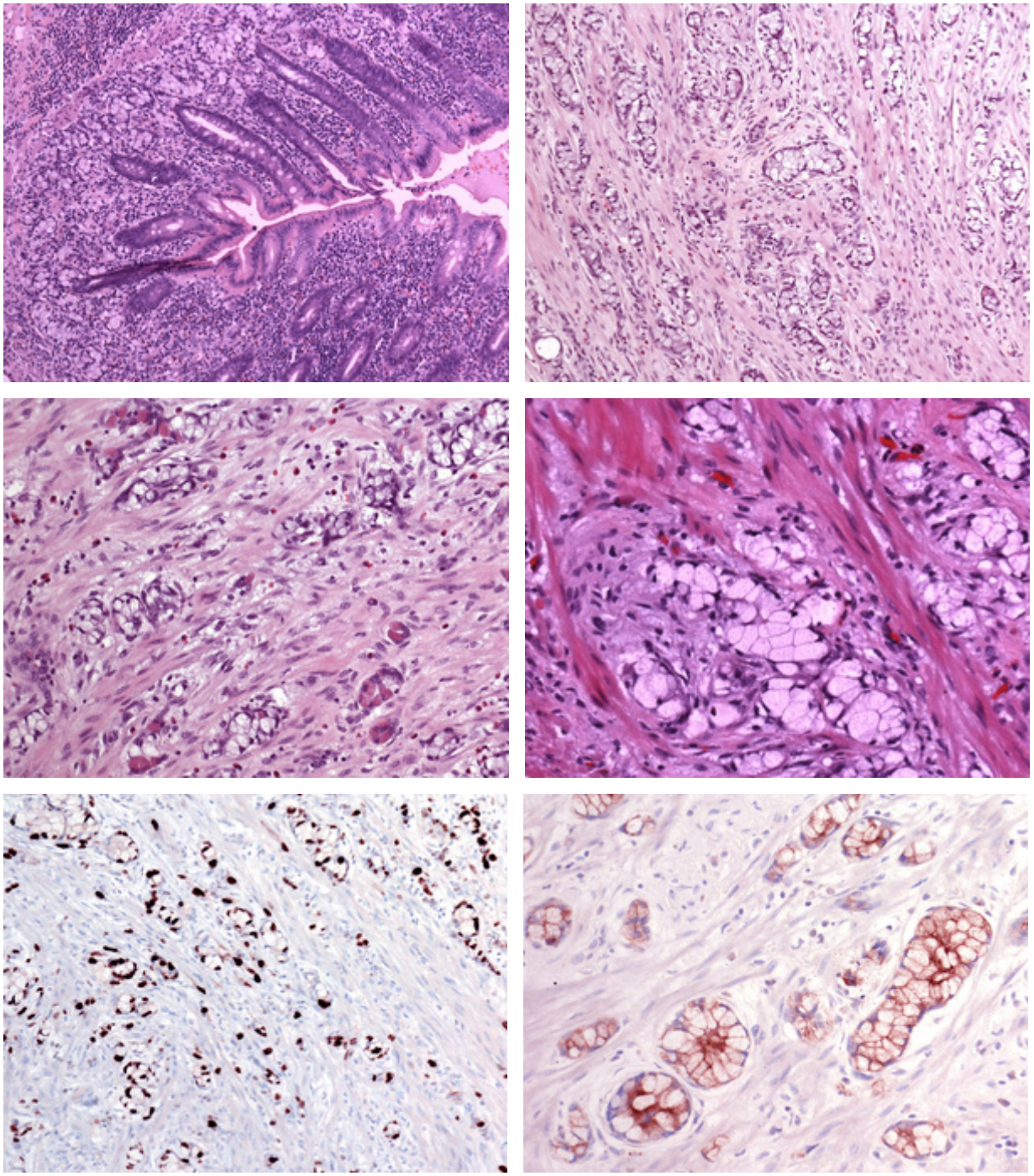
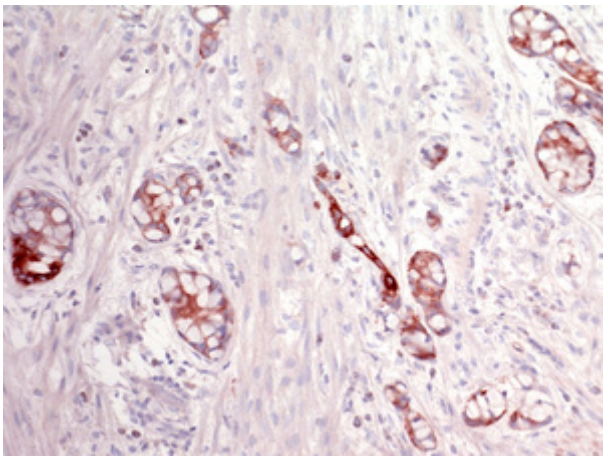
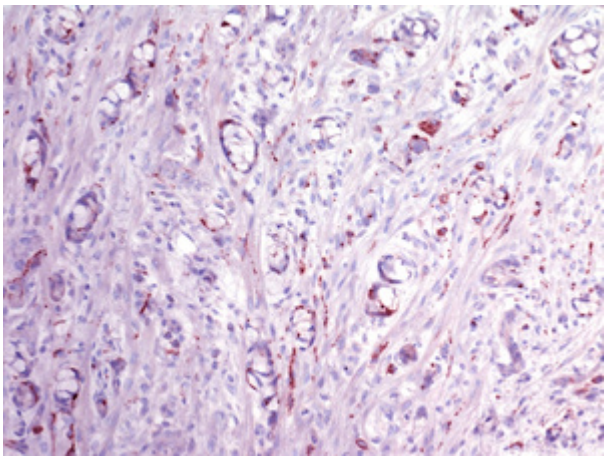
August 2015

32-year-old male with clinical diagnosis of acute appendicitis.

What is your diagnosis?



Diagnosis:

Goblet cell carcinoid of the appendix.

Comment:

A 32 year old male presented with clinical symptoms of acute appendicitis and underwent appendectomy. Macroscopic examination showed a 6.5 x 0.9 cm appendix with fibrinous exudate on the serosal surface and gross perforation. Upon histology, a tumour was identified characterized by predominantly submucosal growth with areas of connection with the base of the crypts of mucosal glands (panel A). The lesion was composed of small nests of signet-ring like cells resembling normal intestinal goblet cells (panel B). Small clusters of Paneth cells were also observed (panel C). The neoplasia invaded into subserosa and mesoappendix and showed prominent perineural invasion (panel D). The neoplastic cells lacked atypia and displayed low mitotic activity on H&E, however Ki67 proliferation index was high (40%) (panel E). Isolated signet-ring cells or extracellular mucin pools were not identified. Immunohistochemistry revealed expression of CEA and CK19 (panel F and G), and focal positivity for synaptophysin (panel H).

Goblet cell carcinoids (GCC) are rare neoplasms of the appendix with distinct pathologic features and outcome. WHO and AJCC classify these lesions according to the criteria of adenocarcinoma because their behaviour appears closer to these than to appendiceal carcinoids. According to ENETS 2012 consensus guidelines, GCC should be considered a rare subtype of mixed adeno-neuroendocrine carcinomas (MANEC), which account for a clinically and therapeutically differing entity from neuroendocrine neoplasms. Clinical presentation is unspecific and most frequently includes symptoms of acute appendicitis, which is usually also present and confirmed on histology.

Several authors have separated GCCs into different histologic subgroups with distinct prognostic properties. Tang et al. described 3 groups with a progressively worse prognosis: typical GCC (group A), adenocarcinoma ex GCC, signet-ring cell type (group B) and adenocarcinoma ex GCC, poorly differentiated adenocarcinoma type (group C). More recently, Taggert et al. separated the lesions into GCC tumour with no adenocarcinoma component (group 1), GCC tumour with less than 50% adenocarcinoma component (group 2) and GCC tumour with more than 50% adenocarcinoma component (group 3). This study supports the notion that the amount of carcinomatous component correlates with the clinical features and disease stage and that it is a major predictor of survival. These authors also described a worse prognosis associated with signet-ring cell adenocarcinoma component compared to other poorly differentiated adenocarcinomas, in contrast with the first study. Poor prognostic features that have been reported include lymph node metastasis, incomplete excision at the base of the appendix, extra-appendiceal spread, increased mitosis (>2/HPF) or increased Ki67 index (>3%) and a large component of adenocarcinoma (>50%).

No genetic association has been reported thus far and therefore there is currently no evidence for any genetic testing.

Right hemicolectomy is recommended after initial appendectomy for the majority of GCC cases since metastatic risk is high and prognosis poor if metastasis occurs. Cytoreductive surgery with adjuvant intraperitoneal chemotherapy may offer prolonged survival in cases with advanced peritoneal dissemination.

For further reading:

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- Tang LH, Shia J, Soslow RA, Dhall D, Wong WD, O'Reilly E, Qin J, Paty P, Weiser MR, Guillem J, Temple L, Sobin LH, Klimstra DS. Pathologic classification and clinical behavior of the spectrum of goblet cell carcinoid tumors of the appendix. Am J Surg Pathol. 2008; 32: 1429-43.
- Taggart MW, Abraham SC, Overman MJ, Mansfield PF, Rashid A. Goblet cell carcinoid tumor, mixed goblet cell carcinoid-adenocarcinoma, and adenocarcinoma of the appendix: comparison of clinicopathologic features and prognosis. Arch Pathol Lab Med. 2015; 139: 782-90.
- Rossi RE, Luong TV, Caplin ME, Thirlwell C, Meyer T, Garcia-Hernandez J, Baneke A, Conte D, Toumpanakis C. Goblet cell appendiceal tumors - management dilemmas and long-term outcomes. Surg Oncol. 2015; 24: 47-53.

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