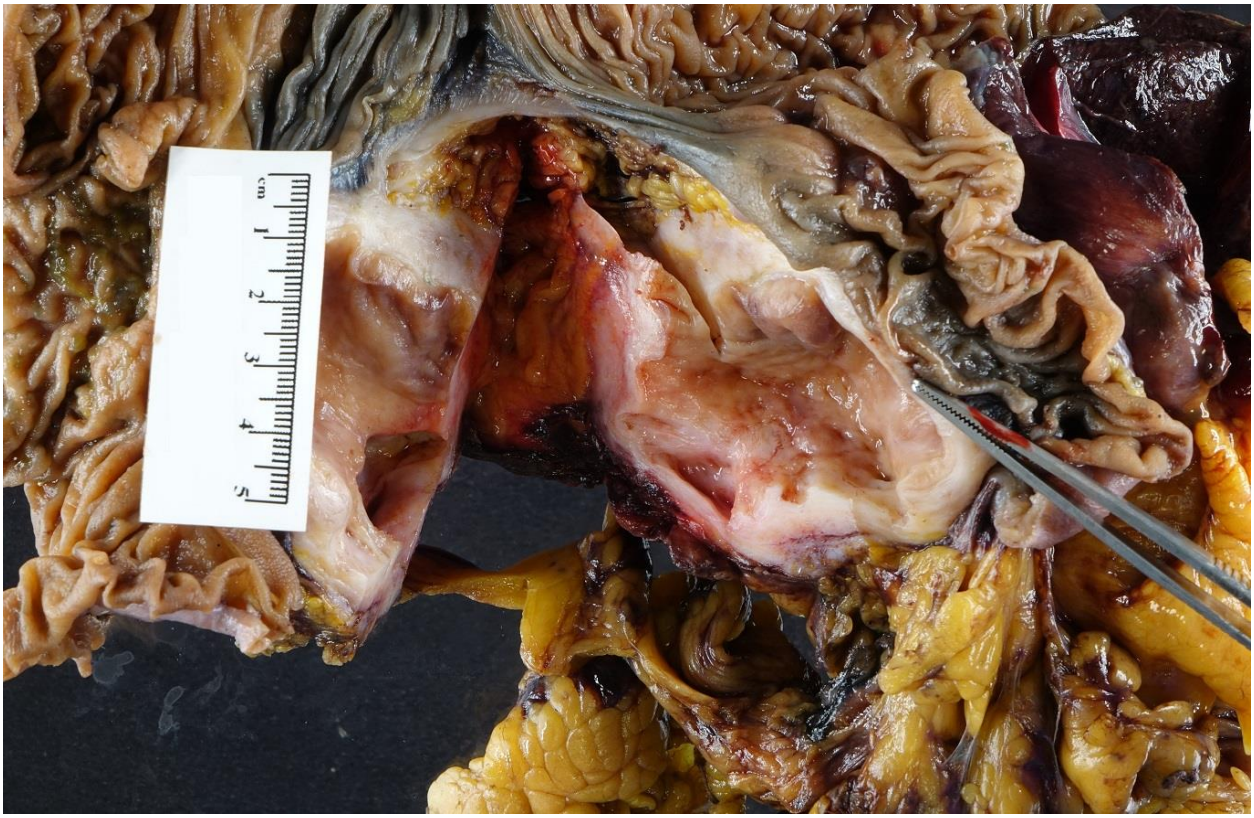
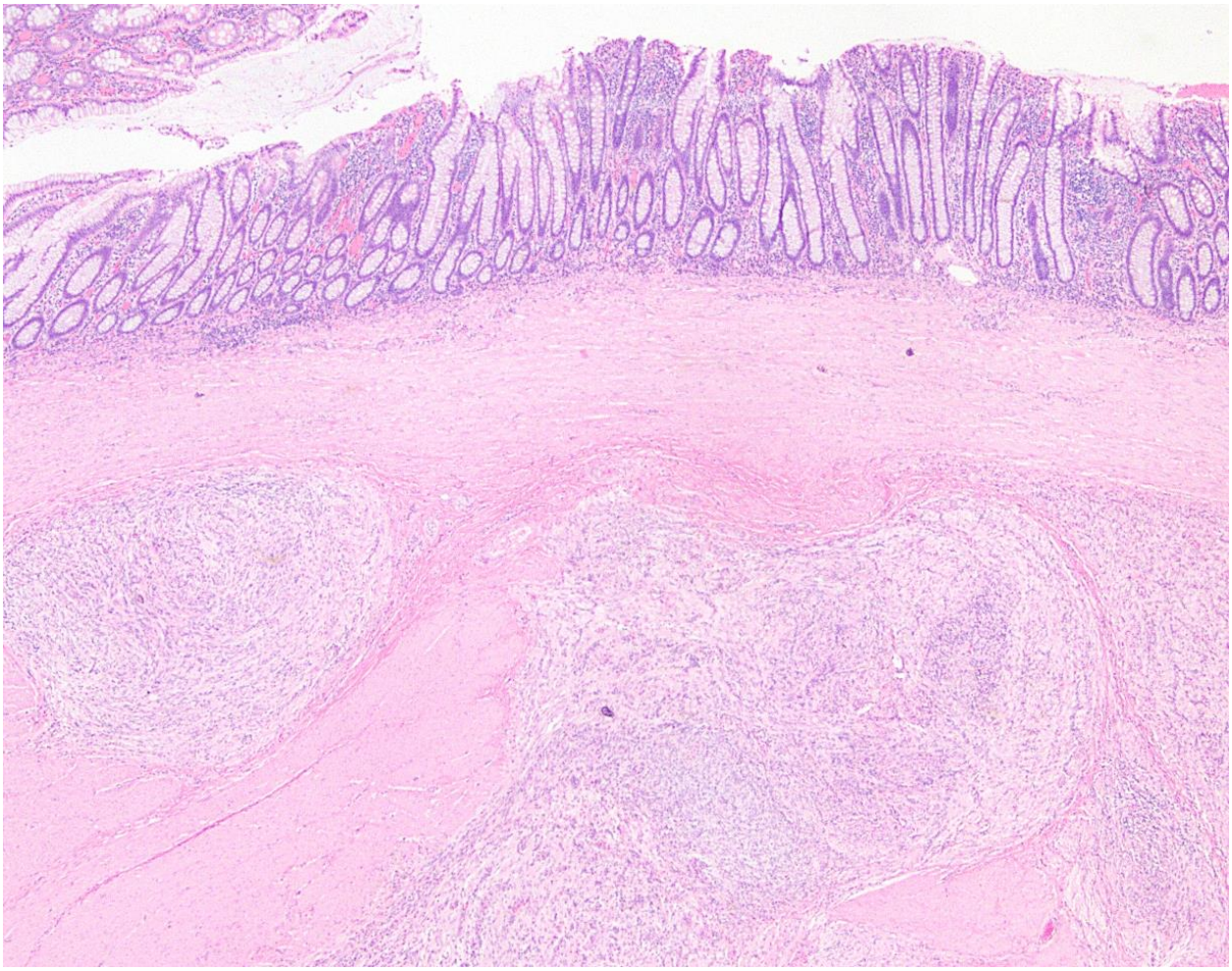
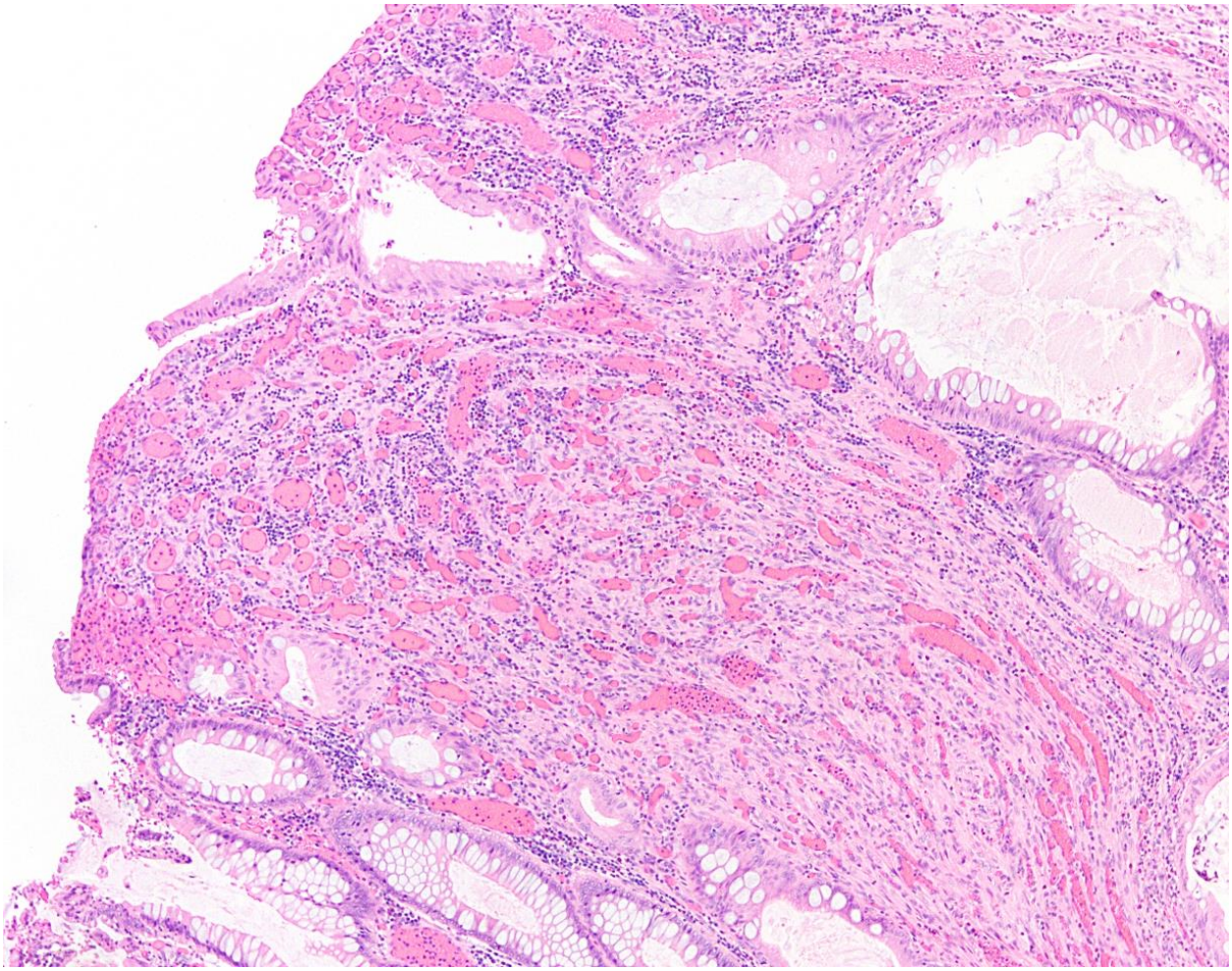
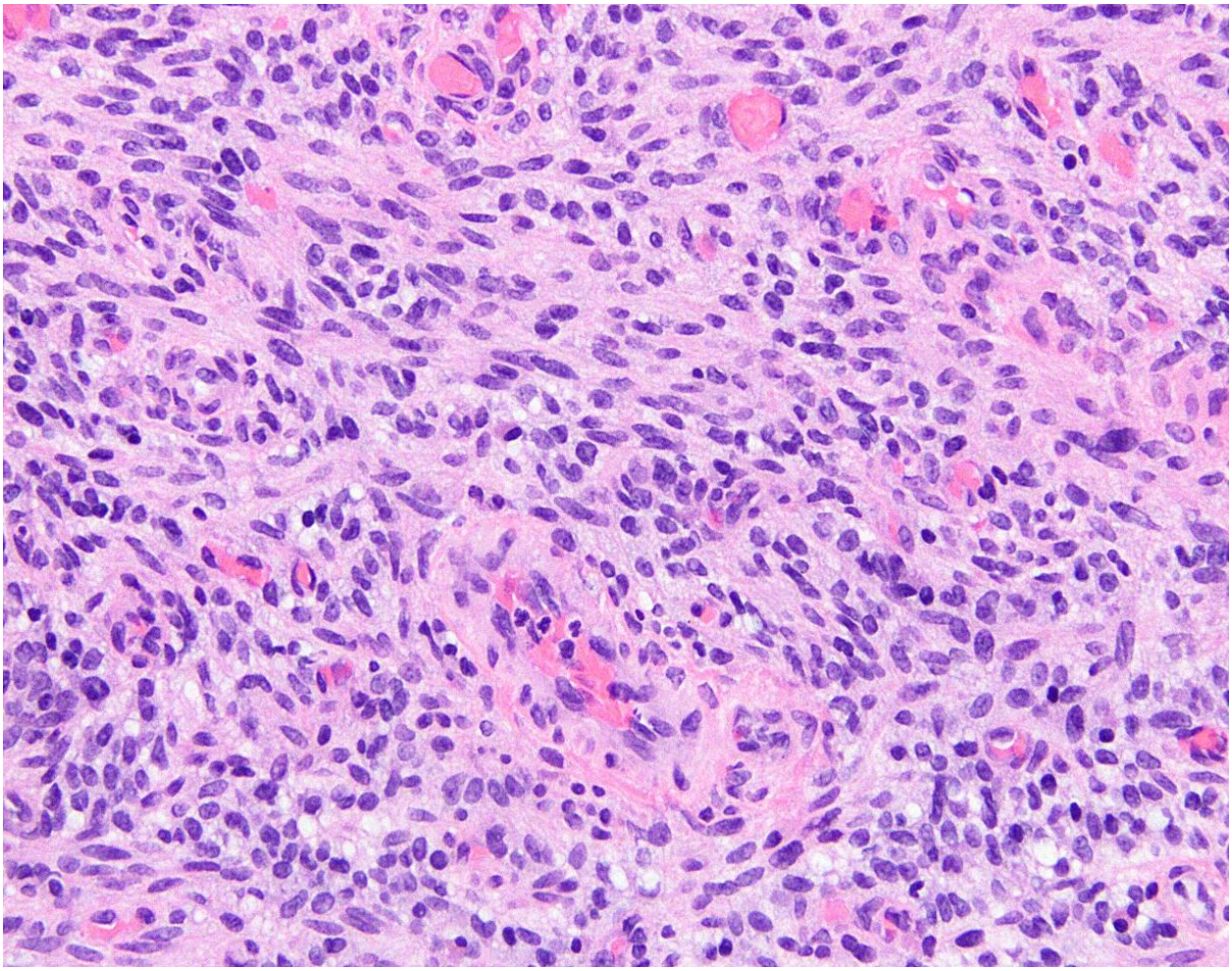
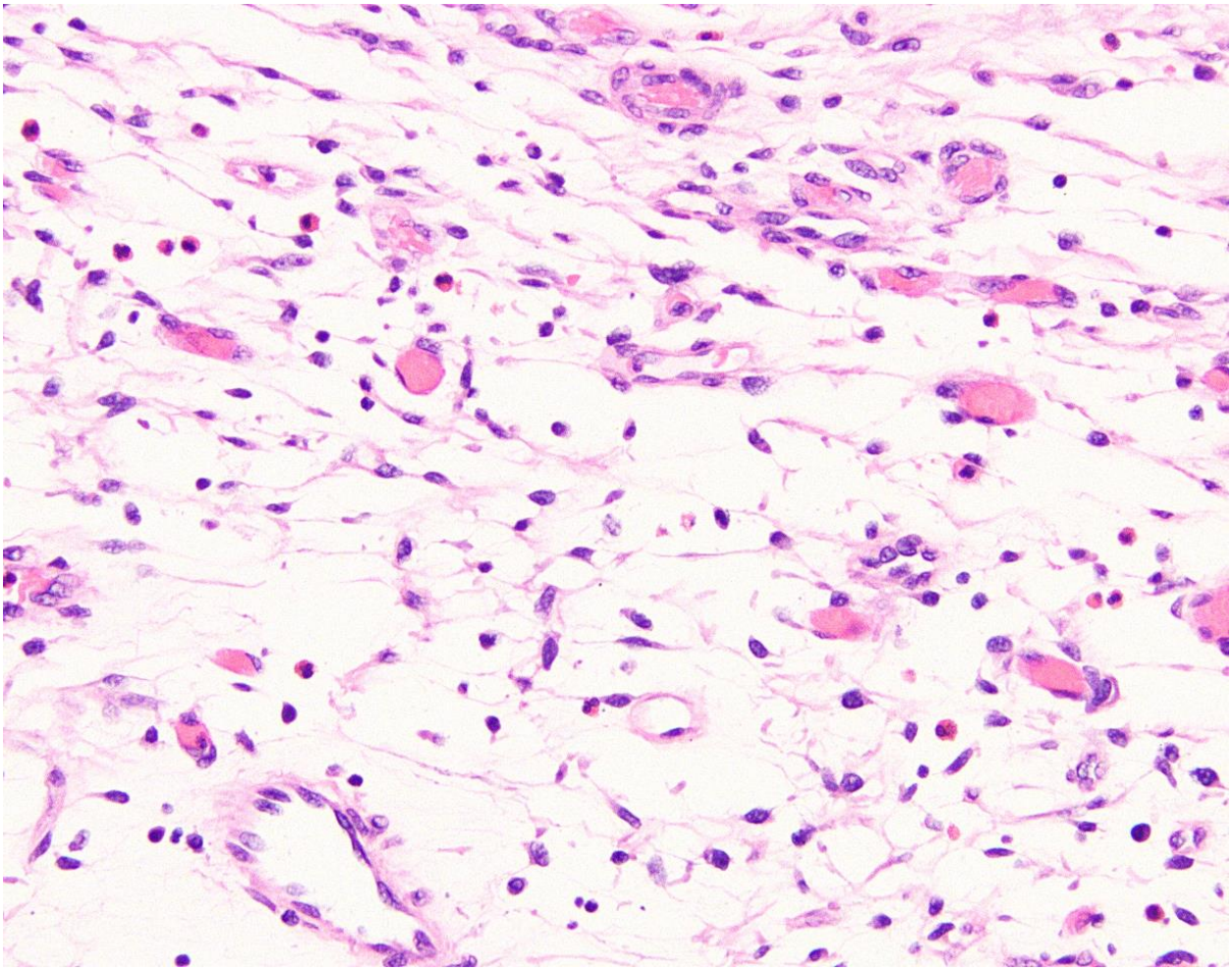
A 43-year-old man with no significant medical history presented with right-sided abdominal pain. CT scan demonstrated a bilobed cystic mass measuring 9.0 x 5.1 cm with thick enhancing walls in the ascending colon. Subsequent colonoscopy revealed an eccentric cystic mass of the ascending colon. Initial superficial biopsies were inconclusive. Due to concerns of the mass growing into the anterior abdominal wall on imaging, the patient underwent a diagnostic laparoscopy and right colectomy. Immunohistochemical stains for SMA and desmin are shown below. Immunohistochemical stains for CD117/c-kit, DOG1, cytokeratin MNF116, S100, ALK1, and CD34 (not shown) were all negative.

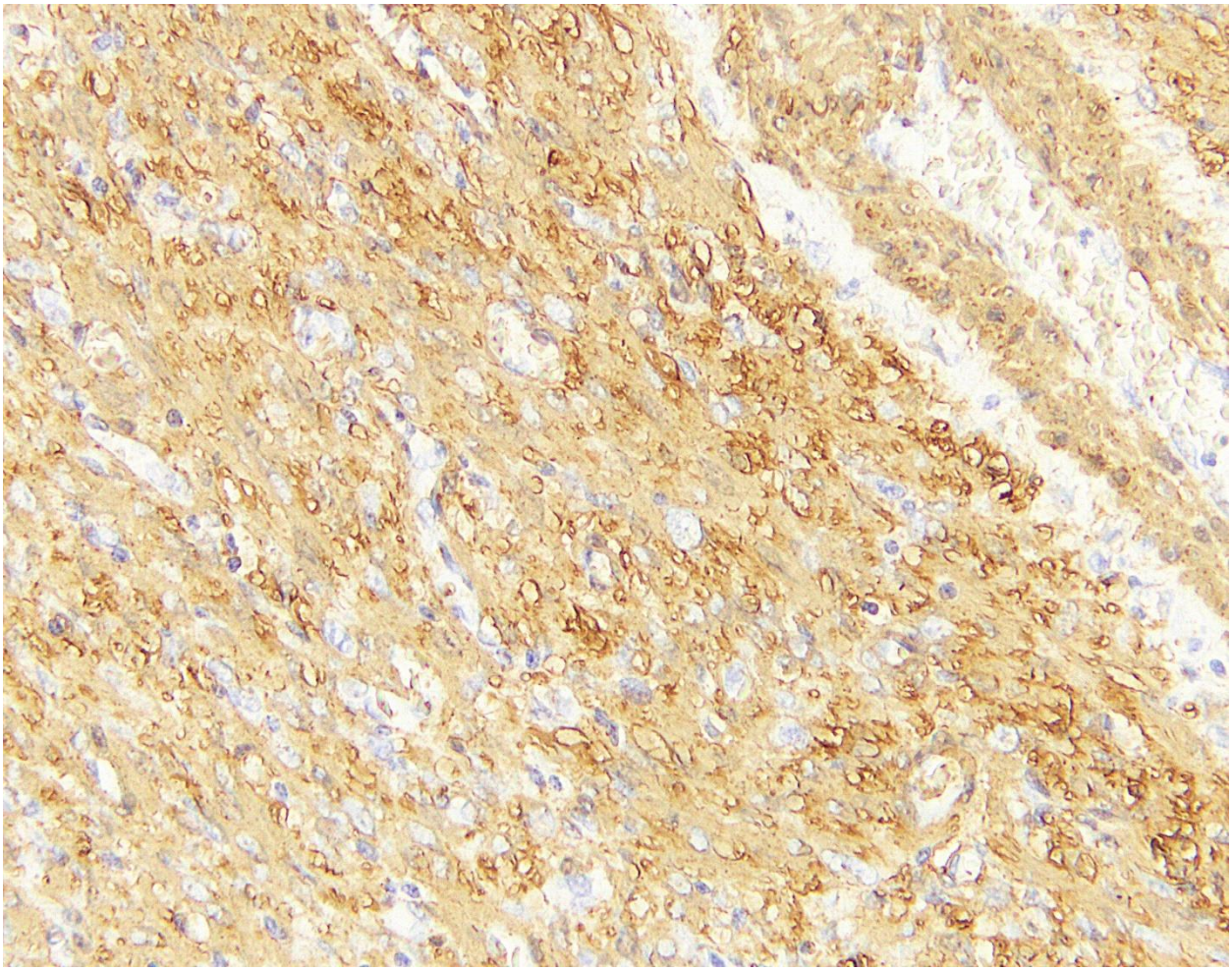




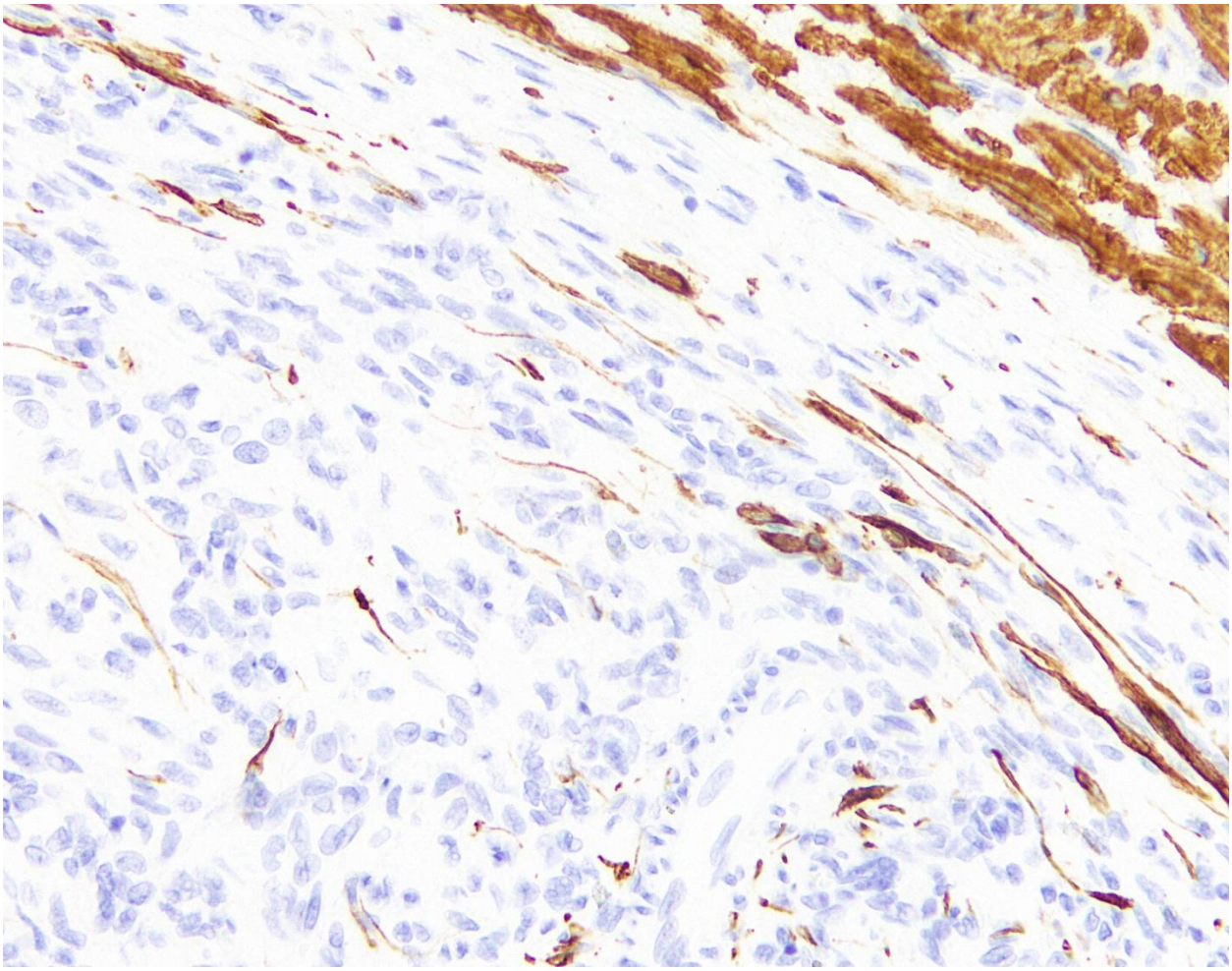








SMA



Desmin

What is the diagnosis?

A. Glomus tumor
B. Inflammatory myofibroblastic tumor
C. Myxoid schwannoma
D. Plexiform fibromyxoma
E. Plexiform neurofibroma
F. Succinate dehydrogenase-deficient gastrointestinal stromal tumor

Answer: D. Plexiform fibromyxoma

Histology demonstrates a multinodular, plexiform lesion with an infiltrative growth pattern in the muscularis propria of the colon, with focal mucosal invasion. The lesion is composed of bland, uniform spindle cells in a fibromyxoid background. Cellularity overall is variable, with the tumor containing both hyper- and hypocellular regions, but prominent vascularity is present throughout. The nuclei themselves are evenly sized, have inconspicuous nucleoli, and show no mitotic activity. Immunohistochemical stains show positive staining for smooth muscle actin, with focal desmin positivity. CD117/c-kit, DOG1, cytokeratin MNF116, S100, ALK1, and CD34 were all negative within the lesional cells. The overall microscopic and immunohistochemical findings are most consistent with a plexiform fibromyxoma of the colon.

Plexiform fibromyxoma is a rare benign mesenchymal tumor first reported by Takahashi et al in 2007 (1-2), with characteristic plexiform architecture. The vast majority of reported cases have occurred in the gastric antrum, but extremely rare examples have been reported in the esophagus, small bowel, and ileocecum (3-5). The age of presentation varies widely, from 7-75 years. Patients present with nonspecific symptoms, including abdominal pain, early satiety, obstruction, or gastrointestinal bleeding, depending on where the tumor is located. Surgical excision appears to be curative, with no reports of recurrence or metastasis to date.

Aside from its characteristic multinodular appearance, plexiform fibromyxoma is typified by bland spindle cells with inconspicuous nucleoli and prominent vascularity. Most lesions are relatively hypocellular. Mitotic activity and necrosis should be rare. The lesional cells are positive for smooth muscle actin and negative for c-kit, DOG1, and S100. Variable CD34 staining is seen. Approximately 18% of plexiform fibromyxomas harbor a t(11;12)(q11;a13) *MALAT1-GLI1* fusion (6); this case was tested and was negative for the fusion.

Glomus tumors are largely benign mesenchymal neoplasms. They are most often seen in the skin but can occur in the digestive system, mostly within the stomach. These tumors consist of solid sheets of cells forming nodules within the muscularis propria. Areas with hyalinization or myxoid change can be present, and tumor cells tend to organize around vessels. Unlike the cells in plexiform fibromyxoma, the cells in glomus tumors are round with uniform nuclei, amphiphilic/eosinophilic cytoplasm, and often well-defined cell membranes. Similar to plexiform fibromyxoma, SMA stains positive, while desmin, CD117, DOG1, and S100 stain negative.

Inflammatory myofibroblastic tumor is a mesenchymal tumor that can occur in the mesentery or colon wall. The tumor consists of bland spindle cells, but unlike plexiform fibromyxomas, they are usually more diffuse and tend to have a more prominent inflammatory cell component and inconspicuous vasculature. Desmin, smooth muscle actin, and (in some cases) ALK1 can be used to highlight the lesional cells. Half of these lesions also contain a t(2;5) *TMP3-ALK* translocation, which can be used to confirm the diagnosis.

Schwannomas of the gastrointestinal tract can have hypercellular and hypocellular areas, though this is often less pronounced than in their soft tissue counterparts. They usually have peripheral lymphoid

aggregates and would manifest as one discrete rounded mass, rather than assuming a plexiform configuration. Rare gastrointestinal examples may have a myxoid background and a reticular/microcytic growth pattern. S100 is positive in gastrointestinal schwannomas.

Plexiform neurofibromas can show multiple enlarged nerve fascicles that may look architecturally similar to a plexiform fibromyxoma. However, it presents more often in neonates and young children and should show additional involvement of nerve fibers, characteristic collagen bundles, and typically positive staining for S100.

SDH-deficient GIST can show a similar plexiform growth pattern but should retain expression of c-kit and DOG1, which were both negative in this case. This type of GIST is also more classically seen in young adults and children and arises almost exclusively within the stomach (as does plexiform fibromyxoma).

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