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Colorectal Mucosal Schwann-cell Hamartoma: A Case Report and Review of the Literature

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Abstract **Background:** Here, we report a sigmoid mucosal Schwann cell hamartoma as an uncommon entity. Though unexpected, the pathologist should consider this among differential diagnoses and be able to distinguish the microscopic features when examining colorectal biopsies. Finally, we have reviewed the literature for similar cases reported over the past two decades. **Case presentation:** A 55-year-old woman was found to have a 5 mm sessile polyp during her screening colonoscopy. The microscopic study revealed colonic mucosa with ill-defined proliferation of uniform spindle-shaped cells arranged in a haphazard pattern within the lamina propria. All cells had elongated bland nuclei with eosinophilic cytoplasm and unclear cell borders. Edema and mild lymphoplasmacytic infiltration were noticed in the lamina propria. No nuclear atypia, necrosis, or mitosis was identified. On immunohistochemistry, Schwann cells showed diffuse and strong nuclear and cytoplasmic positivity for S-100 protein. CD117 (C-kit) and desmin were negative. **Conclusion:** Colorectal MSCH has a benign nature, and the lack of axons and strong immunoreactivity for S-100 protein can help distinguish MSCH from most similar entities.

Keywords: *schwann cell hamartoma, neurofibroma, neuroma, colorectal polyp*

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1. Introduction

Originating from the perineural Schwann cells, colorectal mucosal Schwann cell hamartomas (MSCHs) are classified as nonepithelial tumors and are relatively rare benign tumors. However, over the past years, centers have increasingly been reporting these benign tumors, possibly due to widely used colorectal cancer screening colonoscopies. Here, we are reporting a case of sigmoid MSCH located during a screening colonoscopy. We also review the literature for cases reported over the past two decades.

2. Case Presentation

Clinical Findings: A 55-year-old female with a remote history of HIV infection, status post-HARRT, now with undetectable virus load, was referred for CRC screening.

Gross Features: Colonoscopy showed medium-sized internal hemorrhoids and also a sessile polyp of about 5 mm in the sigmoid colon. (Figure 1-A) The biopsy removed the entire lesion. Computed tomography with intravenous contrast was negative for metastasis or colonic wall thickening.

Histologic Findings: Hematoxylin and eosin stains revealed colonic mucosa with ill-defined proliferation of uniform spindle-shaped cells arranged in a haphazard pattern within the lamina propria. (Figure 1-B) All cells had elongated bland nuclei with eosinophilic cytoplasm and unclear cell borders. Edema and mild lymphoplasmacytic infiltration were noticed in the lamina propria. No nuclear atypia, necrosis, or mitosis was identified. (Figure 1-C)

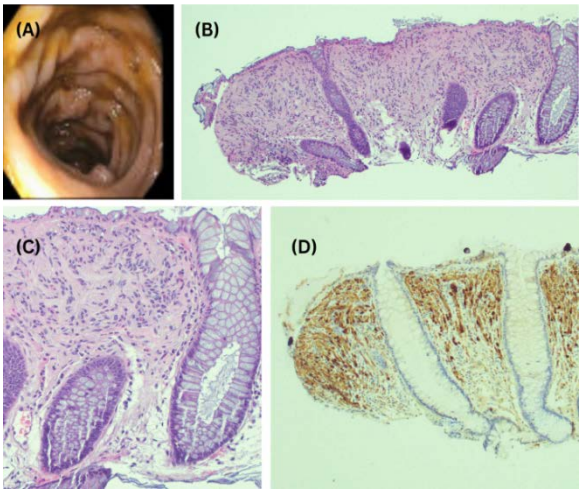

Figure 1. (A) Colonoscopy showing a 5 mm sessile polyp in the sigmoid colon. (B) Low power hematoxylin and eosin stains: Colonic mucosa with ill-defined proliferation of uniform spindle-shaped cells arranged in a haphazard pattern within the lamina propria. (C) High power hematoxylin and eosin stains: Cells show elongated bland nuclei with indistinct cell borders. Edema and mild lymphoplasmacytic infiltration in the lamina propria. (D) **On immunohistochemistry** Schwann cells showed diffuse and strong nuclear and cytoplasmic positivity for S-100 protein.

Immunohistochemical Findings: Schwann cells showed diffuse and strong nuclear and cytoplasmic positivity for S-100 protein. (Figure 1-D) Desmin and CD117 (C-kit) were negative.

Diagnosis: The patient denied any personal or family history suggesting MEN 2B or NF1, including neurofibromatosis, café au lait spots, or adrenal or thyroid diseases. Dermatological examination, laboratory tests, and imaging also found no relevant findings to MEN 2B or NF1. Considering the history and microscopic findings, the diagnosis of the sigmoid colon MSCH was made.

3. Review

Here, we reported a case of an MSCH in a patient with a history of HIV. We also searched PubMed for Mesh and non-Mesh terms related to colorectal mucosal Schwann cell hamartoma. This search found twenty case reports [1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20] (Table 1) and two series. [21,22] (Table 2) We did not include studies that solely reported tactile corpuscle-like bodies or neurofibromal polyps in the gastrointestinal mucosa unless an ultimate diagnosis of Schwann cell hamartoma was made.

In 2009, Gibson et al. [22] reported 26 cases of MSCH with 1– 6 mm colorectal sessile polyps, while most were asymptomatic. After their series, several others presented similar entities as single case reports until Li et al. [21] published the second series, including 48 MSCH patients.

Histologically, MSCHs comprise uniform spindle cells spreading between the glands or crypts in the lamina propria. Cell borders are unclear, and cells appear bland and have eosinophilic cytoplasm with elongated, tapering, or wavy nuclei. MSCH might occasionally show degenerative atypia (ancient change), but nuclear atypia is uncommon, and mitosis is always absent. Immunohistochemically, cells are positive for S100 protein and negative for GFAP, CD34, EMA, CD117, SMA, CD68, and DOG1. [23] The differential diagnoses are GIST and colorectal neural lesions, including neurofibromas, schwannomas, neuromas, perineuriomas, granular cell tumors, ganglioneuromas, and benign mucosal epithelioid nerve sheath tumors.

Distinguishing Schwannoma from Schwann cell hamartoma is often challenging, but colonic schwannomas can occur throughout the colon as an intraluminal polypoid mass with or without mural involvement. [24] Histologically, GI schwannomas are relatively well-circumscribed but unencapsulated lesions showing peripheral lymphoid cuff with germinal centers. Conversely, the microscopic study of the present report found a lack of circumscription and crypt entrapment, which is typical of the MSCH polyps. Given their marked propensity for the rectosigmoid colon, much higher prevalence, and discussed histologic differences, MSCH polyps can be differentiated from Schwannomas. Also, MSCHs are generally smaller in size.

Visceral neurofibromas are known to be highly associated with NF1. Considering the rarity of colorectal sporadic neurofibromas, finding any neurofibroma in the colon should raise the suspicion for NF1. Neurofibromas have a heterogeneous cellular composition, including Schwann cells, perineurial-like cells, fibroblasts, and axons. In contrast, the MSCHs depict uniform cytology, comprised of a pure population of Schwann cells with diffuse immunoreactivity for S-100 protein. Also, while all colorectal neurofibromas contain scattered axons, only a small subset of the MSCHs contain these cellular microstructures. [22]

A more recent body of evidence indicates that GISTs are more common than neurofibromas as GI presentations of NF1. [24] Thus, many noted “leiomyomas” in the past literature might have been GISTs. GISTs are positive not only often for S-100 but also characteristically for c-Kit (CD117), distinguishing them from mucosal Schwann cell hamartomas. [15]

The mucosal neuroma is another differential diagnosis, an infrequent entity highly associated with MEN 2B. [25] Histologically, mucosal neuromas consist of hyperplastic bundles of nerve fibers associated with abundant axons. In contrast, in MSCHs, axons are not frequent, and hyperplastic nerves are absent. [22]

The MSCHs can also be mistaken for ganglioneuromas. Ganglioneuromas are benign lesions of ganglion cells, nerve fibers, and Schwann cells. Colorectal ganglioneuromas can be seen as solitary polypoid ganglioneuromas, diffuse ganglioneuromatosis, and ganglioneuromatous polyposis. Ganglioneuromatous polyposis is associated with Cowden syndrome [26], and ganglioneuromatosis is associated with MEN 2B or NF1. [27] History and the presence of multiple neural polyps can distinguish these two inherited syndromes from MSCH. Also, in contrast to solitary polypoid ganglioneuromas, in terms of IHC study, MSCH is negative for ganglion cells, and axons are usually absent. [22]

Another diagnosis to exclude is intramucosal perineuriomas, most commonly seen in the distal colon as small, sessile polyps. [28] Intramucosal perineuriomas are poorly circumscribed and, like MSCHs, show entrapment of colonic crypts. Still, the stroma is looser and less eosinophilic, and the cells are usually slender or ovoid in a lamellar or whorled pattern. Perineuriomas are negative for S-100 protein, immunoreactive for EMA, and sometimes positive for claudin-1. Finally, not seen in MSCHs, two-thirds of intramucosal perineuriomas are associated with hyperplastic polyps. [28]

Incidentally detected during endoscopy, granular cell tumors are seen as small mucosal nodules, while extracolonic tumors might also be present. Histologically, lesions comprise large cells with small nuclei and ample granular cytoplasm. MSCHs are positive only for S-100, but granular cell tumors are positive for CD68 and S-100. [5]

Finally, similar to the MSCHs, mucosal benign epithelioid nerve sheath lesions can surround crypts, show strong positivity for S-100, and cells lack axons. [25] While the MSCHs are solely restricted to the lamina propria, the mucosal epithelioid nerve sheath tumors often expand into the superficial submucosa. Further studies might answer if these two entities are distinct lesions or parts of the same benign intramucosal Schwann cell proliferation spectrum. [22]

Table 1. Mucosal Schwann cell hamartoma (MSCH) case reports

#	Case reports	Findings
1	Salam et al. 2023 [1]	**Clinical Findings:** A 65-year-old female who was presented for screening colonoscopy in the ground of sigmoid diverticulum, and the family history of pancreatic and breast cancer. **Gross Features:** A 3 mm sessile polyp was identified in the sigmoid colon and removed. **Histologic Findings:** Mucosal spindle cell proliferation consistent with MSCH. **Immunohistochemical Findings:** S-100 was the only stain the spindle cells exhibited, whereas CD34, CD117, desmin, smooth muscle antigen (SMA), and anti-mitochondrial antibody (AMA) were negative. **Work-up and follow-up**: Negative CT chest/Abdomen/Pelvic for metastasis.
2	Mauriz Barreiro et al. 2023 [2]	**Clinical Findings:** A 50-year-old woman who had undergone bilateral adnexectomy due to BRCA1 mutation was referred for colonoscopy. She had two weeks of painless rectal bleeding, and an anal examination revealed no external or internal hemorrhoids. **Gross Features:** The colonoscopy revealed no abnormalities in the entire colon. Rectal retroflexion showed swollen internal hemorrhoids and circumferential mucosal induration of fifty percent, proximal to the dentate line. Biopsies were taken. **Histologic Findings:** Diffuse spindle-shaped cells with eosinophilic cytoplasm and ill-defined cell borders were found in the lamina propria. Mitotic activity and nuclear atypia were not found. **Immunohistochemical Findings:** Cells were diffusely positive for S-100, and CD34, SMA, EMA, and c-kit were all negative. **Work-up and follow-up:** MSCH was a benign lesion, so the patient was released from the hospital without a repeat colonoscopy. Internal hemorrhoids were the cause of the rectal bleeding.
3	Okamoto et al. 2021 [3]	**Clinical Findings:** During the screening colonoscopy of a 64-year-old man with hypertension, diabetes, and atrial fibrillation who was treated with an anticoagulant, an incidental lesion of the sigmoid colon was identified. The patient had no clinical or laboratory features of MEN2B or NF1. **Gross Features:** 12 mm subepithelial lesion, excisional biopsied. **Histologic Findings:** Spindle-shaped cells in the lamina propria, eosinophilic cytoplasm with indistinct cell borders, and tapered or elongated nuclei were present. Crypts and goblet cells were intact. The interstitium was edematous and infiltrated by mild lymphocytes and plasma cells. **Immunohistochemical Findings:** Schwann cells positive for S-100 and negative for CD56, CD34, and NFP were specified. Pan-cytokeratin (AE/AE3), desmin, chromogranin A, and synaptophysin stains were all negative. **Work-up and follow-up:** At follow-up colonoscopy, numerous edematous, submucosal protrusions as skip-lesions were left throughout the sigmoid colon. Some lesions had fine white granular opacities on their surface on narrow-band imaging, all with elongated crypt openings, increased width of intervening parts, and no visible small vessels on magnifying narrow-band imaging. 18-month follow-up colonoscopies did not suggest any change in MSCH lesions of the sigmoid colon. The patient remained asymptomatic without treatment. (Endoscopic ultrasound revealed mild, homogeneously hypoechoic thickening of the first layer (superficial mucosa) with no involvement of the second layer (deep mucosa). CT scan showed no tumor or thickening of the colonic wall.
4	Vaamonde-Lorenzo et al. 2020 [4]	**Clinical Findings:** A 54 years old man with a positive fecal occult blood test was found to have a lesion 35 cm away from the anal margin during a colonoscopy. Eleven years ago, he was diagnosed with pulmonary tuberculosis and a drained perianal abscess. There was no evidence of inflammatory bowel disease, neurofibromatosis, Cowden syndrome, or numerous neuroendocrine syndromes in his family. **Gross Features:** One sessile polyp measuring 10 mm that was located 15 cm from the anal margin was excised with a hot snare. The adjacent mucosa was grossly unremarkable. Also, another sessile polyp measuring 5 mm that was located 35 cm from the external anal margin was excised by a cold snare. **Histologic Findings:** The first polyp, measuring 10 mm, was hyperplastic, and the second polyp, measuring 5 mm, had spindle cell proliferation in its lamina propria composed of elongated bland nuclei without mitotic figures. **Immunohistochemical Findings:** The cells showed immunoreactivity for S100, but SMA, CD34, c-KIT, or epithelial membrane antigen (EMA) were all non-reactive. **Work-up and follow-up:** N/A
5	Feng et al. 2020 [5]	**Clinical Findings:** The screening colonoscopy of a 60-year-old African-American woman, without any history of gastrointestinal disorders or neuronal lesions in her family, revealed a polypoid lesion. **Gross Features:** A 4 mm sessile polyp in the sigmoid colon with no erosion or ulceration. **Histologic Findings:** The microscopic study showed diffuse, unorganized proliferation of benign spindle cells in the lamina propria with intervening intact colonic crypts. The nuclei were wavy and uniform. No nuclear atypia, necrosis, or mitotic figures were identified. **Immunohistochemical Findings:** The spindle cells were strongly reactive for S-100. CD34, SMA, c-Kit (CD117), CD68, and EMA were negative. **Work-up and follow-up:** N/A.
6	Jusue Irurita et al. 2020 [6]	**Clinical Findings:** Colonoscopy was done for a 39-year-old man after acute diverticulitis. The patient had no medical or family history. **Gross Features:** An 8 mm sessile polyp (Paris 0-Is, NICE 1) was removed from the descending colon. **Histologic Findings:** The microscopic study revealed bland spindle cell proliferation in the colonic mucosa. **Immunohistochemical Findings:** Spindle cells were positive for S-100 and CD-34, which is consistent with a benign mesenchymal polyp (Schwann cell hamartoma phenotype) **Work-up and follow-up**: N/A
7	Hashimoto et al. 2019 [7]	**Clinical Findings:** A 40-year-old woman presented with fecal occult blood. She had no significant medical, surgical, or family history but a colonoscopy and removal of a small polyp at 17. **Gross Features:** A 5-mm sessile polyp was resected at the rectosigmoid junction. Also, two ultimately diagnosed tubular adenoma polyps were resected from the ascending and sigmoid colon. **Histologic Findings:** The polyp had an atrophic columnar epithelium without atypia. Spindle cells with dense eosinophilic cytoplasm were present between mucosal crypts with decreased cellularity, imitating fibromuscular obliteration. However, distinct from mucosal prolapse syndrome, spindle cells were more

		abundant in the superficial mucosa than in depth. Nuclear palisading of the spindle cells was partially visible, suggesting neural differentiation. The lesion revealed neither mitotic figures nor lymphocytic foci. **Immunohistochemical Findings:** The spindle cells were diffusely positive for S-100, but claudin-1, α-smooth muscle actin, glucose transporter-1, HMB-45, CD34, Melan-A, and c-Kit were all negative. Neurofilament fibers were scarcely seen. Since partial S-100 positivity and scattered neurofilaments were not present, neurofibroma was excluded. Perineurioma was ruled out, too. The Schwannoma was excluded, considering the absence of supporting cells and a lymphoid cuff. **Work-up and follow-up:** N/A
8	Chintanoboina et al. 2018 [8]	**Clinical Findings:** A screening colonoscopy was performed on a 55-year-old woman who had no symptoms other than a history of multiple sclerosis. She was on Glatiramer acetate (Copaxone) 40 mg three times weekly. Neurofibromatosis, Von Recklinghausen syndrome, Cowden syndrome, familial hereditary polyposis, and colon cancer were not in the family history. Her father was found to have colon polyps of undetermined pathology at 72 years old. **Gross Features:** Two completely excised low-risk tubular adenomas were found in the cecum and ascending colon, each measuring 5 mm. **Histologic Findings:** The ascending colon polyp displayed diffuse spindle cell growth but no ganglion cells in the lamina propria. **Immunohistochemical Findings:** Strong and diffuse immunoreactivity to S100, but not with CD117, neurofilament protein (NFP), or smooth muscle actin (SMA). **Work-up and follow-up**: A follow-up colonoscopy was scheduled for the low-risk tubular adenoma five years later.
9	Garcia-Molina et al. 2018 [9]	**Clinical Findings:** A colonoscopy was performed on a 39-year-old male who screened positive for fecal occult blood, although he had no history of MEN2b, Cowden syndrome, NF, or ulcerative colitis in his family. **Gross Features:** A rectosigmoid polyp was noticed [and biopsied] **Histologic Findings:** Hematoxylin and eosin and periodic acid-Schiff (PAS) stains showed a polypoid area of colonic mucosa with sheets of bland spindle cells in the lamina propria with elongated nuclei. Pleomorphism, mitotic figures, and ulceration of the surface were not observed. **Immunohistochemical Findings:** High reactivity for the S100 protein and negative for EMA, and CD34. **Work-up and follow-up:** N/A
10	Gaspar et al. 2017 [10]	**Clinical Findings:** Our outpatient clinic was notified about rectal bleeding in a 42-year-old male patient who did not have any prior medical history and was not on any medication. Both the physical exam and the laboratory results were within normal limits. **Gross Features:** Upon NBI evaluation, the colonoscopy revealed a flat granular lesion in the rectum measuring 30x15mm, but it did not exhibit the usual pattern of an adenoma. No evidence of dysplasia was identified on biopsies, and the whole tumor was successfully resected by endoscopic submucosal dissection. **Histologic Findings:** Microscopic evaluation showed abundant spindle cells with elongated nuclei in the [lamina propria] with no nuclear atypia, pleomorphism, or mitoses. **Immunohistochemical Findings:** The cells showed strong and diffuse positivity for S-100 protein, with no immunoreactivity to SMA, desmin, or epithelial membrane antigen. **Work-up and follow-up:** N/A
11	Han et al. 2017 [11]	**Clinical Findings:** A follow-up colonoscopy was performed on a 49-year-old man after resection of a tubular adenoma two years ago. He did not have any neuronal lesions or genetic diseases in his family. **Gross Features:** The colonoscopy showed a two-millimeter rectal polyp. **Histologic Findings:** A histologic study revealed ill-defined growth of spindle cells between crypts of the lamina propria. Cells had monomorphic slender nuclei and ample pink cytoplasm with unclear cell boundaries. No dysplasia or mitosis was identified. **Immunohistochemical Findings:** There was strong and diffuse nuclear and cytoplasmic S-100 reactivity. The glial fibrillary acidic protein (GFAP), smooth muscle actin, c-Kit, CD34, EMA, and neurofilament protein (NFP) were all negative. **Work-up and follow-up:** N/A
12	Kanar et al. 2015 [12]	**Clinical Findings:** A follow-up colonoscopy was performed on a 67-year-old African - American man after resection of a tubulovillous adenoma five years ago. On his repeat colonoscopy 1 year later, four tubulovillous polyps identified. There was no history of familial adenomatous polyposis, neurofibromatosis type I, multiple endocrine neoplasia type IIb, or Cowden syndrome in his family; however, his mother was diagnosed with colon cancer when she was 65 years old. The physical examination was within normal limit. **Gross Features:** One 4mm polyp in the descending colon and one 6mm polyp in the sigmoid colon. **Histologic Findings:** Microscopic study of the sigmoid colon revealed polypoid colonic mucosa with expansion of lamina propria containing abundant spindle cells with slender nuclei. On the microscopic study of the descending colon, one tubular adenoma was determined. **Immunohistochemical Findings:** Spindle cells of sigmoid colon polyp were homogenously positive for S-100 but negative for CD34 and CD117. **Work-up and follow-up:** N/A
13	Bae JM et al. 2015 [13]	**Clinical Findings:** A male of 20 years of age with positive family history including colorectal carcinoma in his mother and grandfather, came in complaining of abdominal pain and diarrhea. His physical examination was within normal limit. **Gross Features:** During the work-up proctosigmoidoscopy, one 4mm polyp in the middle portion of the rectum and few polypoid projections in the distal rectum were found. The excisional biopsy of mid-rectum polyp and three random biopsies of distal rectum mucosa were sent for pathology. **Histologic Findings:** Microscopic evaluation of mid rectum polyp and one of the distal lesions showed netlike spindle cell growth in the lamina propria between the surrounding crypts. The lesional cells had slender monomorphic nuclei with pale-pink cytoplasm and unclear cell boundaries. Dysplasia or mitotic figures were not present. **Immunohistochemical Findings:** S-100 was strongly and diffusely positive in proliferating cells, however no activity for CD117, CD34, EMA, synaptophysin, smooth

		muscle actin, and epithelial membrane antigen (EMA) was seen. There were no positive axons highlighted by neurofilament protein (NFP) stain. **Work-up and follow-up:** No functional mutations or mosaicism were detected by gene sequencing of NF1 and RET.
14	Klair et al. 2014 [14]	**Clinical Findings:** A Caucasian 78-year-old female who underwent excision and chemoradiation for rectal cancer fifteen years ago, presented with long standing abdominal pain and acute left lower quadrant tenderness. He has been on rectal steroids for post-radiation proctitis. **Gross Features:** A 5-mm polyp (tubular adenoma) in the ascending colon, a 7-mm polyp in the rectum, and an inflamed and erythematous rectal mucosa with no erosions or ulcerations were discovered during the colonoscopy. **Histologic Findings:** The rectal polyp was stained with hematoxylin and eosin (H&E), which showed an ill- defined, uniform-looking proliferation of elongated cells with deeply eosinophilic cytoplasm. No features of dysplasia were identified. **Immunohistochemical Findings:** Strong reactivity for S-100 in spindle cells and Neurofilament protein (NFP) positivity of scattered axons were noted. Glial fibrillary acidic protein (GFAP), CD34, smooth muscle actin (SMA), c-KIT, EMA, and claudin-1 were not stained. **Work-up and follow-up:** There was no evidence of Cowden syndrome, neurofibromatosis type I, and multiple endocrine neoplasia type 2B in her personal or family history.
15	Neis et al. 2013 [15]	**Clinical Findings:** An annual surveillance colonoscopy was done for a 5-year-old man with a history of ulcerative colitis and associated primary sclerosing cholangitis. He was clinically in remission with oral mesalamine. The only positive medical history was adenomatous polyps of colon found one year ago. He did not have a family history of neurofibromatosis, Cowden syndrome, multiple endocrine neoplasia type 2b (MEN 2b), NF-1 or Cowden syndrome. **Gross Features:** The colonic and ileal mucosa seemed normal throughout the colonoscopy. A 3-mm sigmoid polyp was excised by the cold snare, and the surrounding mucosa was randomly sampled. **Histologic Findings:** Hematoxylin and eosin-stained tissue showed expanded lamina propria inside the colonic polypoid mucosa composed of benign spindle cells with slender nuclei and deeply eosinophilic cytoplasm with indistinct cell borders. No dysplasia or mitotic figures identified. The mucosa around the polypectomy site was negative for dysplasia. **Immunohistochemical Findings:** The spindle cells were significantly positive for S-100. All other markers including Claudin-1, CD117, CD34, and epithelial membrane antigen (EMA were non-reactive. **Work-up and follow-up:** Discussing potential association of the patient's ulcerative colitis and MSCH was deferred. Follow up findings remained unchanged up to the time of the report.
16	Bae MN et al. 2013 [16]	**Clinical Findings:** A 41-year-old woman without any family history of gastrointestinal malignancies, or NF1, was found to have a polyp on her screening colonoscopy. **Gross Features:** Loop snare polypectomy removed the 8 mm polyp in the descending colon, which had no erosion or ulceration. **Histologic Findings:** Included mucosal diffuse spindle cell proliferation in the lamina propria with entrapped colonic crypts. Cells had tapering, elongated nuclei, abundant dense eosinophilic cytoplasm, and faint cell borders but no nuclear atypia, mitosis, or pleomorphism. **Immunohistochemical Findings:** The lesion was strongly positive for the S-100 but negative for CD117, CD34, or smooth muscle actin. A homogeneous proliferation of fusiform Schwann cells was observable. **Work-up and follow-up:** N/A
17	Ferro de Beca et al. 2013 [17]	**Clinical Findings:** A 72-year-old male with no history of colonic polyps or family history of inherited syndromes (including Cowden syndrome, NF-1, or MEN-2B) presented for a screening colonoscopy. **Gross Features:** In colonoscopy, a 5-mm distal sigmoid mucosal polypoid lesion was biopsied. **Histologic Findings:** The lamina propria contained numerous well defined, uniform, bland spindle cells with faint cell borders. The cytoplasm was densely eosinophilic. The nuclei had fine chromatin with occasional inconspicuous nucleoli. The epithelium displayed some glandular hyperplasia without dysplasia or ulceration. **Immunohistochemical Findings:** Spindle cells strongly and diffusely expressed S-100 but did not express CD117 (KIT), smooth muscle actin, epithelial membrane antigen (EMA), or synaptophysin. **Work-up and follow-up:** N/A
18	Sagami et al. 2012 [18]	**Clinical Findings: A 40-year-old male with no history or clinical finding suggestive of MEN-2B or NF1 was referred for the positive fecal occult blood test.** **Gross features: The** colonoscopy indicated numerous small mucosal white nodules in the sigmoid colon. **Histologic Findings:** The lamina propria was affected by the spindle cell proliferation. **Immunohistochemical Findings:** Included strong and diffuse positivity for S-100. **Work-up and follow-up:** Ultrastructural studies were negative for epithelial membrane antigen and neurofilament protein.
19	Rocco et al. 2011 [19]	**Clinical Findings:** A 67-year-old female presented for the follow-up colonoscopy, status post partial-colectomy a year prior, for a 4.5 cm lesion at her descending colon. The resected lesion was diagnosed as tubulovillous adenoma with low-grade dysplasia. She had no family history or clinical findings indicating inherited syndromes like Cowden syndrome, NF-1, or MEN 2B as the possible etiology. **Gross Features:** A cold biopsy excised the 3 mm sessile polyp at 30 cm proximal to the anal verge. **Histologic findings:** The ill-defined lesion had an intact epithelium and muscularis mucosa but showed mucosal diffuse spindle cell proliferation in the lamina propria with entrapped colonic crypts. Cells had tapering, elongated nuclei, abundant dense eosinophilic cytoplasm, and faint cell borders without nuclear atypia, mitosis, or pleomorphism. **Immunohistochemical Findings:** Strongly positive for S-100 but no immunoreactivity for C-KIT (CD117), CD34, or smooth muscle actin. **Work-up and follow-up:** The patient was scheduled for the next year computed tomography and colonoscopy.

20	Pasquini et al. 2009 [20]	**Clinical Findings:** A 60-year-old woman with no family history of colon cancer, NF I, MEN Ⅱb, Cowden, or familial adenomatous polyposis underwent a colonoscopy for positive fecal occult blood. **Gross Features:** A 0.5 cm rectosigmoid sessile polyp with no mucosal ulceration was identified and biopsied. **Histologic Findings:** The lesion core was in the lamina propria without penetration to the muscularis mucosae, showing the diffuse cellular proliferation of uniform spindle cells in whorls pattern and with unclear cell borders, entrapping crypts. Elongated, tapering nuclei were visible but with no nuclear atypia, mitoses, or pleomorphism. Mild chronic inflammation, including some mast cells, was diffusely observable. **Immunohistochemical Findings:** Extensive and strong positivity for the S-100 but negative reactivity to smooth muscle actin, C-KIT (CD117), and CD34. **Work-up and follow-up:** N/A

Table 2. Case series of colorectal mucosal Schwann cell hamartomas (MSCHs)

#	Study	Population	Clinical findings	Gross features	Histologic findings	IHC findings	Work-up and follow-up
1	Li et al. 2020 [21]	48 patients Diagnosed with colonic MSCHs. 23 M, 25 F; The mean age was 60.4 (32–81).	Screening colonoscopy was done for 38 patients: 5 pts for GIB, 2 for diarrhea, 1 for CRC follow-up, 1 for constipation, and 1 for abdominal pain.	Twenty-three lesions were from the descending, eight from the sigmoid, and seven from other parts of the colon. The range of polyps size was 1–10 mm with a mean of 3.7 mm.	MSCH diagnoses were made by studying 46 targeted biopsies, one random biopsy in a diarrhea work-up, and one biopsy from a 2 cm cecal high-grade dysplastic tubulovillous adenoma. Forty-four MSCH cases were found in normal mucosa as isolated polyps, and four MSCHs were identified as a part of sessile serrated, inflammatory, or hyperplastic polyps. All polyps showed ill-defined growth of diffuse spindle cells with indistinct borders and slender benign nuclei associated with large eosinophilic cytoplasm occupying the lamina propria. Muscularis mucosa and submucosa were uninvolved. Few lymphocytes and eosinophils were identified. No evidence of granuloma, mitoses, ganglion cells, or necrosis was seen.	Immunohistochemistry revealed nuclear and cytoplasmic S100 reactivity in all lesions. The markers for SMA, EMA, desmin, CD117, CD34, CD68, and DOG1 were negative in all cases except for one descending colon lesion with CD34 positivity and a cecal lesion with patchy desmin reactivity.	No genetic syndromes, including NF1, were present.
2	Gibson et al. 2009 [22]	26 patients 16 F, 10 M, Age 46-88	All had polyps identified during colonoscopy. Eighteen asymptomatic pts for CRC screening; 2 for diarrhea, 3 for lower LGIB, and one follow-up for prior CRC, two unknown indications.	15 cases in the rectosigmoid, 2 in the transverse, 2 in the ascending colon, and 7 cases in the descending colon. All polyps were sessile (1 to 6 mm). No one had more than one neural polyp, but some patients had non-neural polyps simultaneously.	All polyps revealed ill-defined expansion of the lamina propria with benign spindle cells with slender and wavy nuclei, wide pink cytoplasm, and unclear cell borders. The nuclei had homogenous chromatin and few invisible nucleoli. Crypts were engulfed by lesional cells. Nuclear atypia, mitotic figures, and mucosal ulceration were not found. Palisading, whirling, or fascicular patterns were not seen.	All polyps [with the later diagnosis of MSCH] showed strong and diffuse S-100 reactivity, and NFP was (+) in 7 lesions. Other tested markers were negative, including GFAP, EMA, claudin-1, CD34, SMA, and KIT. Five biopsies from NF-1-associated neurofibromas showed the same spindle cell proliferation as non-NF1 polyps but less uniformly cellular and more heterogeneous in cytology and IHC. (i.e., scattered S-100 positivity)	The three-month to 17.5 years follow up of the thirteen patients revealed no neuronal lesions or evidences of genetic syndromes including NF1, MEN 2B or Cowden syndrome.

4. Conclusions

In conclusion, we described an incidentally noted sigmoid mucosal Schwann cell hamartoma found during a screening colonoscopy. To our knowledge, this is the first report of this mucosal anomaly in a patient with a history of treated HIV. Clinically, this lesion is benign and is not associated with inherited polyposis syndromes, and follow-up colonoscopy is not different from the recommended schedule in the healthy population. Strong immunoreactivity for S-100 protein and lack of axons can help distinguish MSCHs from similar entities.

ACKNOWLEDGEMENTS

Not applicable.

Statement of Competing Interests

Not applicable.

List of Abbreviations

MSCH, mucosal schwann-cell hamartoma; CRC, colorectal cancer; GIST, gastrointestinal stromal tumor; IHC, immunohistochemistry; LGIB, lower gastrointestinal bleeding; NFP, neurofilament protein; GFAP, glial fibrillary acidic protein; EMA, epithelial membrane antigen; SMA, smooth muscle actin; NF1, neurofibromatosis 1; MEN, multiple endocrine neoplasia.

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