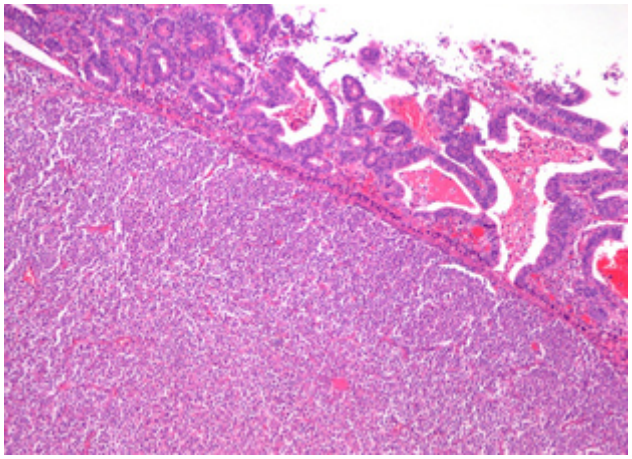
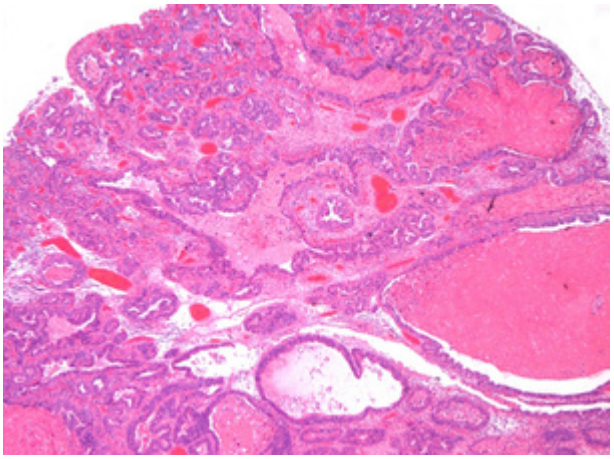
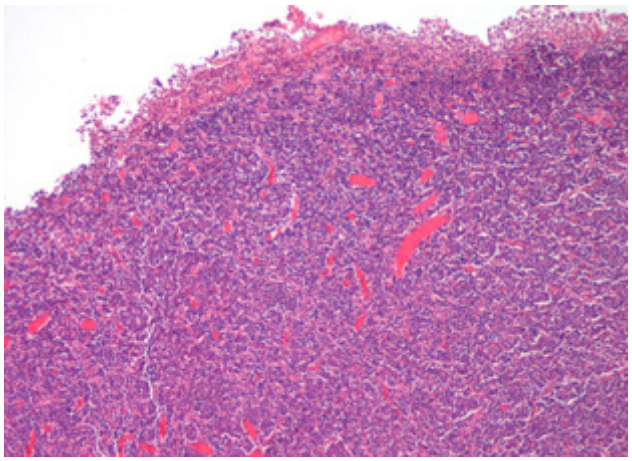
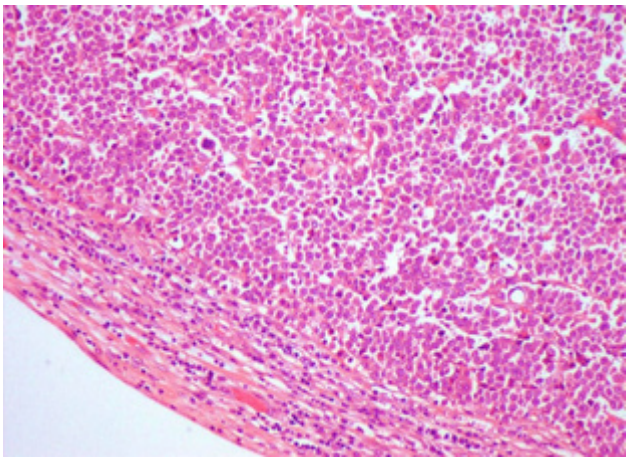
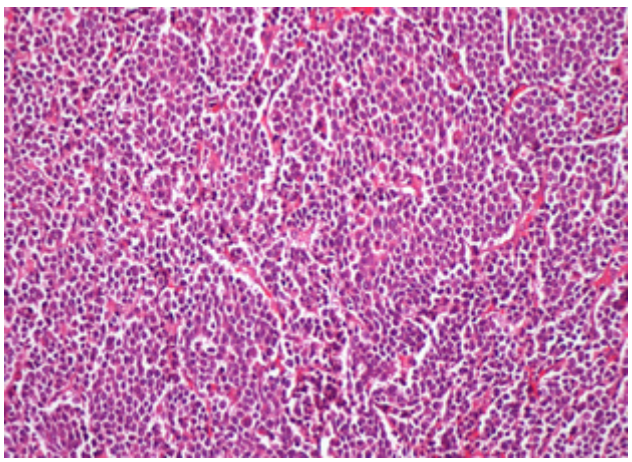
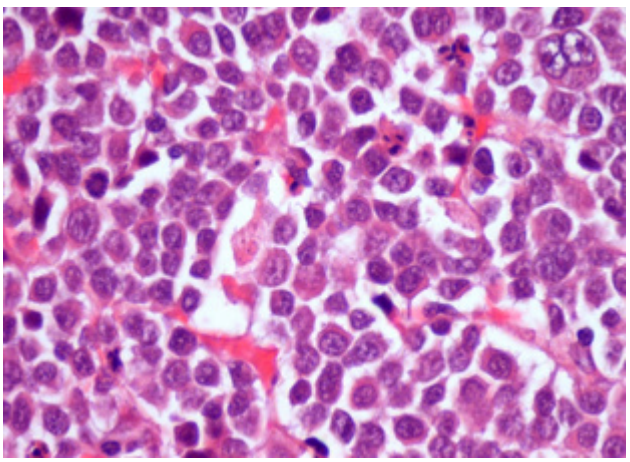
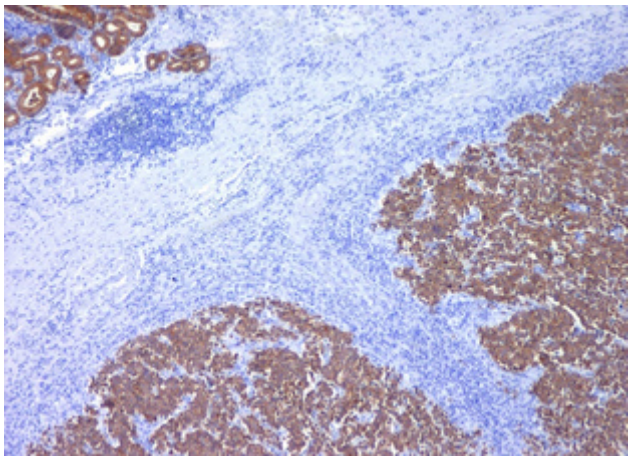
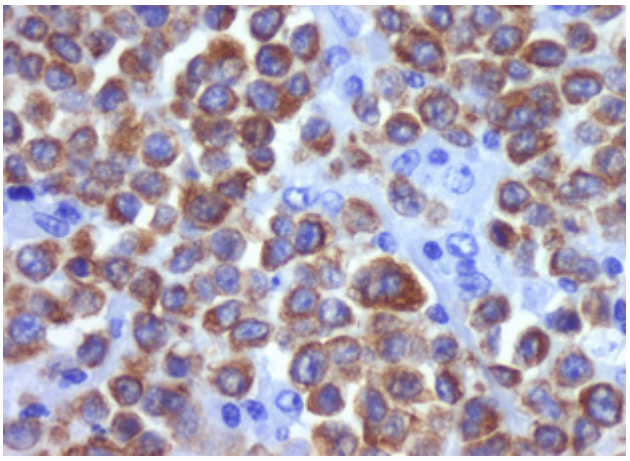
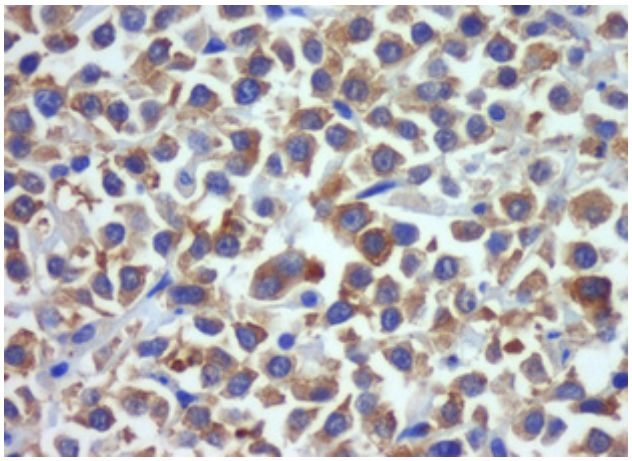
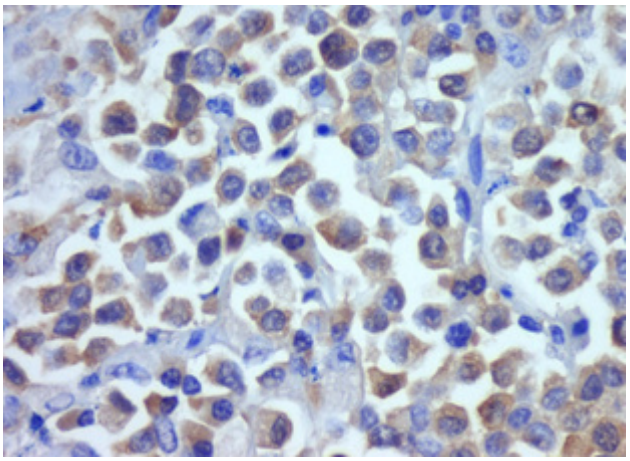
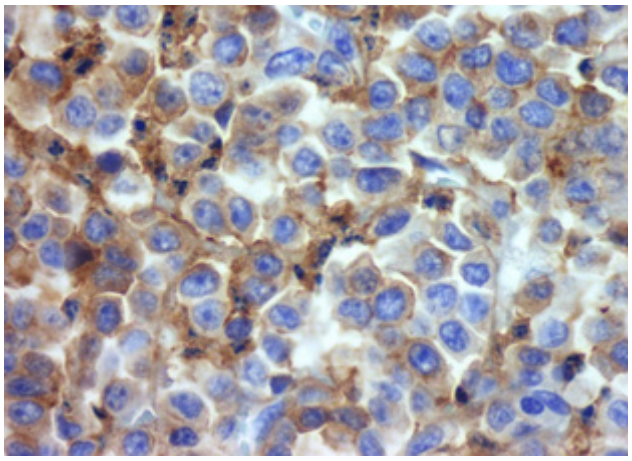
December 2015

Ulcerated lesion in the gastric antrum of a 63-year-old female.

What is your diagnosis?

Diagnosis:

Mixed adenoneuroendocrine carcinoma (MANEC).

Comment:

A 63-year-old female with no relevant medical history, presented with a 5-month history of anorexia and anemia. Endoscopy showed a nodular and ulcerated neoplasia in the gastric antrum involving the pylorus. The biopsy revealed poorly differentiated neoplasia and the patient underwent distal gastrectomy.

Histology showed a two-component neoplasia (Panel A). Superficially, the lesion was consistent with a moderately differentiated adenocarcinoma (Panel B). The second component was composed of epithelioid and polygonal cells, disposed in sheets and nests, extending through the muscularis propria and adipose tissue, but not involving the serosal surface (Panel C-D). The neoplastic cells had round to oval nuclei, occasional prominent nucleoli and well delimited eosinophilic cytoplasm, with a mitotic count of 74 per 10 HPF (Panels E and F). Upon immunohistochemistry, these neoplastic cells were positive for CAM 5.2 (Panels G and H) and neuroendocrine markers, such as synaptophysin (Panel I), NSE (Panel J) and CD56/NCAM (Panel K). The

glandular component was negative for neuroendocrine markers. Lymphoid markers, S100, HMB-45, CD117 and DOG1 were negative in both components. A diagnostic of mixed adenoneuroendocrine carcinoma (MANEC) was rendered.

MANECs are relatively rare in the stomach with less than 40 cases reported in literature. According to the WHO definition, they are morphologically recognizable as both gland-forming and neuroendocrine neoplasms with an arbitrary requirement of at least 30% of either component. They are defined as carcinomas because both components are histologically malignant. The neuroendocrine component may be that of a small or large cell neuroendocrine carcinoma (NEC). It is of note that a minor component of cells with neuroendocrine differentiation (less than 30%) occurs rather frequently in gastric adenocarcinomas. However, this does not qualify for a diagnosis of MANEC and should not alter the diagnosis of adenocarcinoma.

The available data on the genetics of MANECs is scant. There appears to be a higher frequency of chromosomal abnormalities in the NEC vs. the adenocarcinoma component. However, shared LOHs at chromosomes 5q, 11q, 17p and 18q suggest a close histogenetical relationship of both tumor components and a possible multistep progression from a common precursor lesion.

MANECs seem to have a poor prognosis, and platinum-based chemotherapy should be the first-line treatment in advanced disease. Gastrectomy should be considered for early-stage lesions or cases with gastric outlet obstruction.

For further reading:

- Kim KM, Kim MJ, Cho BK, et al. Genetic evidence for the multi-step progression of mixed glandular-neuroendocrine gastric carcinomas. Virchows Arch 440: 85-93, 2002.
- La Rosa S, Marando A, Sessa F, Capella C. Mixed Adenoneuroendocrine Carcinomas (MANECs) of the Gastrointestinal Tract: An Update. Cancers (Basel) 4: 11-30, 2012.
- Kwok CM. Mixed Adenoneuroendocrine Carcinoma of the Stomach. Case Rep Gastroenterol 9: 241-5, 2015.
- Gurzu S, Kadar Z, Bara T, et al. Mixed adenoneuroendocrine carcinoma of gastrointestinal tract: report of two cases. World J Gastroenterol 21: 1329-33, 2015.

Presented by:

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