

Case: A 50 year-old man presented with hematochezia. He had a history of diverticulitis and bloody stools requiring multiple hospitalizations. A nuclear medicine study showed active bleeding from the sigmoid colon; a CT showed moderate colonic diverticulosis with short segment mural thickening. The patient underwent sigmoid colonic resection. Dense adhesions were identified at the time of the procedure and the sigmoid colon was long, tortuous, and inflamed. Histologic sections were obtained from the colonic wall and pertinent findings are illustrated in the following figures.

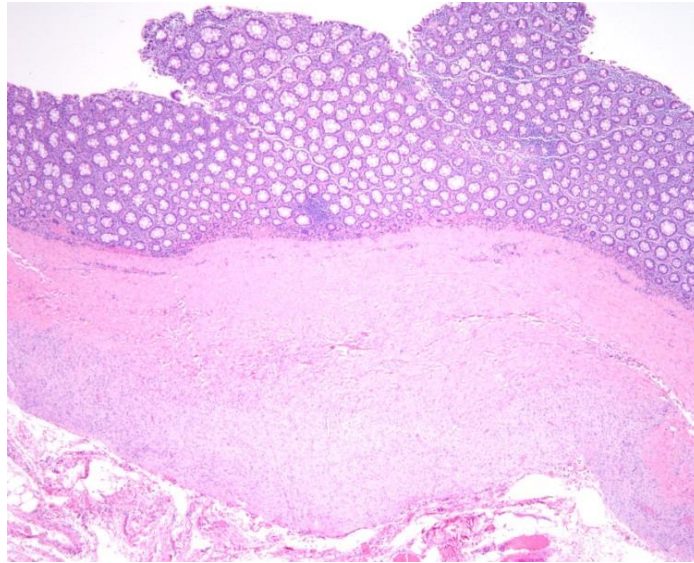


Figure 1. H&E, (40x)

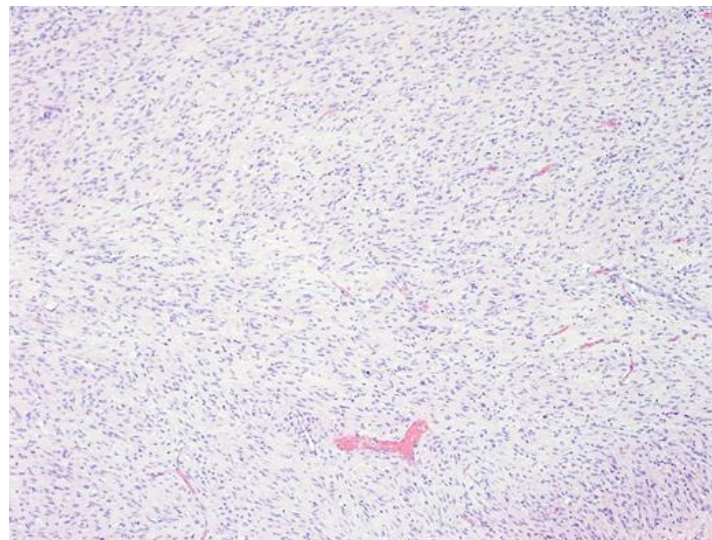


Figure 2. H&E, (100x)

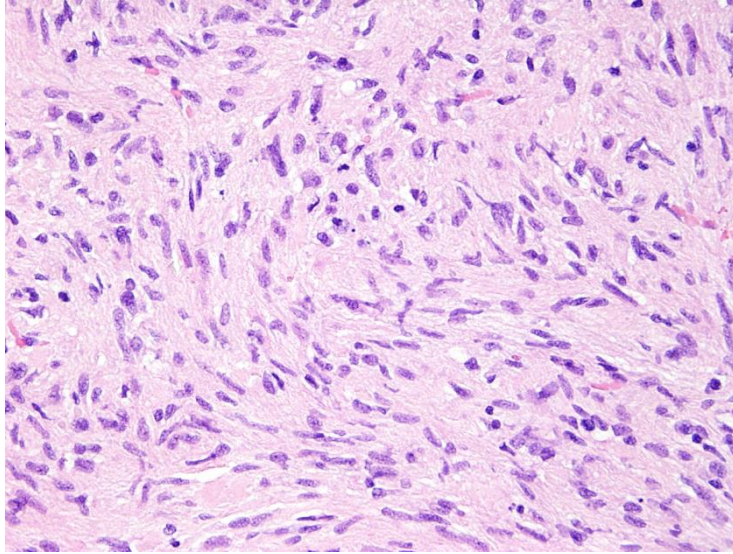


Figure 3. H&E (400x)

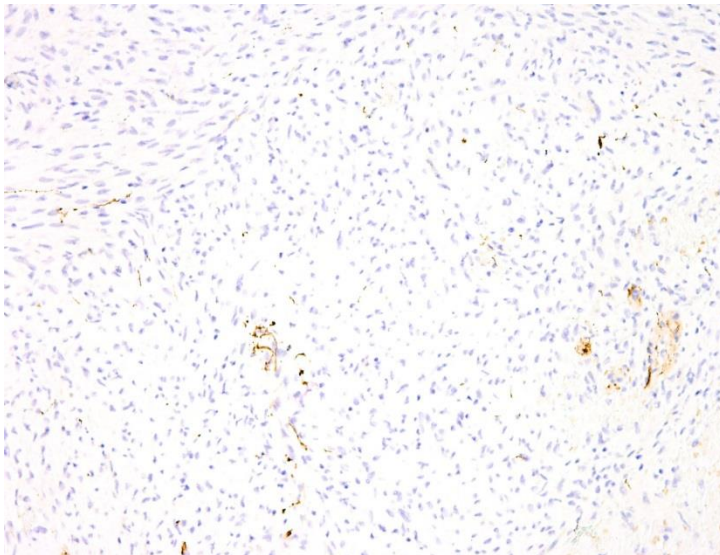


Figure 4. Calretinin, immunohistochemical stain (200x).

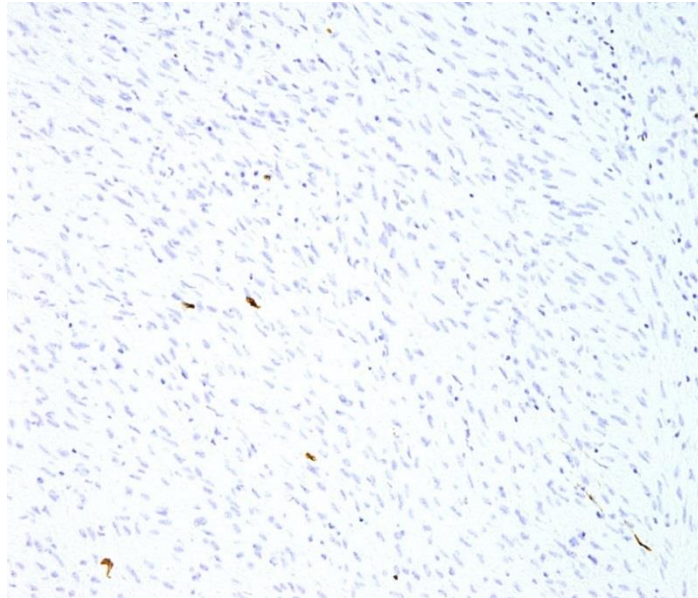


Figure 5. S100, immunohistochemical stain (200x).

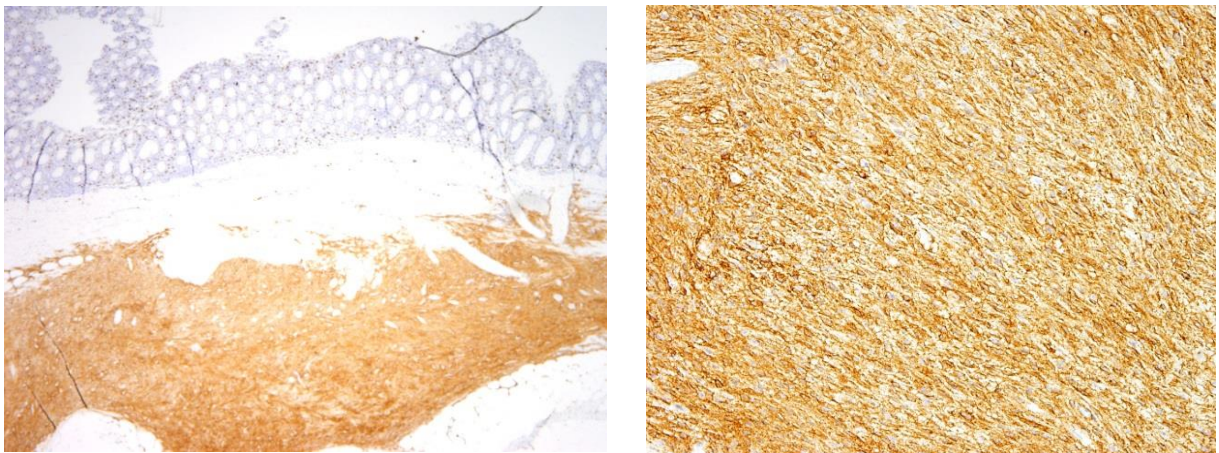


Figure 6. CD117, immunohistochemical stain (40x and 200x).

What is your diagnosis?

- A. Segmental hyperplasia of the interstitial cells of Cajal
- B. Schwannoma
- C. Diffuse gangioneuromatosis
- D. Gastrointestinal stromal tumor
- E. Mesenteric fibromatosis

(SCROLL DOWN TO NEXT PAGE FOR CORRECT ANSWER.)

Answer and Discussion:

Segmental hyperplasia of the interstitial cells of Cajal (ICC)

Segmental hyperplasia of the interstitial cells of Cajal (ICC) is a microscopic finding characterized by the presence of a focal or diffuse CD117-expressing spindle cell proliferation involving the myenteric plexus; it does not form a grossly evident mass. Hyperplasia of ICC is most commonly associated with hereditary syndromes involving germline mutations in *c-kit* or *PDGFRA* genes that predispose patients to multiple gastrointestinal stromal tumors throughout the gastrointestinal tract. It has been associated with Carney triad, congenital intestinal neuronal dysplasia, and von Recklinghausen disease [1, 2]. Although commonly an incidental finding, ICC hyperplasia has been reported in patients with chronic constipation, bleeding, and abdominal pain [3]. One previous case was described within a true diverticulum [1].

ICC hyperplasia is most frequently encountered in serially sectioned stomachs (35%) followed by gastroesophageal specimens (9%); intestinal proliferations are rare (<0.1%) [2]. Lesions are composed of spindle cells with strong CD117 immunostaining. Molecular analysis from one study of 12 lesions revealed *c-kit* exon 11 mutations in 25% of cases [2]. Chen and Hirota *et al* reported polyclonality in two separate cases of ICC hyperplasia [4]. Whether these lesions are early neoplastic gastrointestinal stromal tumors or non-neoplastic hyperplasia is not clear.

The histologic differential diagnosis includes several entities. **Schwannomas (choice B)** are circumscribed masses that involve the muscularis propria and submucosa. They are highly cellular and contain spindle cells with elongated nuclei. Fibrovascular septa contain interspersed lymphocytes and plasma cells, and most lesions show a cuff of benign lymphoid hyperplasia at the periphery. The cells are strongly positive for vimentin, glial fibrillary acidic protein, and S-100 protein. They may show focal staining for CD34, but are negative for CD117, neurofilament, smooth muscle actin and desmin [3].

Diffuse ganglioneuromatosis (choice C) is a hamartomatous lesion composed of Schwann cells and ganglion cells. Diffuse ganglioneuromatosis usually manifests as bowel wall thickening with diffuse, fusiform expansion of the submucosal plexus or myenteric plexus. Spindle cells are positive for S100, neurofilament and neuron specific enolase and negative for CD117. Diffuse ganglioneuromatosis is associated with syndromes including neurofibromatosis type 1, multiple endocrine neoplasia type 2B, juvenile polyposis, and non-familial adenomatous polyposis, although it can be an isolated finding in some cases [4].

Gastrointestinal stromal tumors (GIST) (choice D) recapitulate the phenotype of interstitial cells of Cajal. They occur most frequently in the stomach, but can be seen throughout the small bowel and, less commonly, the colorectum. Tumors can be either benign or malignant; prognosis and staging depend on both tumor size and mitotic activity. Histologically, GISTs can be categorized predominantly as spindle cell, epithelioid cell, and mixed cell types. The former contain whorls and intersecting fascicles of elongated cells with fibrillary cytoplasm, while epithelioid cells contain abundant eosinophilic cytoplasm with round nuclei. Tumor cells are positive for CD117, DOG1, and often CD34, but are usually negative for desmin, S100, and smooth muscle antigen [4-6].

Mesenteric fibromatosis (choice E) involves the mesentery, but can encroach on and involve the bowel wall. Tumors are large and firm with infiltrative borders and contain fascicles of bland, spindle cells enmeshed in densely collagenous stroma. Thin-wall, dilated vessels are surrounded by extravasated

erythrocytes and thick-walled arteries are typically present. The spindle cells are positive for nuclear B-catenin and smooth muscle antigen, but negative for CD117 and desmin [4, 7].

References:

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