Perineurioma is a relatively rare benign peripheral nerve sheath tumor composed of cells resembling normal perineurium. Although this tumor may arise in the context of a nerve (intra-neural perineurioma), extraneural perineurioma does occur, frequently involving the soft tissues of the lower and upper extremities, trunk and head and neck. Rarely it has also been reported in visceral organs, including gastrointestinal tract. We herein describe the clinicopathologic features of a rare case of a perineurioma presenting as a polypoid lesion of the sigmoid colon, emphasizing the pathologic diagnostic clues.

Case report

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

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Key words

Perineurioma • Colon • Immunohistochemistry

Summary

Perineurioma is a relatively rare benign peripheral nerve sheath tumor composed of cells resembling normal perineurium. Although this tumor may arise in the context of a nerve (intra-neural perineurioma), extraneural perineurioma does occur, frequently involving the soft tissues of the lower and upper extremities, trunk and head and neck. Rarely it has also been reported in visceral organs, including gastrointestinal tract. We herein describe the clinicopathologic features of a rare case of a perineurioma presenting as a polypoid lesion of the sigmoid colon, emphasizing the pathologic diagnostic clues.

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 females.1 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 benign. Colorectal perineurioma was firstly described in 2004 by Eslami-Varzaneh as fibroblastic polyp. 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 cells. The striking morphologic, immunohistochemical and ultrastructural similarities between fibroblastic polyps and perineuriomas led some authors 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 far. 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 described. 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 interaction. 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 cells. 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.

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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 perineuriosas but not in lesions containing fibroblasts, neurons and smooth muscle cells.

The aim of the present paper is to describe the clinicopathologic 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. Histological examination showed a marked expansion of the lamina propria with separation of the colonic crypts. Neither mucosal ulceration nor adenomatous or hyperplastic epithelial changes was noticed (Haematoxylin & Eosin). Lamina propria is largely replaced by a bland-looking spindle cell proliferation (Haematoxylin & Eosin). The spindle cells show bipolar and focally ramifying slender cytoplasmic processes which often formed an anastomosing network (Haematoxylin & Eosin).

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 (Haematoxylin & Eosin). (C) Lamina propria is largely replaced by a bland-looking spindle cell proliferation (Haematoxylin & Eosin). (D) The spindle cells show bipolar and focally ramifying slender cytoplasmic processes which often formed an anastomosing network (Haematoxylin & 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 no-
ticed (Fig. 1B, C). Higher magnification showed a pro-
liferation of bland-looking, fibroblast-like spindle cells
mainly arranged in short fascicles or exhibiting a whor-
ling pattern (Fig. 1C). The spindle cells showed bipo-
lar and focally ramifying slender cytoplasmic processes
which often formed an anastomosing network (Fig. 1D).
Nuclei were ovoid to elongated. Nuclear atypia and mi-
toses were absent. The stroma was collagenous with fo-
cal edematous changes (Fig. 1D). Immunohistochemi-
cally 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 morpho-
logical and immunohistochemical features, the diagno-
sis of “perineurioma” was rendered.

Discussion

Perineuriomas of the colon-rectum are usually asym-
ptomatic 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 histologi-
cal diagnosis of intra-neural perineurioma is usually
straightforward due to its typical localization and cyto-
logical features, it is more challenging for its extraneural
counterpart which can pose differential diagnostic prob-
lems with other spindle cell lesions. In addition the diag-
nosis is more difficult when pathologist is facing an ex-
traneural perineurioma which occurs at an unusual site,
including the gastro-intestinal tract. Endoscopic features
of perineurioma are not specific and the diagnosis is his-
tologically based.

We herein report a case of a polypoid lesion of the
sigmoid colon with the morphological and immuno-
histochemical 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

![Fig. 2. Immunohistochemically most of the neoplastic cells were stained with both CD34 (A) and EMA (B). (A, B: immunoperoxidase staining).](image)
polyps, also in perineurioma with associated serrated/ hyperplastic changes confirming a close association between the two lesions. According to Agaimy et al. perineurioma that harbour BRAF mutation and morphological features of hyperplastic polyp should be considered as true mixed epithelial-stromal entity composed by prominently serrated superficial crypts associated with stromal proliferation with perineurial differentiation. Conversely Pai et al. suggest that perineurioma is the result of a reactive process, likely induced by the BRAF-mutated serrated epithelium. However the same authors admit, albeit rarely, the existence of true colic perineurioma. As our case lacks serrated or hyperplastic epithelial changes, we suggest that we are dealing with a true colic perineurioma.

Differential diagnosis mainly included schwannoma, neurofibroma, ganglioneuroma, GIST (gastro-intestinal stromal tumor) and leiomyoma of the muscularis mucosae. Schwannoma is benign tumor which may occasionally occur in gastrointestinal tract, especially as an intramural unencapsulated mass. Unlike schwannoma, perineurioma lacks the typical lymphocytic cuff, Antoni A and Antoni B areas, as well as the Verocay bodies. In addition immunohistochemistry is extremely helpful in the differential diagnosis in that perineurioma lacks100 protein expression, a marker which is strongly and diffusely expressed in schwannoma. Conversely, EMA expression is indicative of perineurial differentiation, supporting the diagnosis of perineurioma. Neurofibroma consists of an admixed proliferation of heterogeneous mixture of differentiated Schwann cells, fibroblasts and axons embedded in a predominantly myxoid stroma. Although both neurofibroma and perineurioma share CD34 expression, the latter lacks S100 protein expression. Ganglioneuromas usually present as sporadic, solitary polypoid lesions but may also occur as multiple in association with MEN IIb or NF1 syndrome. Histologically they are composed of bland-looking spindle cells with the features of schwannian and ganglion cells. The immunohistochemical detection of the neurofilament protein-positive axons and S-100 protein-positive Schwann cells is helpful in the differential diagnosis. Although more common in stomach and small intestine, GIST can also arise in the colon. Unlike perineurioma, GIST is positive for c-kit (CD117) and DOG-1. Colorectal leiomyomas usually arise from the muscularis mucosae, showing spindle cells arranged in well-formed fascicles with well circumscribed borders. Immunohistochemically, leiomyomas are positive for α-smooth muscle actin, desmin and h-caldesmon, which are not expressed in perineuriomas.

Conclusions
The present paper emphasizes that the diagnosis of colorectal perineurioma can be confidentially achieved if the pathologist is aware of the possibility that this uncommon lesion may occur in an unusual site, including the colo-rectum. Although perineurioma may be histologically confused with other morphologic mimics, immunohistochemistry is mandatory for a correct diagnosis.

References


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.