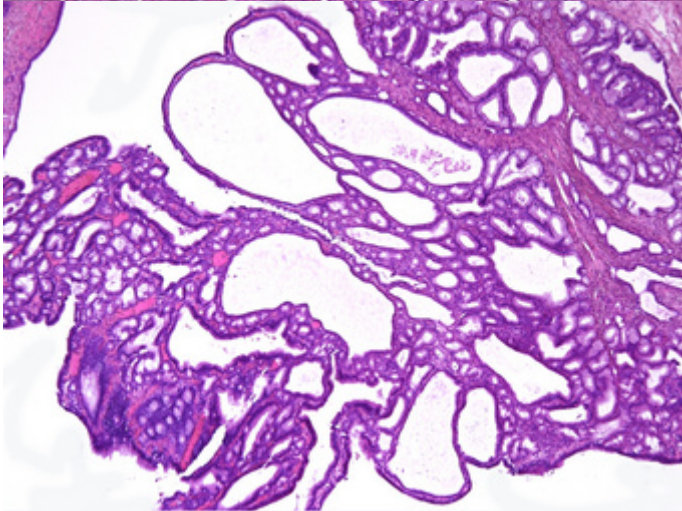
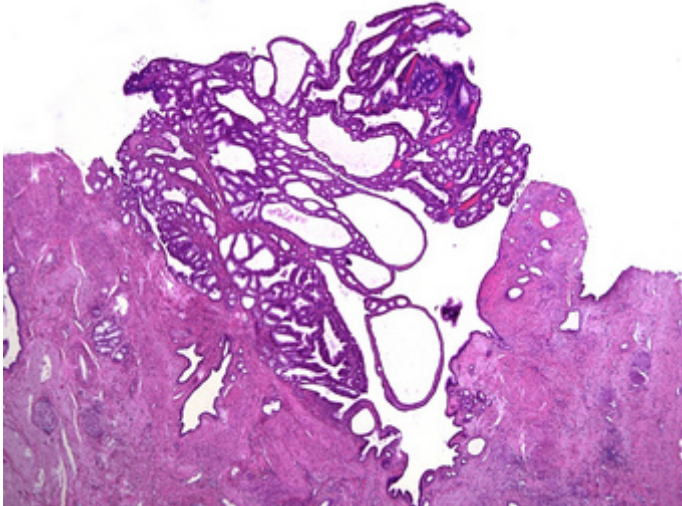
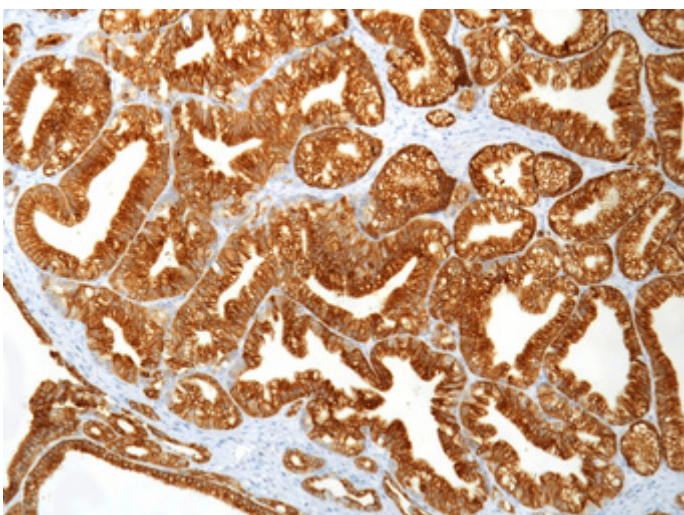
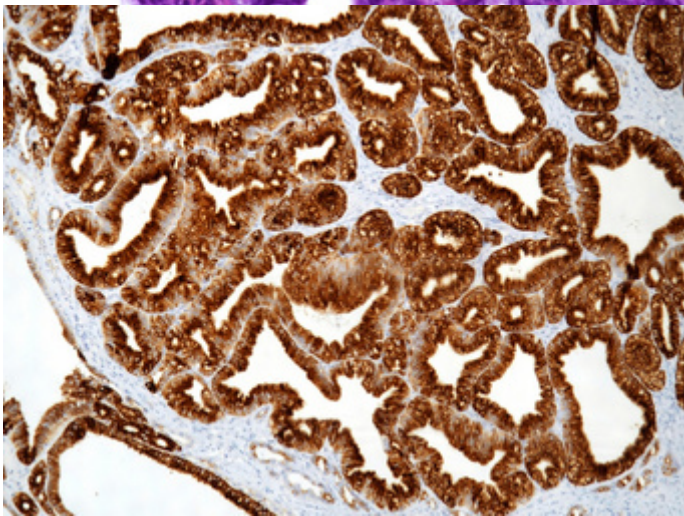
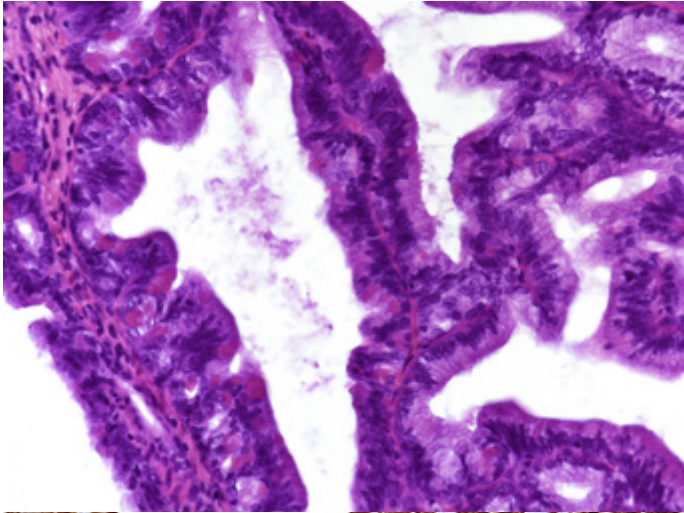
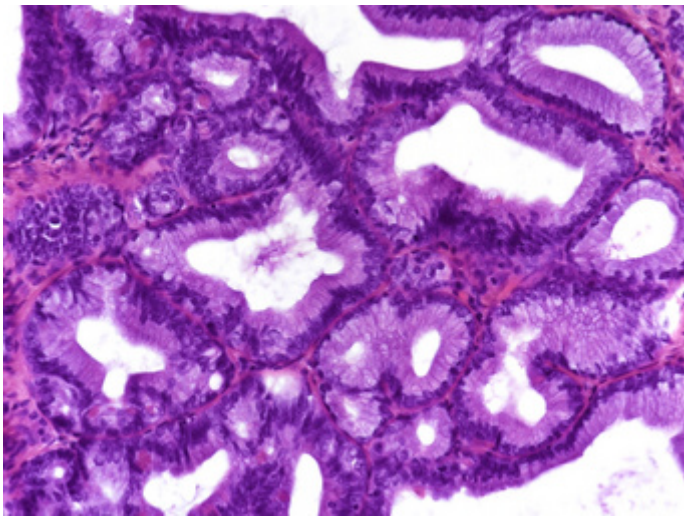


# December 2018

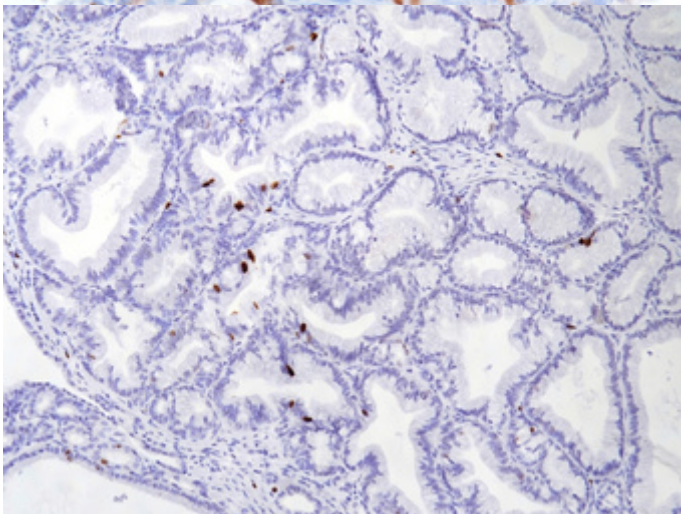
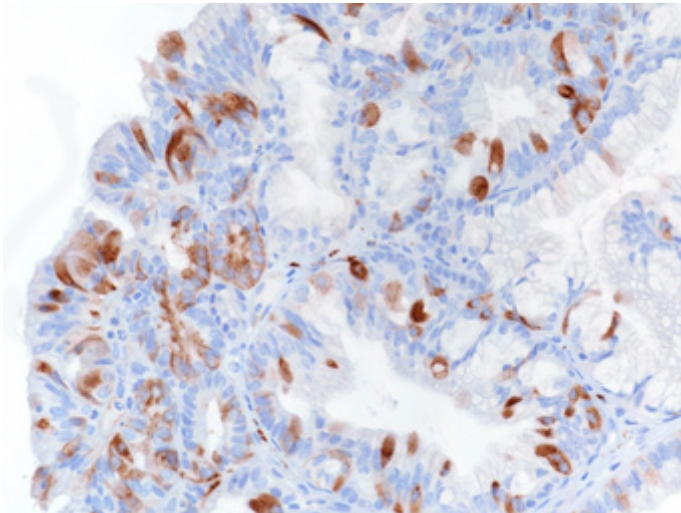
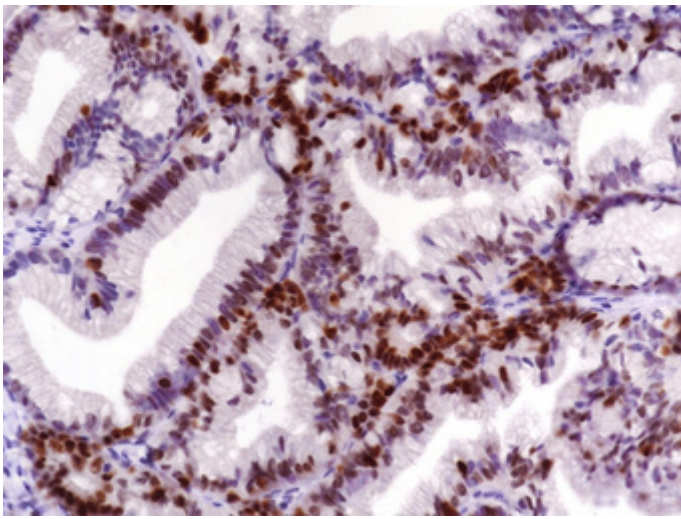
Cholecystectomy specimen obtained from a 66-year-old female with the incidental finding of a small mucosal polyp.

What is your diagnosis?









### Diagnosis:

Intracholecystic papillary-tubular neoplasms (ICPN) of the gallbladder, syn. pyloric gland adenoma (low grade dysplasia).

### Comment:

On low power, histology shows an exophytic, predominantly tubular lesion composed of closely packed glands in lamina propria, some of which are cystically dilated (Panels A-B). Most tubules are lined by tall columnar cells with abundant apical foamy mucin and basally located nuclei with mild atypia, bearing resemblance of pyloric phenotype (Panels C-D); some of the glands contain more hyperchromatic, elongated, pseudostratified

nuclei, with an undulating contour of the glandular lumen. These cells are admixed with numerous neuroendocrine cells with brightly eosinophilic cytoplasm (Panel E). Mitoses are exceptionally rare, features of high grade dysplasia or malignancy are not seen.

The neoplastic cells show diffuse cytoplasmic immunoreactivity for MUC6 (Panel F), but also for MUC1 (Panel G). Additionally, there is focal, strong nuclear expression of CDX-2 in the area with pseudost stratified nuclei (Panel H). MUC2 and MUC5AC are completely negative. The neuroendocrine cells show strong synaptophysin positivity (Panel I). The Ki-67 (MIB-1) stain reveals minimal proliferative activity (Panel J).

The classification and nomenclature of mass forming preinvasive neoplasms of the gallbladder is confusing, a lot of terminology exists in the literature. The 2010 WHO Classification described two separate categories for these precursors: adenomas and intracystic papillary neoplasms (with low-, intermediate- and high-grade dysplasia / intraepithelial neoplasia). However there is a significant overlap between these two groups and interobserver agreement placing tumors in these categories is poor even among experts. Therefore Adsay et al. suggested a broad category of intracholecystic papillary-tubular neoplasms (ICPN) to include all tumoral intraepithelial neoplasms (including adenomas, such as pyloric gland adenoma, and intracystic papillary neoplasms) arising in the gallbladder, parallel to the approach taken recently in the pancreas and biliary tract.

This new unifying concept takes into consideration the peculiar immunoprofile of the presented case. In contrast to pyloric gland adenomas of the stomach, which are invariably positive for MUC6 (and MUC5AC), but lack expression of MUC1 and CDX-2, the same type of tumour occurring in the gallbladder may show a mixed immunophenotype with pyloric gland (MUC6), pancreatobiliary (MUC1) and intestinal (CDX-2) expression.

It is of note that the presented lesion is smaller than 10 mm in maximum diameter. Some authors adopted the 10-mm criterion for these tumors to maintain the parallelism with the pancreatobiliary tract (i.e. intraductal papillary mucinous neoplasm, IPMN of the pancreas), and to distinguish these lesions from so-called polypoid pyloric metaplasias. Although the presented lesion does not fulfill this size criterion, we believe it to be neoplastic, that is, a true adenoma.

### For further reading:

- › Adsay V, Jang KT, Roa JC, et al. Intracholecystic papillary-tubular neoplasms (ICPN) of the gallbladder (neoplastic polyps, adenomas, and papillary neoplasms that are  $\geq 1.0$  cm): clinicopathologic and immunohistochemical analysis of 123 cases. *Am J Surg Pathol.* 2012 Sep;36(9):1279-301.
- › Balci S, Akkas G, Roa JC & Adsay NV. Intracholecystic Papillary Tubular Neoplasm of the Gallbladder With Microinvasive Carcinoma. *Pathol Case Rev.* 2014;19: 283–288.
- › Dekate J, Serra S & Chetty R. Intracholecystic papillary-tubular neoplasm. *Diagn Histopathol.* 2015, 21(4), 169–172.
- › He C, Fukumura Y, Toriyama A, et al. Pyloric Gland Adenoma (PGA) of the Gallbladder: A Unique and Distinct Tumor from PGAs of the Stomach, Duodenum, and Pancreas. *Am J Surg Pathol.* 2018 Sep;42(9):1237-1245.
- › Vieth M & Montgomery EA. Some observations on pyloric gland adenoma: an uncommon and long ignored entity!*J Clin Pathol.* 2014 Oct;67(10):883-90.

### Presented by:

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