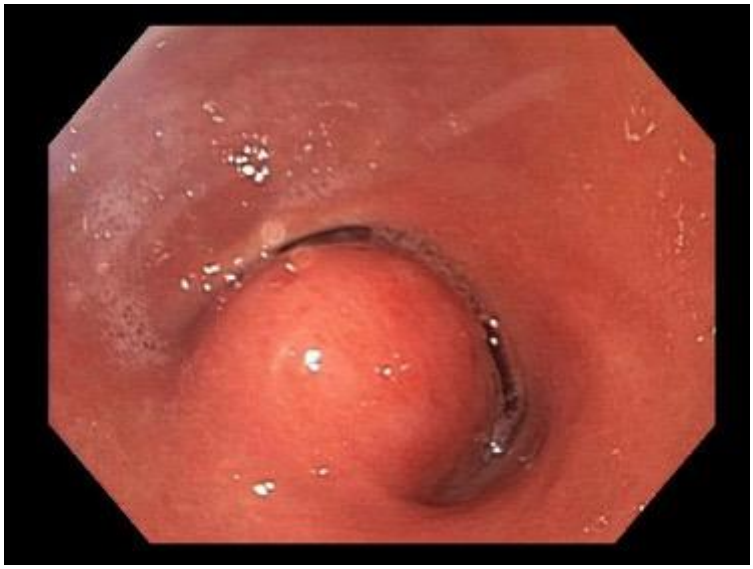
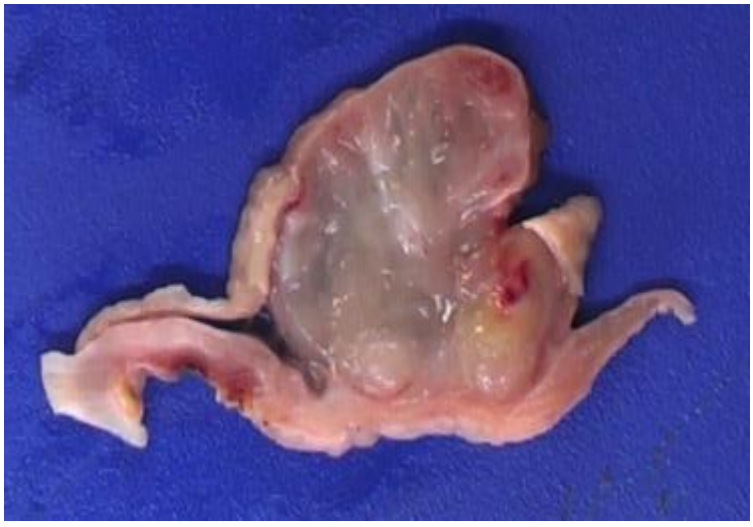
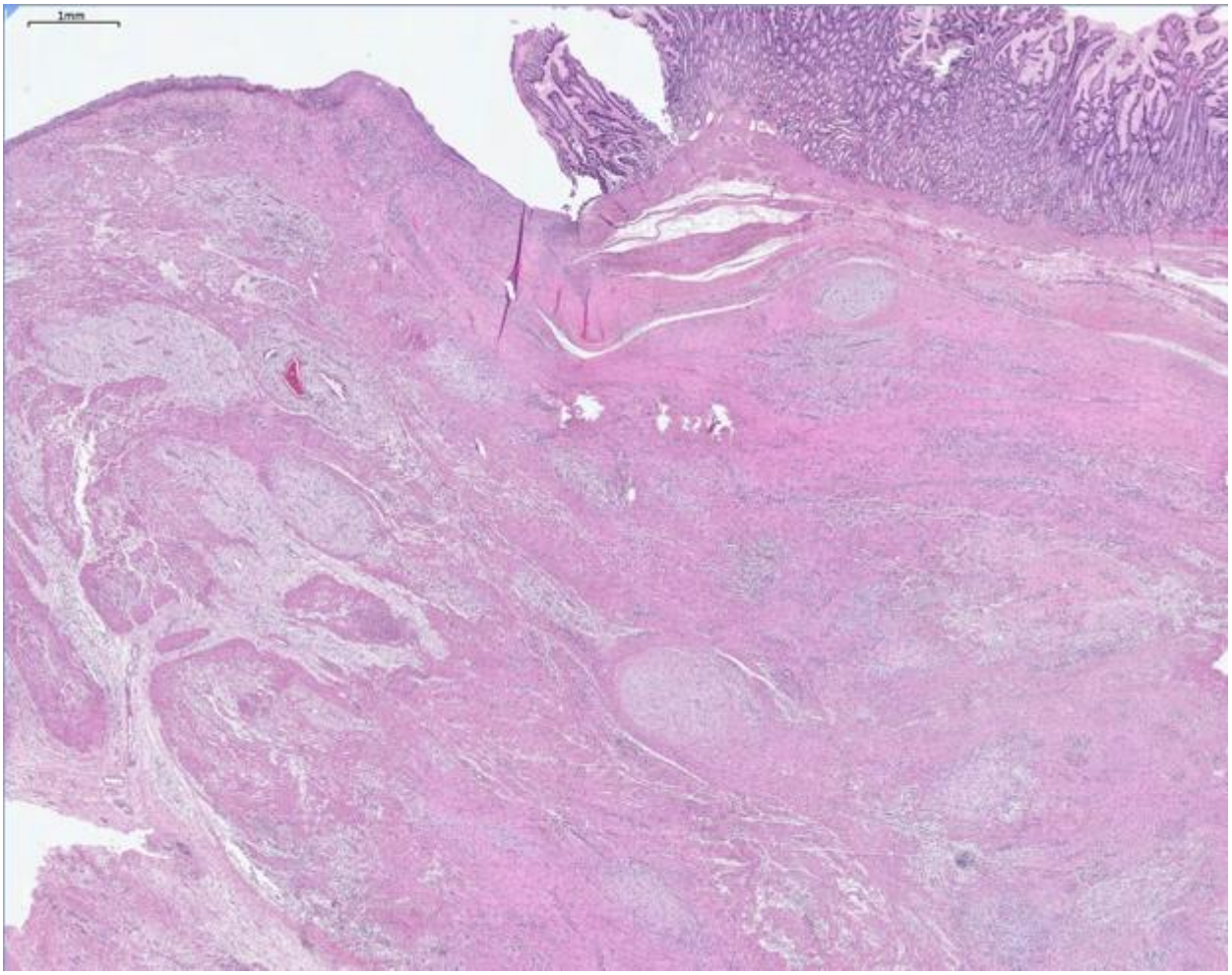
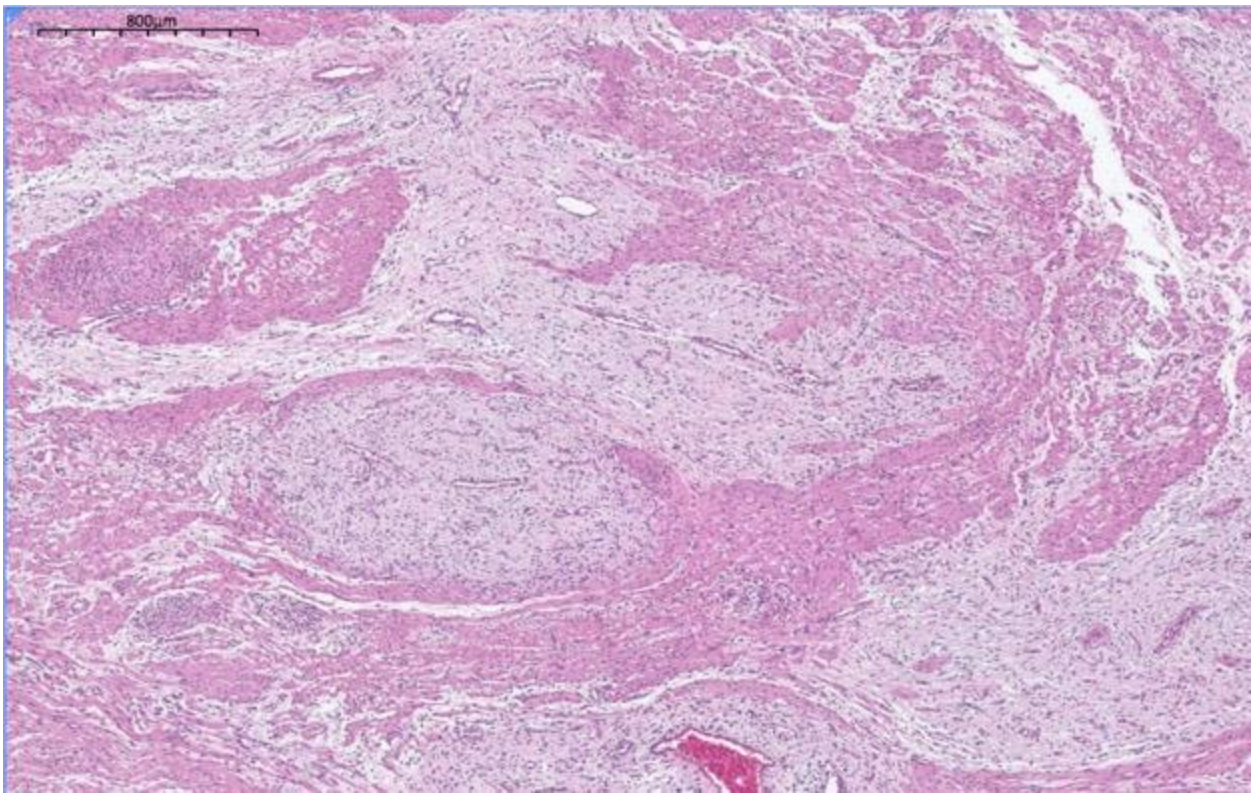
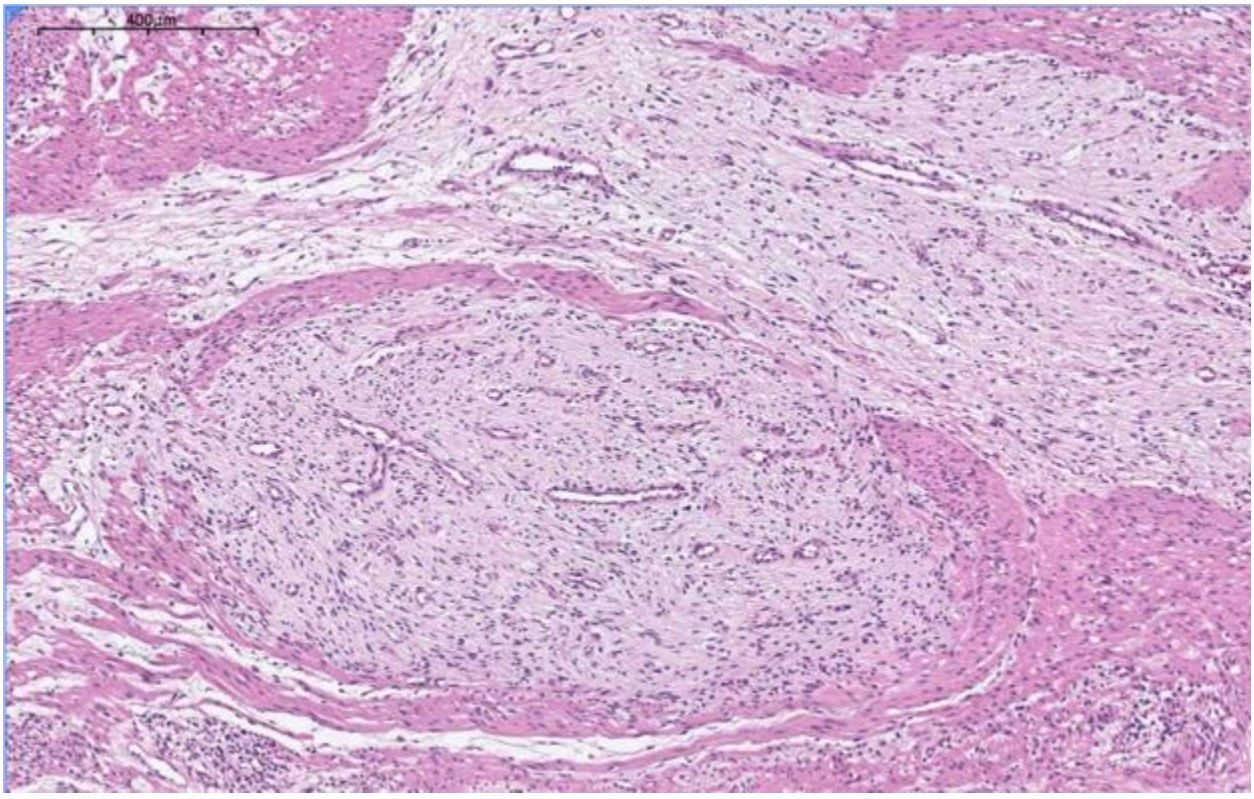
A 58 year old man with multiple medical problems (ulcerative colitis, alcohol abuse, hypertension, cardiovascular disease) presented with dizziness, hematemesis and hematochezia. An EGD showed a 5.0 cm submucosal nodule in the pyloric channel of the stomach as well as multiple ulcers and erosions. The patient underwent a partial gastrectomy and a cross section of the mass is shown. Representative H&E images depict a lesion with a multinodular growth pattern within the muscularis propria. A smooth muscle actin immunostain is included below. Immunostains for desmin, KIT, DOG1, and S100 were negative (not shown).

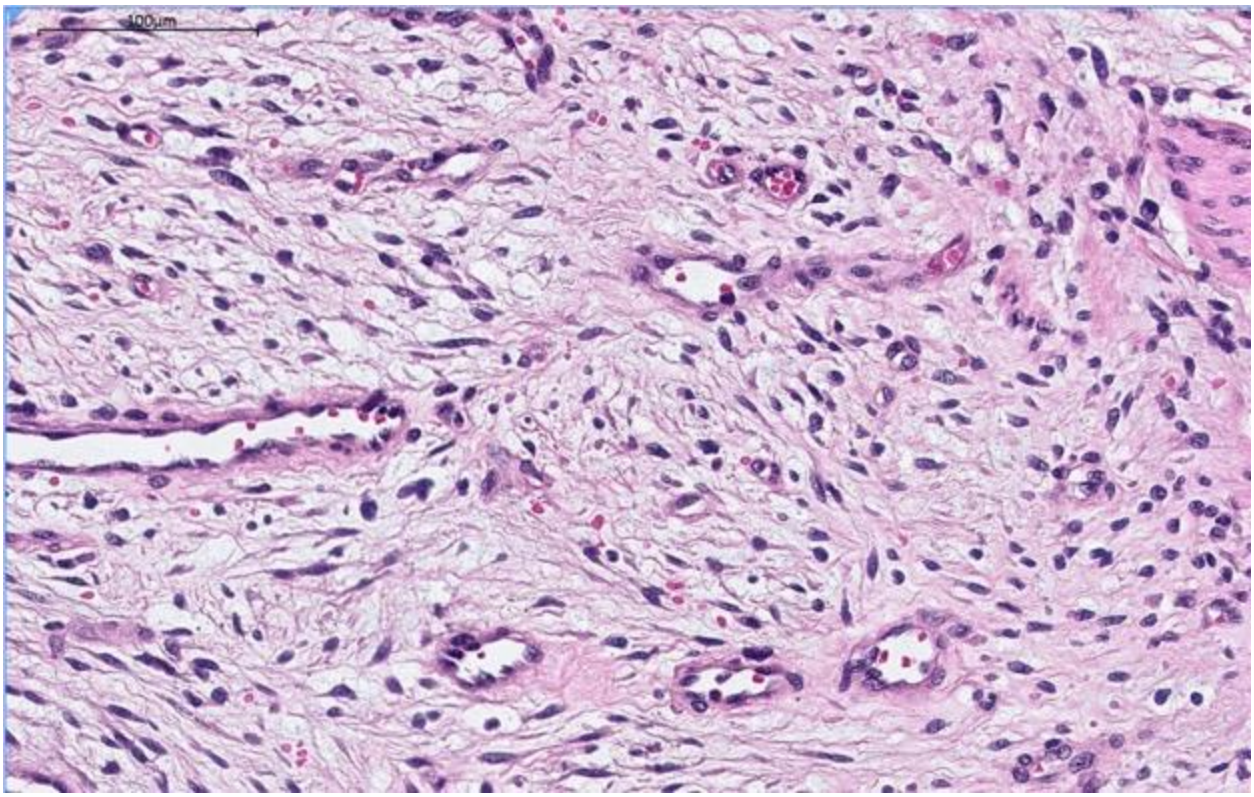


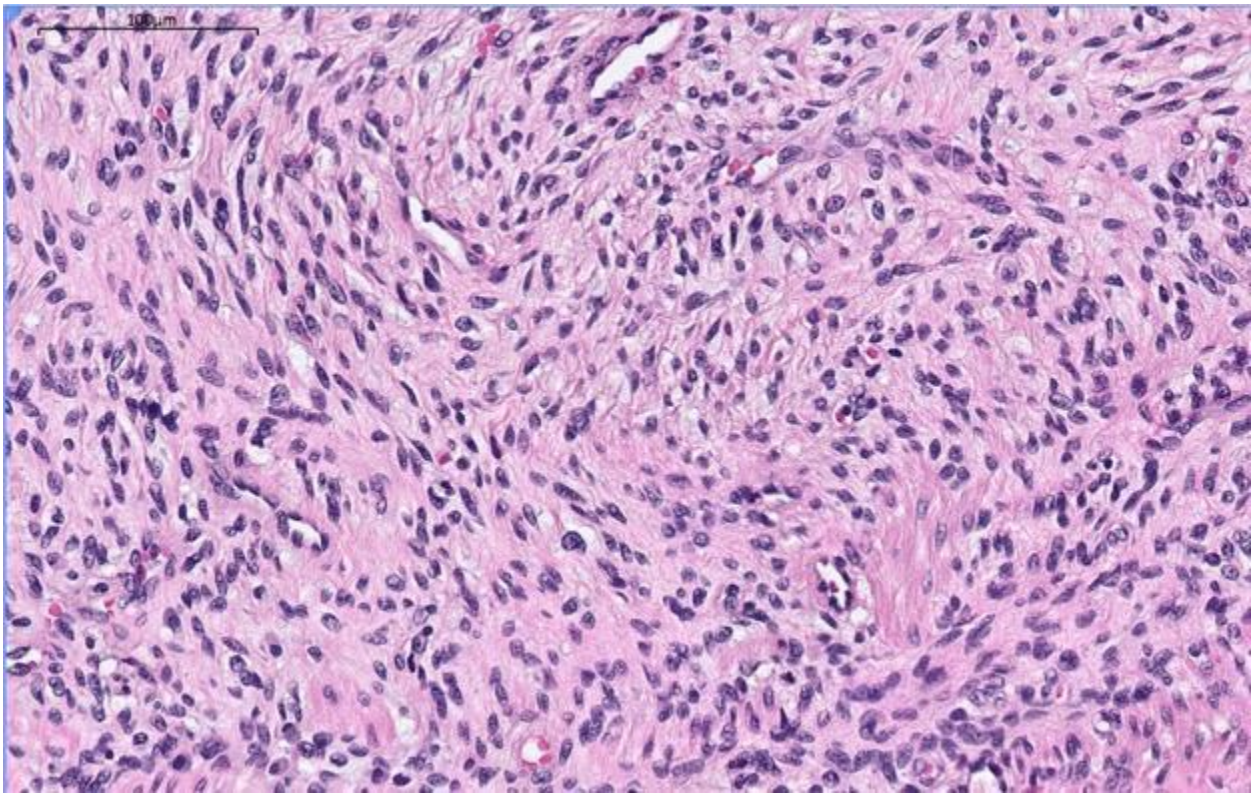



1mm

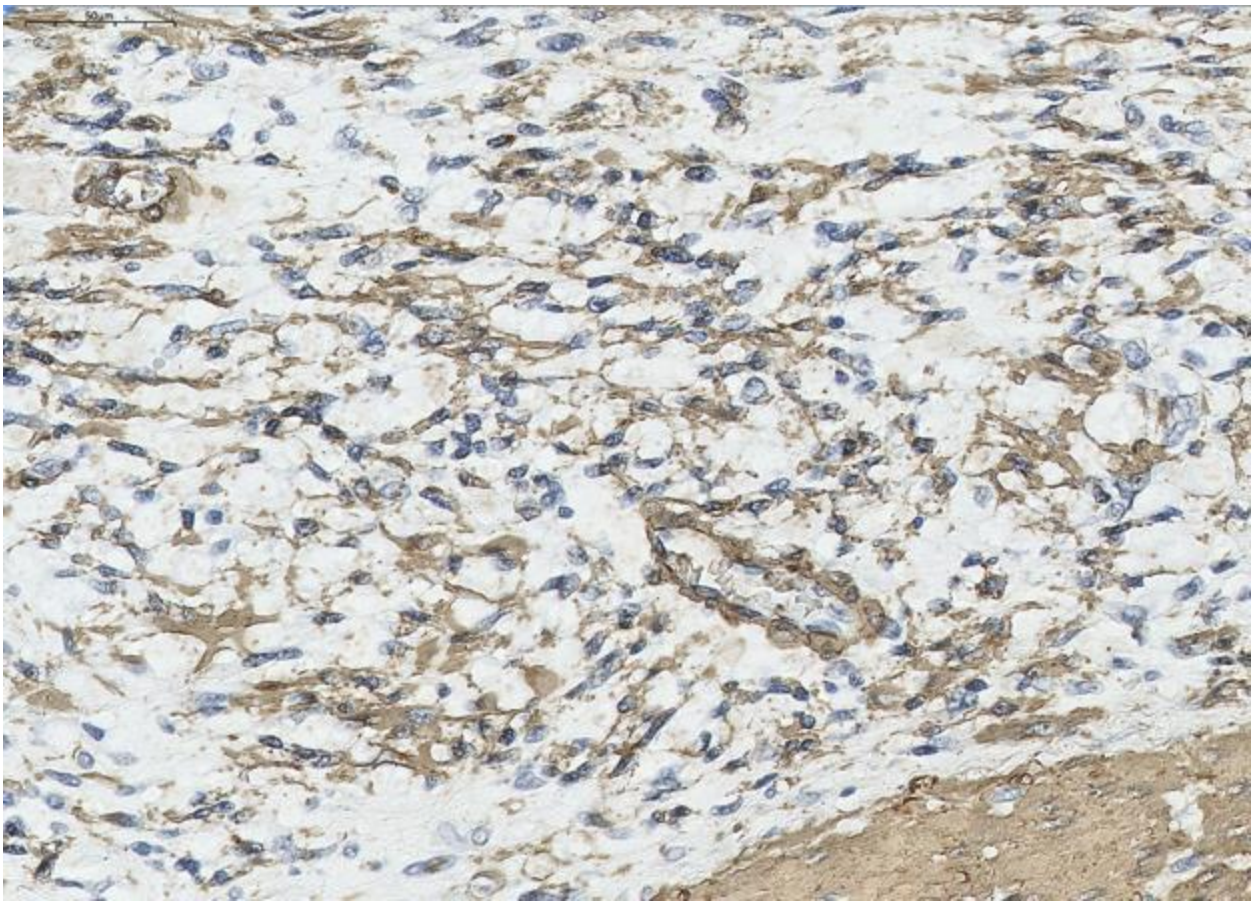

800 µm


400 µm


100 µm


100 µm

Smooth muscle actin



What is the diagnosis?

A. Succinate dehydrogenase deficient gastrointestinal stromal tumor (SDH-deficient GIST)
B. Plexiform fibromyxoma
C. Plexiform schwannoma
D. Neurofibroma
E. Inflammatory fibroid polyp

ANSWER AND DISCUSSION ON NEXT PAGE

Answer and discussion:

Plexiform fibromyxoma (choice B) is the correct answer. Cut sections showed a well circumscribed, unencapsulated, lobulated mass with gelatinous tan-gray cut surfaces that appeared to arise from the muscularis propria with extension into the submucosa. Microscopically, the lesion had a multinodular (plexiform) architecture with fibromyxoid nodules interspersed within the muscularis propria. The mild to moderately cellular nodules were composed of a proliferation of bland, monomorphic spindle cells with inconspicuous nucleoli and eosinophilic cytoplasm. The lesion had a prominent capillary network within a fibromyxoid stroma. Only rare mitotic figures were seen. The lesional cells were positive for smooth muscle actin, and were negative for KIT, DOG1, desmin, and S100. Overall, these findings are diagnostic for plexiform fibromyxoma.

Plexiform fibromyxoma (also known as plexiform angiomyxoid myofibroblastic tumor) is a neoplasm that occurs almost exclusively in the antrum/pylorus, usually in the fifth decade of life. Presenting symptoms include nausea, gastric outlet obstruction, gastric ulcer and anemia. Recurrences or metastases have not been reported after surgical resection. No consistent molecular aberrations have been described and current literature suggests that this neoplasm is benign. The histologic features are demonstrated in our example [1-7].

SDH-deficient GIST (choice A) occurs almost exclusively in the stomach and typically exhibits a plexiform growth pattern in the muscularis propria and a hypercellular, epithelioid cell morphology, but prominent and diffuse myxoid features have only rarely been reported [8-10]. By immunohistochemistry, the tumor cells of SDH-deficient GISTs show loss of succinate dehydrogenase subunit B (SDHB) but are positive for KIT and DOG1. In contrast to the majority of other GISTs, SDH-deficient GISTs are KIT and PDGFRA wildtype by molecular analysis [8-9].

Schwannoma (choice C) rarely occurs in the GI tract, but when it does, it most commonly occurs in the stomach. Tumors can arise from the submucosa or muscularis propria. Microscopically, tumors often have a characteristic peritumoral lymphoid cuff. Myxoid change can be seen in up to 27% of cases, but the plexiform variant is rare, estimated to represent 1-2% of all gastric schwannomas [11]. S100 and Sox10 should be strongly and diffusely positive in schwannoma, including the plexiform variant, but negative in plexiform fibromyxoma [12].

Neurofibroma of the GI tract usually occurs in the setting of patients with neurofibromatosis type I (NF1, formerly known as von Recklinghausen disease), although rare sporadic cases occurring in the stomach have been reported [13-16]. In contrast to schwannoma, neurofibroma is composed of a mix of cells: Schwann cells, perineurial cells, and endoneurial fibroblasts [17]. Neurofibromas have been described as polyps arising from the submucosa [18], and in patients with NF1, can have a plexiform pattern [19]. Like schwannoma, neurofibroma should also be diffusely positive for S100 and Sox10.

Inflammatory fibroid polyp (choice D) is also rare in the GI tract, but most commonly occurs in the stomach [20]. Inflammatory fibroid polyps are submucosal lesions that do not usually extend into the muscularis propria when they occur in the stomach [2, 4, 21]. Microscopically, in addition to the spindle cell proliferation, there should be an associated eosinophil-rich mixed inflammatory infiltrate as well as

thin- and thick-walled blood vessels throughout the tumor; spindle cells can show an “onion skin” arrangement around vessels [2, 4]. Spindle cells are typically positive for CD34 and fascin; spindle cells can also be positive for smooth muscle actin in 25% of cases [2, 4, 22].

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