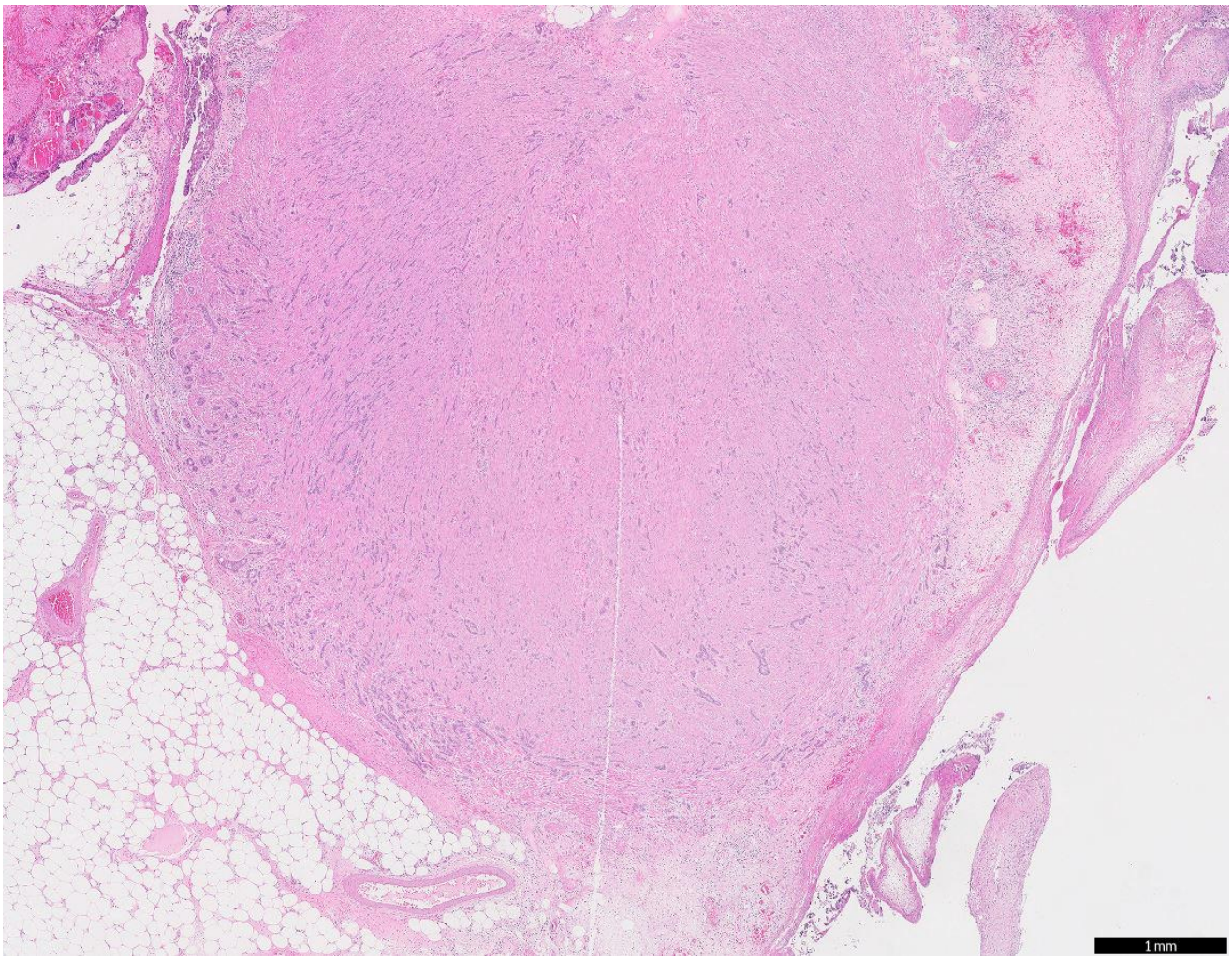
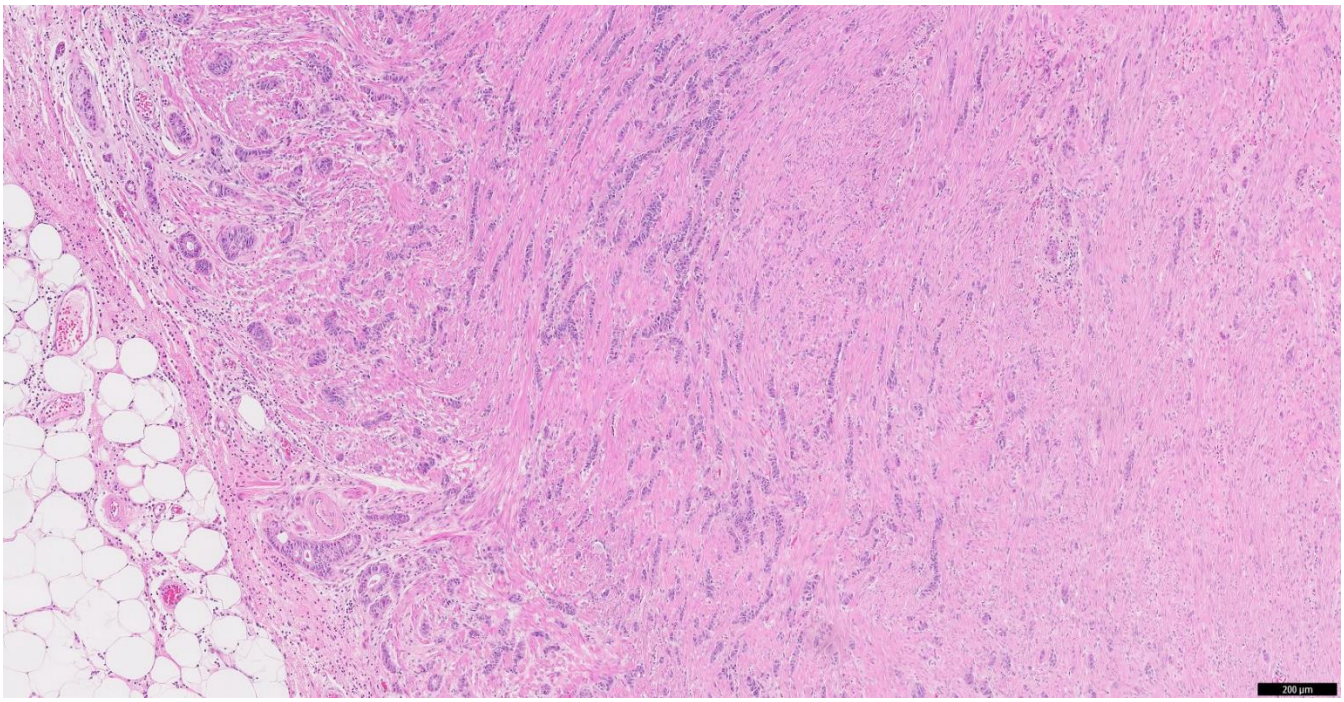
**Clinical History**

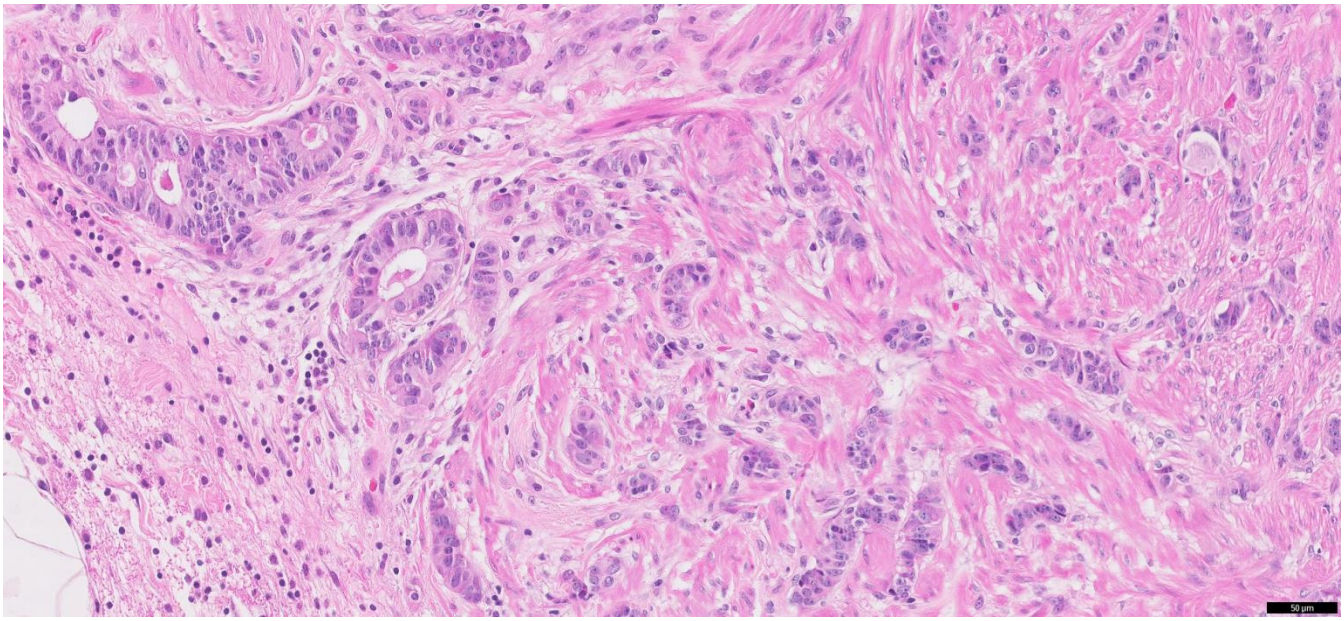
A 42-year-old male presented to the emergency department with complaints of abdominal pain. Whole body computerized-tomography showed an uncomplicated appendicitis with no evidence of rupture or abscess. The patient underwent laparoscopic appendectomy; intraoperatively a perforated appendix was noted. On microscopic examination, acute appendicitis was present, but in addition, a 0.9 cm lesion was seen in the appendiceal tip.



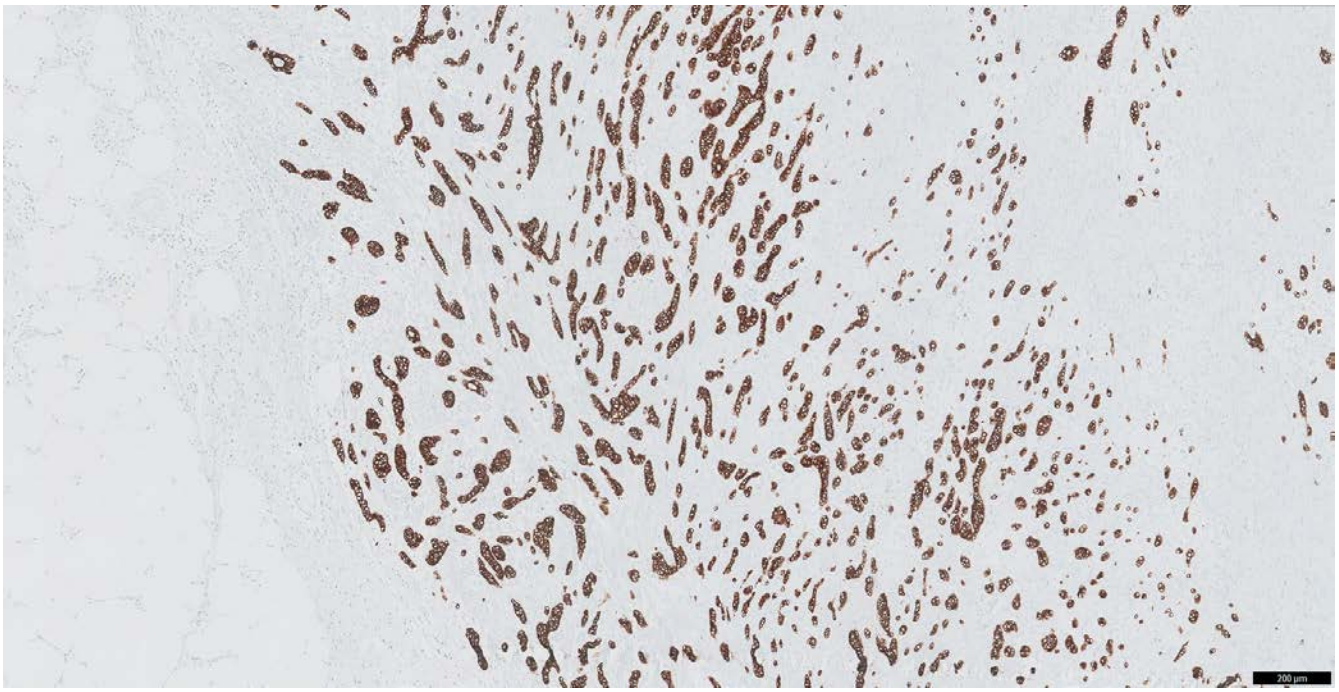

**Tip of the appendix, H&E stain.**



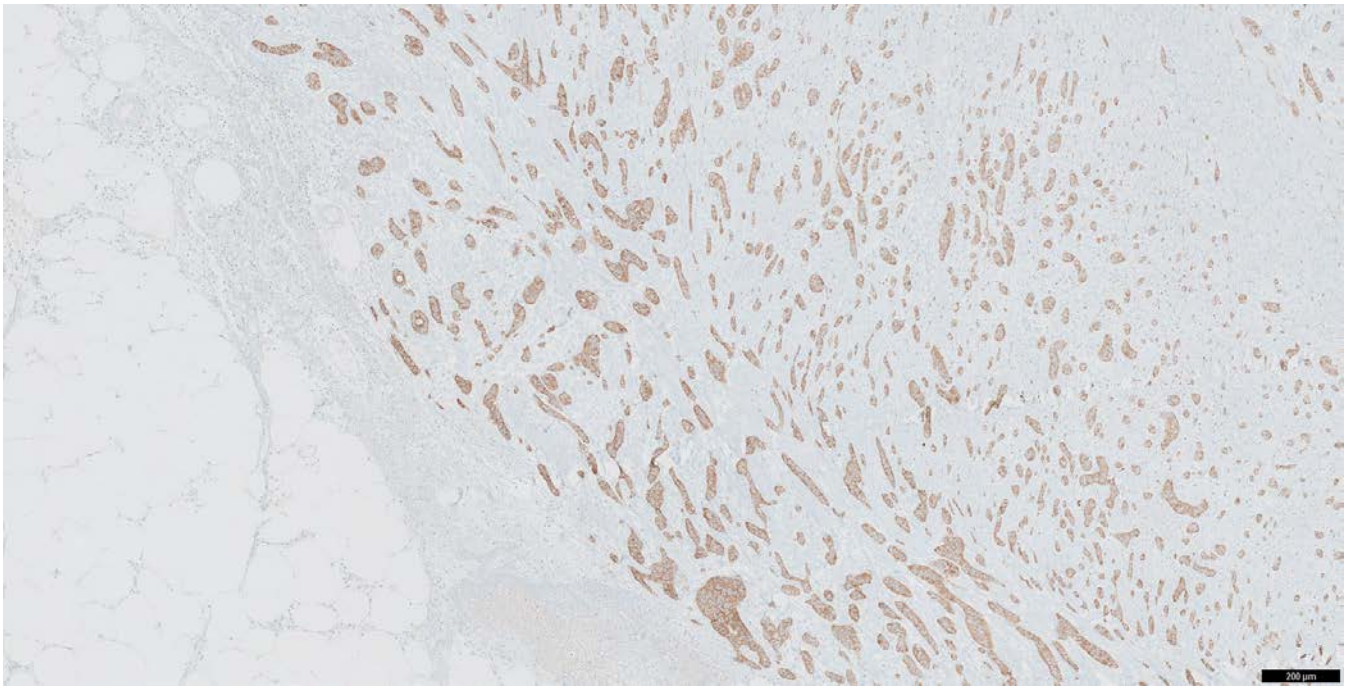

**Tip of the appendix, H&E stain.**



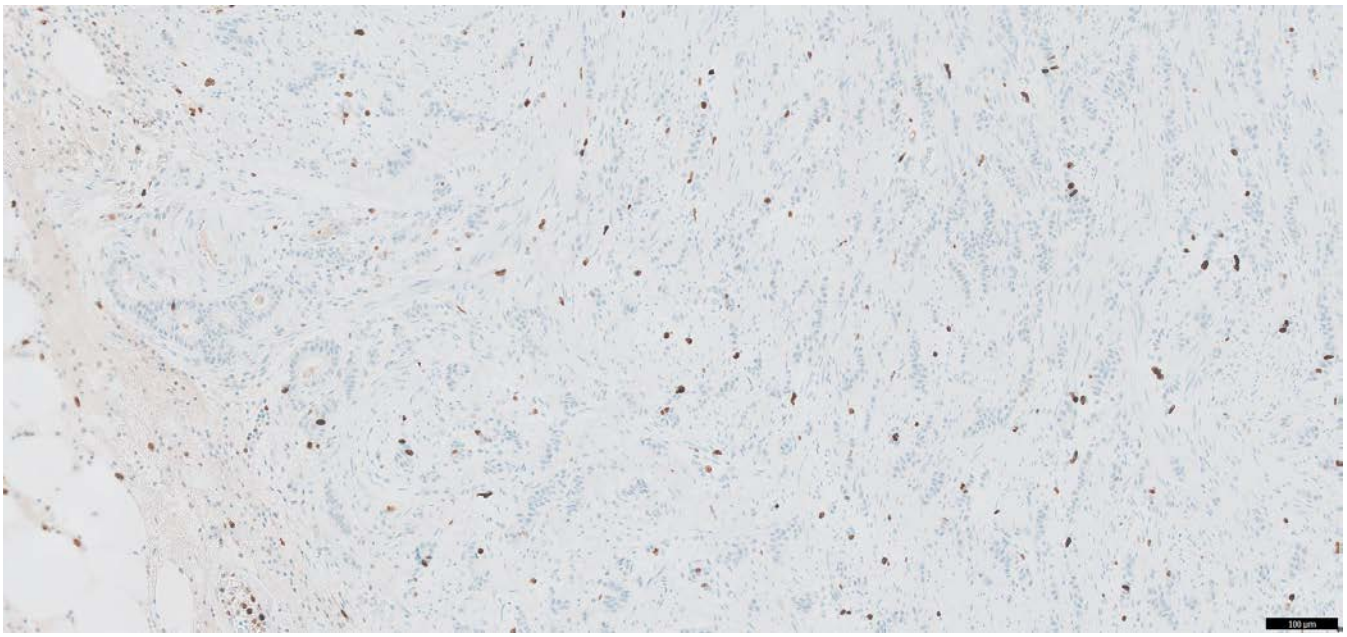

**Tip of the appendix, H&E stain.**




**CAM5.2**




**Synaptophysin**



**Ki-67**

**What is the diagnosis of the additional lesion?**

A. Metastatic adenocarcinoma with neuroendocrine features
B. Mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN)of the appendix
C. Tubular carcinoid
D. Goblet cell carcinoid

**Correct answer:**

C. Tubular carcinoid

**Discussion**

Appendiceal neuroendocrine neoplasms are exceedingly rare with an incidence of 0.3 to 0.9% in appendectomy specimens, and are usually diagnosed incidentally (1, 2). Most of them are well-differentiated tumors and are considered cured with appendectomy alone, if less than 2 cm in diameter; in cases larger than 2 cm, a right hemicolectomy is recommended (2–4).

Tubular carcinoid is a special variant of well differentiated neuroendocrine tumor that has been described exclusively in the appendix. It is commonly seen in young adults and is diagnosed incidentally. Tubular carcinoids have not been reported to metastasize and local excision is curative (4–6). Microscopically they are characterized by the presence of discrete separate tubules lined by cuboidal to columnar cells with round to oval bland nuclei with indistinct nucleoli, variable amount of cytoplasm and absent mitotic activity (4–7). Mucin is typically seen in the lumen of the tubules. A classic carcinoid component consisting of small nests and trabeculae is often admixed (5).Tubular carcinoids are reactive with antibodies to cytokeratin CAM5, CEA, glucagon (not all antibody clones), to neuroendocrine markers, such as synaptophysin and CD56. Anti-chromogranin A immunoreactivity is variable.

A. Metastatic adenocarcinoma can mimic tubular carcinoid due to its infiltrative appearance and luminal mucin production. The predominantly mucosal/submucosal localization, diffuse expression of neuroendocrine markers, presence of a classic carcinoid component and absence of mitotic activity help to rule out adenocarcinoma. Expression of cytokeratin-7 and -20 is varied in tubular carcinoid and was not found to be helpful in the differential diagnosis (5).

B. Mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN) has two distinct morphologic components of any histologic type and grade, one of which is a neuroendocrine component. The lesser components should comprise at least 30% of the tumor. In the GI tract, MiNEN usually consist of a high-grade neuroendocrine carcinoma and adenocarcinoma components, classified in WHO 2010 edition as mixed adenoneuroendocrine carcinoma (MANEC) (8, 9).

D. Goblet cell carcinoids have a characteristic morphology of small rounded or oval cohesive clusters or simple small tubular formations containing goblet or signet ring-like cells. These tumors show dual mucinous and neuroendocrine differentiation (4).

**References**


1. Kim JY, Hong SM. Recent updates on neuroendocrine tumors from the gastrointestinal and pancreatobiliary tracts. Arch Pathol Lab Med. 2016;140(5):437–48.
2. Shapiro R, Eldar S, Sadot E, Papa MZ, Zippel DB. Appendiceal carcinoid at a large tertiary center: Pathologic findings and long-term follow-up evaluation. Am J Surg [Internet]. 2011;201(6):805–8. Available from: http://dx.doi.org/10.1016/j.amjsurg.2010.04.016
3. Deschamps L, Couvelard A. Endocrine Tumors of the Appendix. Arch Pathol Lab Med. 2010;134:871–5.
4. Carr NJ, Sobin LH. Neuroendocrine tumors of the appendix. Semin Diagn Pathol. 2004;21(2):108–19.
5. Matsukuma KE, Montgomery EA. Tubular carcinoids of the appendix: The CK7/CK20 immunophenotype can be a diagnostic pitfall. J Clin Pathol. 2012;65(7):666–8.
6. Goddard MJ, Lonsdale RN. The histogenesis of appendiceal carcinoid tumours. Histopathology. 1992;20(4):345–9.
7. Burke AP, Sobin LH, Federspiel BH, Shekitka KM, Helwig EB. Goblet cell carcinoids and related tumors of the vermiform appendix. Am J Clin Pathol. 1990;94(1):27–35.
8. la Rosa S, Marando A, Sessa F, Capella C. Mixed adenoneuroendocrine carcinomas (MANECs) of the gastrointestinal tract: An update. Cancers (Basel). 2012;4(1):11–30.
9. La Rosa S, Sessa F, Uccella S. Mixed Neuroendocrine-Nonneuroendocrine Neoplasms (MiNENs): Unifying the Concept of a Heterogeneous Group of Neoplasms. Endocr Pathol 2016;27(4):284–311.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