



A Case of Multiple Perineuriomas in the Colon With Underlying Neurofibromatosis Type I

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ABSTRACT

A 45-year-old woman was referred to us after a positive fecal occult blood test. Colonoscopy revealed a 20-mm polyp in the transverse colon and a 10-mm polyp in the sigmoid colon. Endoscopic mucosal resection was performed as a diagnostic treatment. Both resected polyps were histologically diagnosed as perineuriomas. She was later found to exhibit multiple café-au-lait spots on the skin and subsequently diagnosed as having neurofibromatosis type I (NF-1). Perineuriomas are rare benign peripheral nerve sheath tumors, with no reports of multiple colonic lesions in a patient with NF-1 to date. NF-1 might be associated with the onset of multiple perineuriomas.

INTRODUCTION

A perineurioma is a rare benign peripheral nerve sheath tumor composed of perineural cells.¹ Perineuriomas in the gastrointestinal (GI) tract were first described as benign fibroblastic polyps (BFPs) in the colon in a series of 14 cases by Eslami-Varzaneh et al² in 2004. Most reported cases of perineurioma in the GI tract occur in the sigmoid colon or rectum as a solitary lesion,³ with no cases of multiple perineuriomas in the colon reported to date. Neurofibromatosis type I (NF-1) is an autosomal dominant genetic condition affecting the brain, spinal cord, nerves, and skin. Although patients with NF-1 sometimes exhibit peripheral nerve sheath tumors presenting as neurofibromas, the relationship between NF-1 and perineurioma remains unknown. We report the first case of multiple perineuriomas in the colon with underlying NF-1.

CASE REPORT

A 45-year-old woman from Japan was referred to our hospital after a positive fecal occult blood test. She had no significant complaints or abnormal findings on physical examination at presentation. Complete blood count findings demonstrated no anemia, and blood chemistry results were normal. Colonoscopy revealed a 20-mm polyp (Paris classification 0-IIa + Isp) in the transverse colon and a 10-mm polyp (Paris classification 0-Isp) in the sigmoid colon. The transverse colon lesion was polypoid, red, and granular, with an appearance similar to that of a gastric hyperplastic polyp (Figure 1A). The sigmoid colon lesion was also red and polypoid, but no granular component was noted (Figure 1B). Given these findings, both polyps were deemed to be inflammatory or hyperplastic polyps. Endoscopic mucosal resections were performed for the lesions. Both polyps showed histologically similar features. Congestive and hyperplastic changes without cytological atypia were found on the surface epithelium. Spindle cells with ovoid nuclei were distributed densely, mainly in the lamina propria (Figure 2A,B). Immunohistochemically, the spindle cells were diffusely positive for EMA and focally positive for GLUT1, which were compatible with the features of perineurioma (Figure 2C,D). Accordingly, the diagnosis of multiple colon perineuriomas was made. Afterward, the patient mentioned several brown patches on her back that were considered café-au-lait spots. She was referred to a dermatologist who also identified multiple neurofibromas on the skin. The patient was ultimately diagnosed as having underlying NF-1.

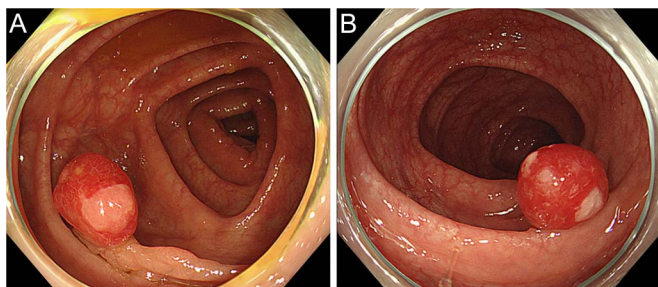


Figure 1. Colonoscopy findings. (A) The transverse colon lesion was polypoid, red, and granular, with an appearance similar to that of a gastric hyperplastic polyp. (B) The sigmoid colon lesion was also red and polypoid, but no granular component was noted.

DISCUSSION

We encountered a patient with multiple perineuriomas in the colon and accompanying NF-1. To the best of our knowledge, this is the first case report not only of multiple colon perineuriomas but also of GI perineuriomas in the context of NF-1. In 2004, Eslami-Varzaneh et al² first described a series of 14 cases of BFPs in the colon. BFPs are currently thought to be the same entity as perineuriomas histologically and immunohistochemically.⁴ Colon perineuriomas are rare, accounting for only 0.1%–1.46% of colon polyps.^{2,5} Most colon perineuriomas are found in the sigmoid colon or rectum, and most cases (69%) are identified by screening colonoscopy.^{3,6} The age of patients at diagnosis ranges from 37 to 84 years (mean age 60 years), with a female preponderance among reported cases.^{2,3,5}

Reports describing the endoscopic findings of perineuriomas are scarce. Jama et al⁷ found the endoscopic findings of perineuriomas to be solitary, sessile, well-circumscribed mucosal lesions that ranged from 0.2 to 1.5 cm in size. Our case exhibited a hyperplastic and inflammatory appearance, which differed from earlier findings. According to the microscopic results, this discrepancy may have been caused by chronic inflammatory changes because of the traction by the tumor's own weight.

Histologically, perineuriomas are characterized by spindle cell proliferation within the lamina propria and without cytological atypia, mitosis, or necrosis. The epithelial surface is typically intact but occasionally displays superficial erosions.⁵ Immunohistochemically, the spindle cells are positive for EMA, GLUT1, and claudin-1, which are considered specific perineurial cell markers.^{8,9} EMA, GLUT1, and claudin-1 show positivity in 78%, 85%, and 88% of perineuriomas, respectively, whereas CD34, c-kit, α SMA, and S100 are typically negative. The differential diagnoses of spindle cell tumors arising in the stroma include leiomyoma, GI stromal tumor, schwannoma, neurofibroma, and inflammatory fibroid polyp.

NF-1 is a genetic condition with an autosomal dominant pattern of inheritance affecting the skin, bone, and part of the nervous system. NF-1 causes benign and malignant tumors along the nervous system, which can grow anywhere in the

body. Neurofibromas are the most typical tumors associated with NF-1, usually developing on the skin, deep soft tissues, and other organs. Hybrid peripheral nerve sheath tumors are also seen in patients with NF-1. Harder et al¹⁰ reported that 26% of patients with hybrid neurofibroma/schwannoma were diagnosed as having neurofibromatosis type 2, and 9% of them had NF-1. Malignant peripheral nerve sheath tumors have also been described in patients with NF-1; approximately half of malignant peripheral nerve sheath tumor cases are associated with NF-1.¹¹ For the GI tract, NF-1 is associated with neurofibroma, neuroendocrine tumors, and GI stromal tumor. However, there have been no reports of GI perineuriomas accompanied with NF-1 to date.

A total of 3 published case reports exist on perineuriomas associated with NF-1,^{12–14} citing lesions from the chest wall, lower leg, and breast, respectively. NF-1 is caused by alterations in the *NF-1* gene, which is responsible for tumor suppression. *NF-1* encodes neurofibromin, a cytoplasmic protein controlling cellular proliferation.¹⁵ The mechanism by which this gene causes tumors in patients with NF-1 remains unclear. The present case showed the rare phenomenon of multiple perineuriomas arising in the colon, suggesting a possible relationship between multiple lesions and genetic abnormalities in NF-1. Further reports of similar cases may help elucidate the mechanism of tumorigenesis in NF-1.

In summary, we present the first known case of a patient with multiple perineuriomas in the colon and underlying NF-1. Although their precise relationship is unclear, NF-1 may play a role in multiple lesion development. Clinicians should pay attention to accompanying NF-1 and consider a whole-body

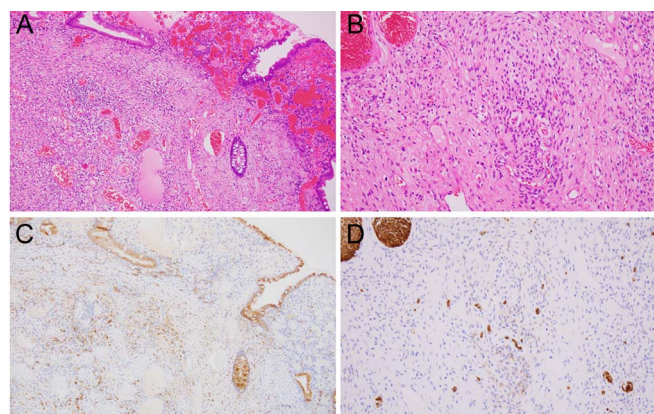


Figure 2. Histological and immunohistochemical examination of a transverse polyp EMR specimen. (A) Congestive and hyperplastic changes without cytological atypia were found on the surface epithelium (hematoxylin and eosin stain, 10 \times magnification). (B) Spindle cells with ovoid nuclei were distributed densely, mainly in the lamina propria (hematoxylin and eosin stain, 20 \times magnification). (C) Spindle cells were diffusely positive for EMA (anti-EMA staining, 10 \times magnification). (D) Spindle cells were focally positive for GLUT1 (anti-GLUT1 staining, 20 \times magnification). EMR, endoscopic mucosal resection.

checkup when encountering multiple perineuriomas in the colon.

DISCLOSURES

Author contributions: T. Tsuchiya, Y. Iwaya, T. Okamura, T. Nagaya, and T. Umemura wrote the manuscript. M. Iwaya revised the manuscript for intellectual content. T. Tsuchiya, Y. Iwaya, M. Iwaya, T. Okamura, T. Nagaya, and T. Umemura approved the final manuscript. Y. Iwaya is the article guarantor.

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