Perineurioma of the colon: an uncommon tumor with an unusual location. Report of a case and review of the literature

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Summary

Introduction
The gastrointestinal perineuriomas usually develop both as intramucosal or submucosal lesions. They can occur at any age but are more common in middle-aged adults with slightly predominance in females¹. Endoscopically they usually present as small (< 0.6 cm), solitary, polypoid lesions, often indistinguishable from epithelial polyps. Perineuriomas are discovered incidentally during a screening colonoscopy in middle-aged adults, and their clinical course is benign². Colorectal perineurioma was firstly described in 2004 by Esami-Varzaneh as fibroblastic polyp³. Later Hornick and Fletcher reported a series of polypoid lesions displaying clinical and histological features identical to those of fibroblastic polyps previously mentioned but with immunohistochemical and ultrastructural features of perineurial cells⁴. The striking morphologic, immunohistochemical and ultrastructural similarities between fibroblastic polyps and perineuriomas led some authors⁵,⁶ to speculate that these lesions may represent different variants of the same tumor entity. To the best of our knowledge, approximately 150 cases of perineuriomas have been reported in the colon-rectum so far⁵-¹⁶. Histologically, gastrointestinal perineurioma is composed of spindle cells with long slender, pale eosinophilic, cytoplasmatic processes, arranged in a storiform, whorled or short fascicular patterns and set in a collagenous stroma. Cytological atypia and mitotic activity are only rarely described²,¹⁷. The spindle cell proliferation involves the lamina propria, often with a periglandular arrangement. There is the possibility that the overlying mucosa shows hyperplastic or adenomatous changes. Originally believed as a reactive phenomenon related to the stromal proliferation, it may be rather a true neoplastic epithelial proliferation that harbors a mutation similar to those seen in other serrated polyps. In a recent study Pai et al. emphasize this relationship suggesting that the common finding of serrated crypts in colonic perineuriomas are suggestive of an epithelial-stromal interaction¹⁶. Immunohistochemically the spindle cells of perineurioma are positive for EMA, claudin-1, GLUT-1 and focally for CD34. Although EMA was originally considered to be a specific epithelial marker, over time its expression has been found in several other cytotypes, including the perineurial cells¹⁸. Claudin-1 is a tight junction-associated protein expressed by perineurial cells. It has been reported as a highly sensitive and specific marker of perineurium
and soft tissue perineurioma, showing a diffuse and strong granular membranous reactivity. GLUT-1 is regarded as a relatively specific marker of perineurial differentiation since it has been found in soft tissue perineuriomas but not in lesions containing fibroblasts, neurons and smooth muscle cells. The aim of the present paper is to describe the clinico-pathologic features of a perineurioma of the sigmoid colon. Pathologists should be aware of the possibility that perineurioma may present as a colorectal polypoid lesion, and thus performing appropriate immunohistochemical analyses for confirming the diagnosis.

Case report

A 40-year old woman with a family history of colorectal cancer, was referred to our gastroenterology section for routine colonoscopy. Physical examination, laboratory tests and her past medical history were unremarkable. No lower GI bleeding was detected, nor abdominal pain, nausea or vomiting. Endoscopically a pedunculated lesion of the sigmoid colon, approximately 8 mm in its greatest diameter, was identified (Fig. 1A). No mucosal erosion/ulceration was noted. According to the endoscopic appearance, the lesion seemed to involve the submucosal layer. The lesion was completely resected. The patient is well after a follow-up period of 6 months.

Materials and methods

The surgical sample was fixed in 10% buffered formalin, embedded in paraffin, and sectioned at 4 µm. Standard stains, including haematoxylin and eosin, as well as immunohistochemical analyses were performed. Immunohistochemical studies were performed with the labeled streptavidin-biotin peroxidase detection system using the Dako automated immunostainer (Dako autostainer link 48, Glostrup, Denmark). The following antibodies were tested: EMA, claudin-1, α-SMA, desmin, CD117, h-caldesmon, S-100 protein, CD99, CD34, B-cell lymphoma 2 protein, β-catenin, STAT-6 and cytokeratins (AE1/AE3 clone).

Pathological findings

Gross examination revealed a lesion measuring 8 mm in its greatest diameter, with a polypoid appearance. Histo-

Fig. 1. (A) Endoscopic view: pedunculated lesion of the sigmoid colon. Lesion seems to involve the submucosal layer. (B) Histological examination showing a marked expansion of the lamina propria with separation of the colonic crypts. Neither mucosal ulceration nor adenomatous or hyperplastic epithelial changes was noticed (Hematoxylin & Eosin). (C) Lamina propria is largely replaced by a bland-looking spindle cell proliferation (Hematoxylin & Eosin). (D) The spindle cells show bipolar and focally ramifying slender cytoplasmic processes which often formed an anastomosing network (Hematoxylin & Eosin).
logically, at low magnification, a marked expansion of the lamina propria with separation of the colonic crypts was evident (Fig. 1A, B). Neither mucosal ulceration nor adenomatous or hyperplastic epithelial changes was noticed (Fig. 1B, C). Higher magnification showed a proliferation of bland-looking, fibroblast-like spindle cells mainly arranged in short fascicles or exhibiting a whorling pattern (Fig. 1C). The spindle cells showed bipolar and focally ramifying slender cytoplasmic processes which often formed an anastomosing network (Fig. 1D). Nuclei were ovoid to elongated. Nuclear atypia and mitoses were absent. The stroma was collagenous with focal edematous changes (Fig. 1D). Immunohistochemically the spindle cells were stained with CD34 (Fig. 2A), EMA (Fig. 2B), and claudin-1. No staining was obtained with the other antibodies tested. Based on the morphological and immunohistochemical features, the diagnosis of “perineurioma” was rendered.

Discussion

Perineuriomas of the colon-rectum are usually asymptomatic and incidentally discovered lesions during screening colonoscopy for colorectal carcinoma. Since their first description in 2004 by Eslami-Varzaneh, about 150 cases of perineuriomas have been reported in the colon-rectum to date. Although the histological diagnosis of intra-neural perineurioma is usually straightforward due to its typical localization and cytological features, it is more challenging for its extraneural counterpart which can pose differential diagnostic problems with other spindle cell lesions. In addition the diagnosis is more difficult when pathologist is facing an extraneural perineurioma which occurs at an unusual site, including the gastro-intestinal tract. Endoscopic features of perineurioma are not specific and the diagnosis is histologically based.

We herein report a case of a polypoid lesion of the sigmoid colon with the morphological and immunohistochemical features of perineurioma. Since its first description the association between perineurioma and hyperplastic changes in the overlying epithelium was noted. In addition Agaimy et al. and Pai et al. discovered BRAF mutation, commonly seen in serrated...


24 Miettinen M, Sarlomo-Rikala M, Sobin LH. Mesenchymal tumors of muscularis mucosae of colon and rectum are benign leiomyomas that should be separated from gastrointestinal stromal tumors—a clinicopathologic and immunohistochemical study of eighty-eight cases. Mod Pathol 2001;14:950-6.