Case History

A 30-year-old female with family history of colon polyps presented with rectal bleeding and change in bowel habits. Colonoscopy and endoscopic ultrasound were performed, revealing a 10.5-mm oval, homogeneous, hypoechoic, well-defined mass with smooth borders that appeared to arise from the submucosa of the sigmoid colon. Initial fine-needle biopsy of this mass was non-diagnostic with only scant colonic mucosa and blood.

A subsequent targeted fine needle biopsy of the mass demonstrated cords and clusters of compact cells with oval-to-irregular nuclei and variable amounts of cytoplasm (Fig.1). No mitotic activity was appreciated. Immunohistochemical stains revealed diffuse positive staining for S100 and SOX-10 with focal positive staining for MART-1, GFAP, and MiTF; negative immunostains included cytokeratins (AE1/AE3 and MNF116), EMA, CD68, chromogranin, synaptophysin, DOG-1, KIT, SMA, HMB45, and inhibin. The proliferative index by Ki-67/MIB-1 staining was 1%. The final diagnosis was "neuroectodermal proliferation" with the following explanatory note "… while the morphology and immunophenotype of the cells is suggestive of neural crest or possibly melanocytic differentiation, it is not characteristic of a particular entity… possibilities include a neoplastic proliferation of neuroectodermal or neural crest derived cells, or less likely a hamartomatous lesion or congenital rest." Additional sampling if clinically indicated was recommended.

The patient subsequently underwent a sigmoid colon resection for definitive diagnosis of the submucosal lesion. The gross, histologic and key immunohistochemical features of the lesion are illustrated in Figs. 2-6.

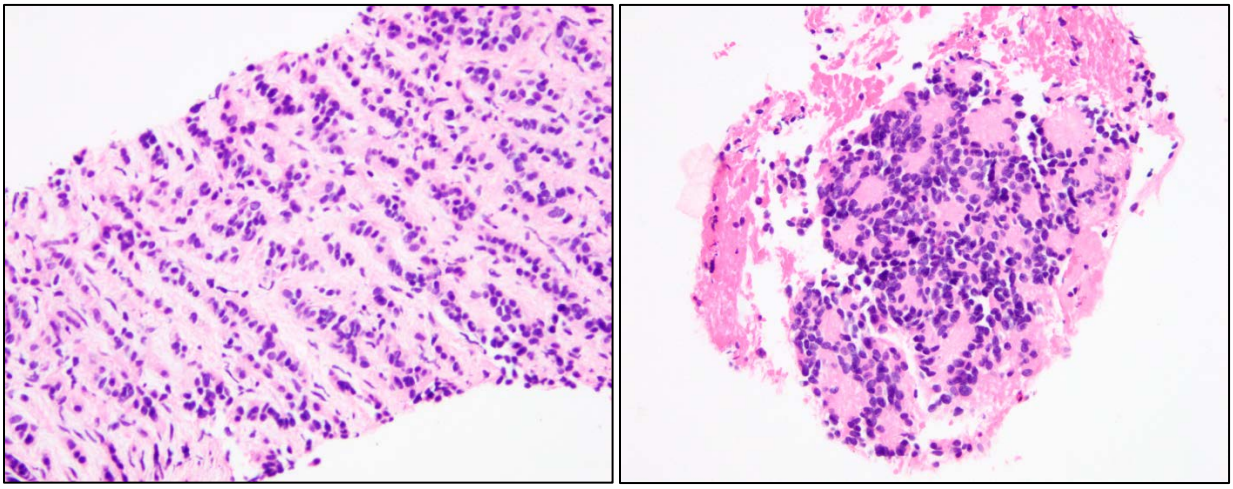

Fig 1. Fine needle biopsy of sigmoid mass, H&E (20x).

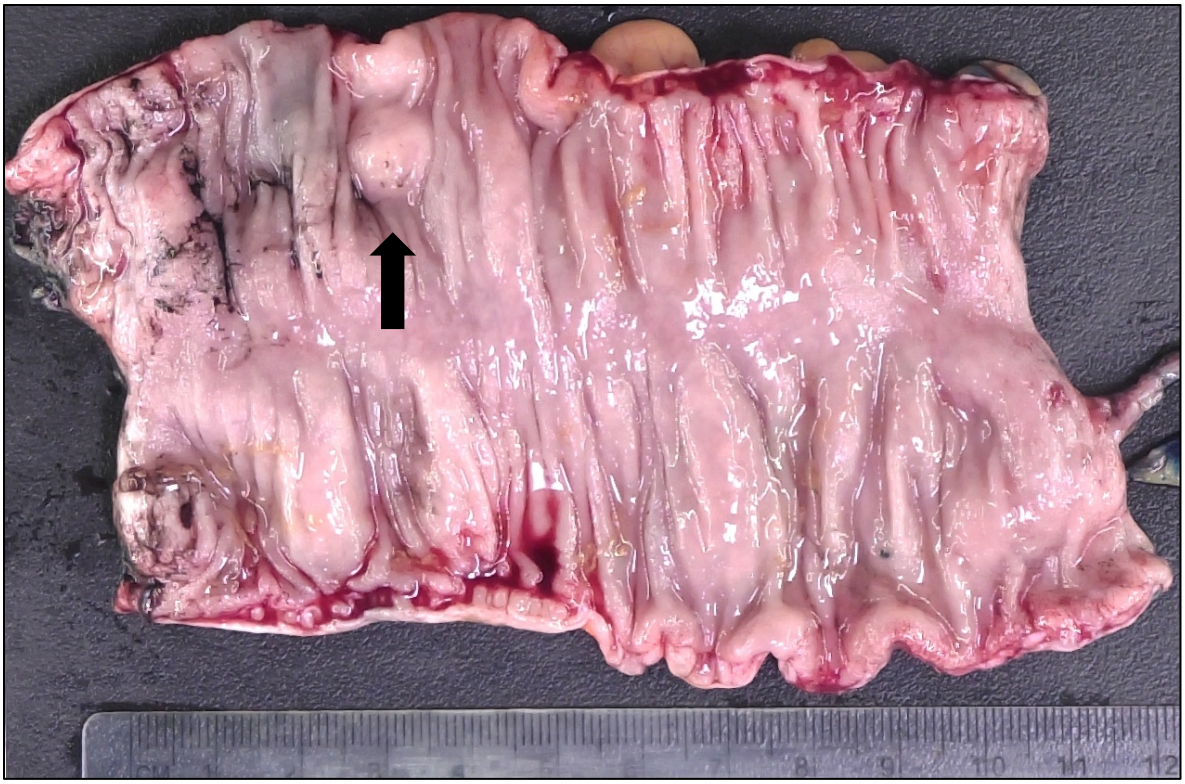

Fig 2. Submucosal mass, sigmoid colon resection.

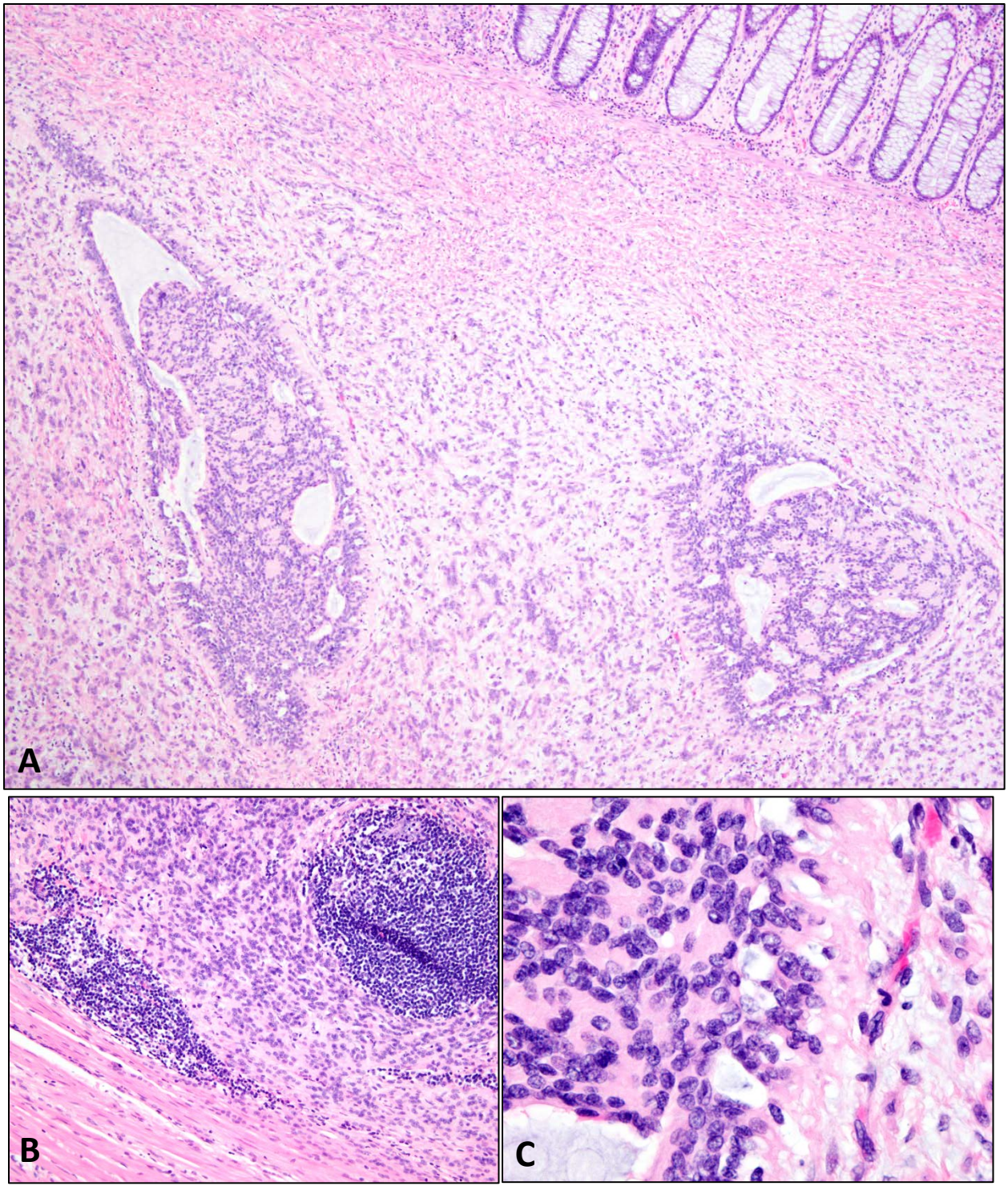

Fig 3. Sigmoid mass resection, H&E. A. Low power showing a biphasic tumor with spindled and epithelioid areas (4x). B. Mature lymphocytes at the periphery (10x). C. Interface between epithelioid area containing rosettes (left) and background spindle cells (right; 40x).

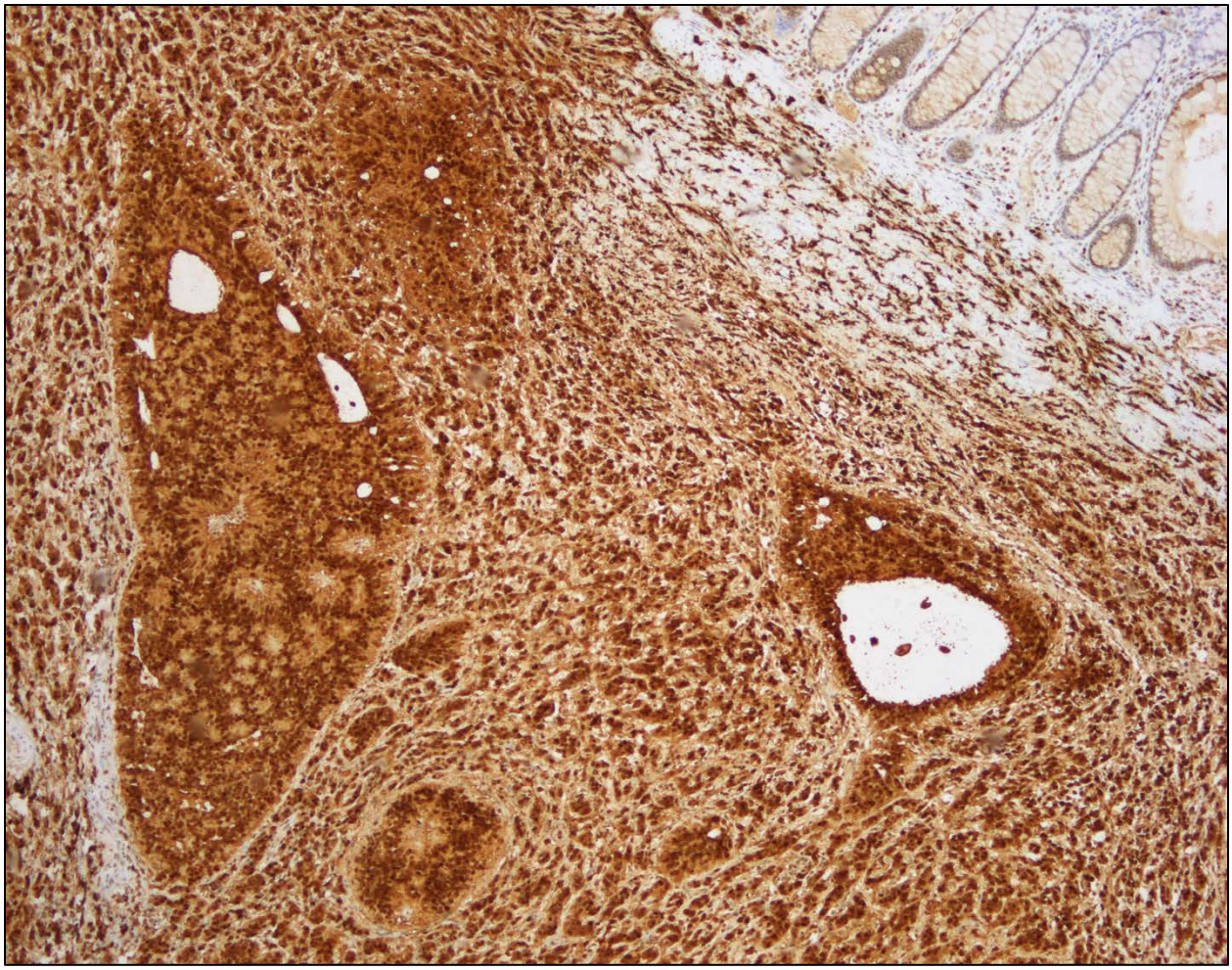

Fig 4. Sigmoid mass resection, S100 (10x).

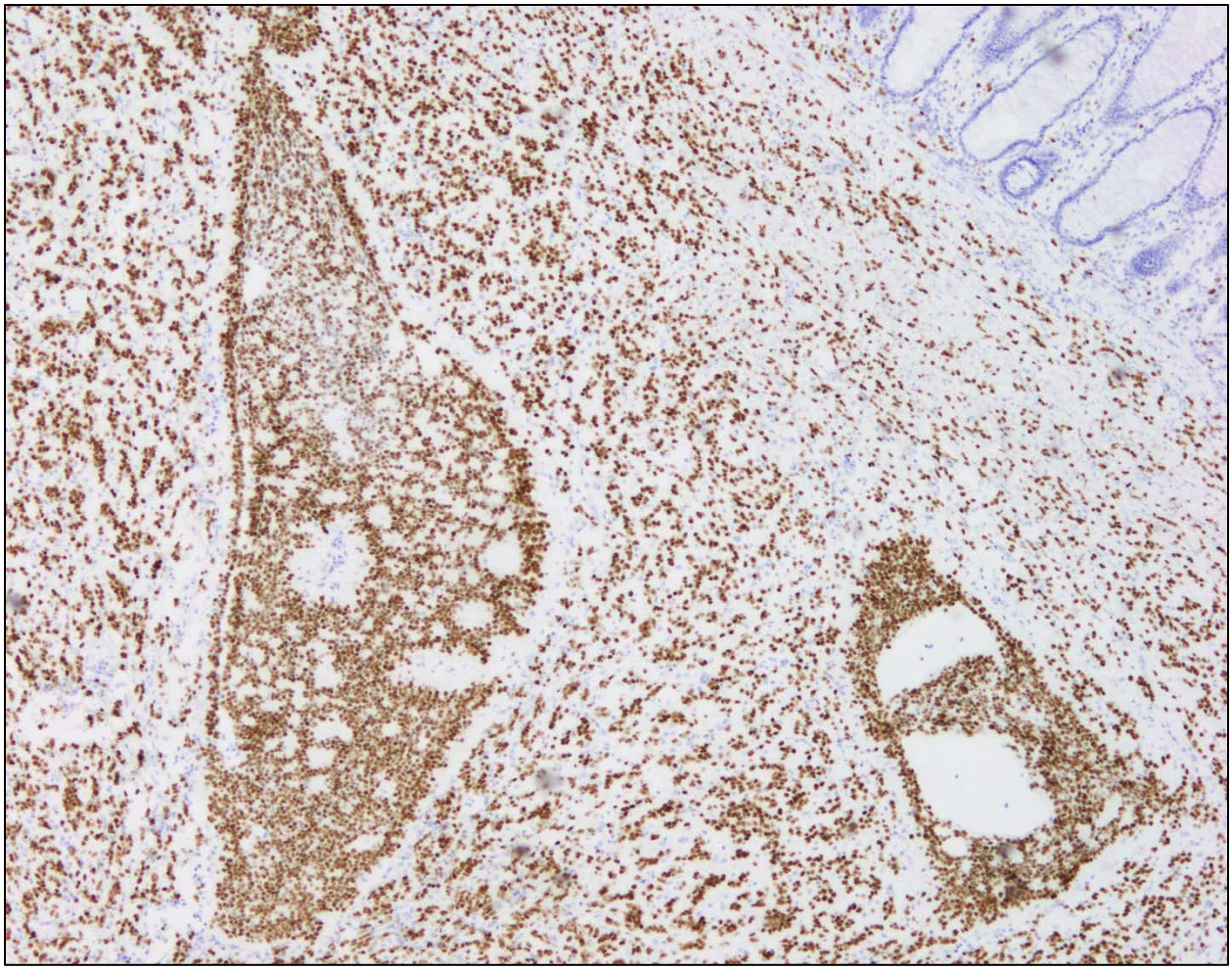

Fig 5. Sigmoid mass resection, SOX-10 (10x).

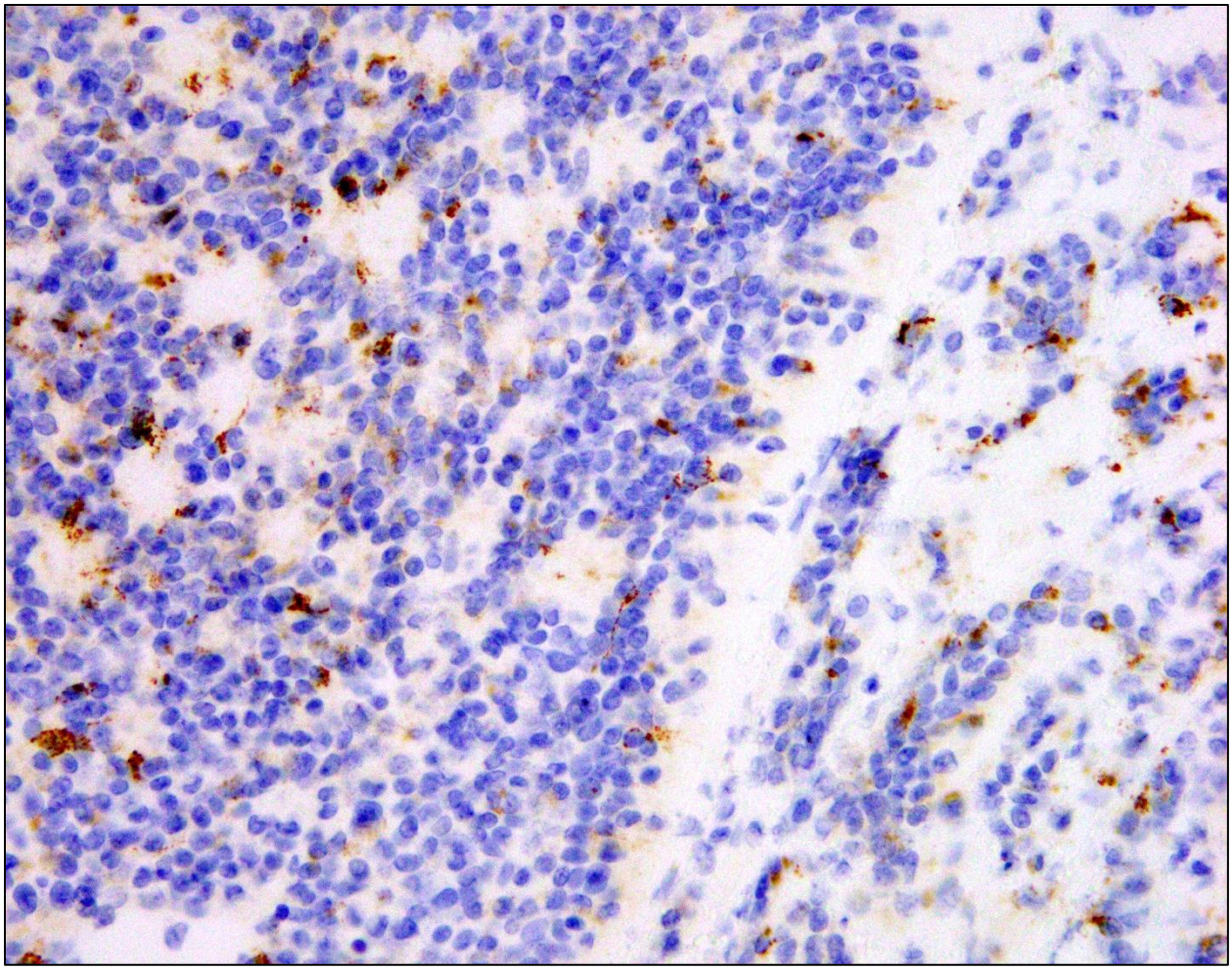

Fig 6. Sigmoid mass resection, Melan-A/MART-1 (20x).

What is the most likely diagnosis?

a. Gastrointestinal stromal tumor
b. Malignant gastrointestinal neuroectodermal tumor
c. Neuroblastoma-like schwannoma
d. Epithelioid malignant peripheral nerve sheath tumor
e. Metastatic melanoma

Correct Diagnosis

c. Neuroblastoma-like schwannoma

Description of Findings and Differential Diagnosis

Macroscopically, the sigmoid colon resection specimen demonstrated a 14-mm well-circumscribed, tan-white, submucosal mass with homogeneous cut surface. Histologically, the tumor was non-encapsulated and showed relatively well-circumscribed, biphasic proliferation of spindle cell and epithelioid cells with surrounding mild lymphocytic inflammation. The spindle cell component consisted of bland, plump cells organized in short fascicles; areas of palisading were noted. The epithelioid areas were well-delineated from the spindled component and were composed of round, epithelioid cells with delicate chromatin and moderate amount of eosinophilic cytoplasm. Several foci of rosettes with morphologic features suggestive of Homer-Wright rosettes were noted. No significant mitotic activity, nuclear pleomorphism, or necrosis was appreciated. In addition to the above described immunophenotype, an immunostain for SMARCB1/INI-1 showed intact nuclear staining.

The histologic features of this case suggest a differential diagnosis of well-differentiated neuroendocrine tumor, neuroblastoma, schwannoma, epithelioid malignant peripheral nerve sheath tumor, and malignant gastrointestinal neuroendocrine tumor. The negative staining for cytokeratin, chromogranin and synaptophysin rules out a neuroendocrine tumor, and the positive staining for S100 and SOX-10 supports a neural origin for this neoplasm. Gastrointestinal stromal tumor is a possibility, however, immunostains for DOG-1 and KIT were negative. Diffuse staining for S100 and SOX-10 is seen in malignant gastrointestinal neuroectodermal tumors; however, these tumors generally feature sheets and nests of epithelioid cells with more pleomorphic nuclei than seen in this case, as well as aggressive features such as mucosal or transmural infiltration, hemorrhage, necrosis, or mitotic activity. Neuroblastoma would also demonstrate malignant histologic features in addition to classic “small round blue cell” morphology, which are not seen in this case; also, the patient’s age and the immunophenotype exclude neuroblastoma.

The focal positive staining for Melan-A/MART-1 brings metastatic melanoma into the differential diagnosis. However, the histologic features are not in keeping with melanoma, as the histology does not show significant nuclear pleomorphism or mitotic activity. In addition, a small percentage (~10-15%) of nerve sheath tumors are known to show positive staining for melanocytic markers. This patient’s lack of history of melanoma is also helpful.

Given the epithelioid morphology of the cells and the strong S-100 expression, an epithelioid malignant peripheral nerve sheath tumor is a consideration. These lesions can infrequently contain areas of primitive neuroepithelial differentiation showing small cells in cords, nests, or very rarely, rosettes. In this case, immunohistochemistry for INI-1 was performed, as it is lost in approximately 50% of epithelioid malignant peripheral nerve sheath tumors. In this case, INI-1 was intact, and the histology is cytologically bland without evidence of invasion, arguing against this diagnosis.

Schwannoma is known to rarely demonstrate areas of small, epithelioid Schwann cells with rosette formation. This is known as the neuroblastoma-like variant of schwannoma. Several features in this case favor a schwannoma: the morphology of the spindle cell component with a peripheral rim of lymphocytes, the characteristic immunophenotype, and the lack of malignant features. Taken together, the findings are diagnostic of neuroblastoma-like schwannoma. These lesions have a benign natural history and are most common in cutaneous soft tissue locations, but have been also reported in pleural, intradural, skull base, and orbital locations [1]. To our knowledge, this is the first report of occurrence in the gastrointestinal tract.

1. Mahjoub WK, Jouini R, Khanchel F et al. Neuroblastoma-like schwannoma with giant rosette: A potential diagnostic pitfall for hyalinizing spindle cell tumor. Journal of Cutaneous Pathology. 2019; 46:234-237.

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