

Isolated colonic neurofibroma, a rare tumor: A case report and review of literature

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Abstract

BACKGROUND

Neurofibromas are tumors comprised of peripheral nerve sheath and connective tissue components. They can occur sporadically or as part of familial syndromes such as neurofibromatosis type 1. Isolated colonic neurofibroma without systemic manifestations is a rarely reported clinical entity. Here we present a case of a 51 years old male with an isolated colonic neurofibroma seen on a screening colonoscopy.

CASE SUMMARY

Fifty-one years old male who was otherwise healthy without a significant family history of cancer underwent a screening colonoscopy and was found have a 2.3 cm × 1.4 cm lesion in the colon. Tissue biopsy revealed a spindle cell tumor. Magnetic resonance imaging of the pelvis was negative for adenopathy. He underwent an endoscopic ultrasound that showed an ill-defined avascular lesion of mixed echogenicity measuring 2.8 cm × 15.2 cm in the submucosa with no communication with muscularis mucosa or propria. Immunohistochemistry staining of the tumor was strongly positive for S100, with rare penetrating axons deep within the tumor. Tumor cells were negative for c-kit and desmin and had low Ki-67 index. These findings were consistent with a solitary colonic submucosal neurofibroma. A detailed history and physical examination did not reveal any evidence of extraintestinal neurofibromatosis. He underwent transanal surgical resection of the tumor. The patient tolerated the procedure well without any complications.

CONCLUSION

While neurofibromas have been well described in literature, an isolated colonic neurofibroma is a rare pathological entity. Malignant transformation of

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neurofibromas has been reported in patients with neurofibromatosis syndromes. We report a case of isolated colonic neurofibroma and highlight the importance of resection due to the increased risk of tumorigenesis.

Key words: Neurofibroma; Colonoscopy; Neurofibromatosis type 1; Neurofibromatosis type 2; Spindle cell tumor; Endoscopic ultrasound; Case report

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Core tip: Neurofibromas are composed of neural and connective tissue components. They are associated with hereditary syndromes such as neurofibromatosis type 1 and 2. They have systemic manifestations and may involve multiple organs. Malignant transformation of this tumor has been reported in literature. Isolated colonic neurofibroma is a rarely reported pathological entity. Clinical follow-up after surgical resection is recommended as solitary colonic neurofibromas might be the first sign of neurofibromatosis type 1.

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INTRODUCTION

Neurofibromas are peripheral nerve sheath tumors that consist of Schwann cells, perineural cells and myofibroblasts^[1-3]. They occur sporadically or as part of familial syndromes such as neurofibromatosis type 1 (NF1) (von Recklinghausen's disease), NF2 (central or bilateral neurofibromatosis), multiple endocrine neoplasia type IIb, or intestinal neurofibromatosis^[2]. NF1 and 2 are both autosomal dominant syndromes with variable clinical manifestations^[1-3]. The genes for NF1 and NF2 are found on chromosomes 17 and 22, respectively^[3]. Both genes encode tumor suppressor proteins. NF1 has no sex predilection and occurs with a prevalence of 1 in every 3000 individuals^[3,4]. About 50% of patients have a positive family history. In the remaining 50% of patients, the disorder represents a sporadic new mutation^[3,4]. The diagnosis of NF1 is largely based on clinical criteria established by the National Institutes of Health and involves the presence of two or more of the following features: Six or more café au lait patches, two or more neurofibromas, one plexiform neurofibroma, freckling in the axillary or groin region, Lisch nodules, optic glioma, a first degree relative with NF1 and/or the presence of osseous dysplasia^[3].

Gastrointestinal involvement is seen in NF1 but not NF2^[4]. Abdominal neoplasms in NF1 can be divided into five categories: Neurogenic tumors, neuroendocrine tumors, gastrointestinal mesenchymal tumors, embryonal tumors and miscellaneous tumors. Neurogenic neoplasms seen in the abdomen include neurofibroma, plexiform neurofibroma, malignant sheath peripheral nerve sheath tumor, triton tumor and ganglioneuroma^[3-4]. Sporadic intestinal neurofibromas mainly arise in the small or large intestine and affect middle age adults^[5]. In the gastrointestinal tract, neurofibromas have been reported in the following order of decreasing frequency: the jejunum, stomach, ileum, duodenum and colon^[3-7]. Isolated colonic neurofibromas are rare with a few cases reported in literature (Table 1)^[8-23]. Here we present a case of an isolated colonic neurofibroma seen on a routine screening colonoscopy.

CASE PRESENTATION

Chief complaints

A 51-year-old Caucasian male was referred to our gastroenterology clinic for a routine screening colonoscopy. He had no complaints.

History of present illness

He was otherwise healthy and denied having bloody stools, fevers, chills or unintentional weight loss.

Table 1 Case reports of isolated colonic neurofibromas reported in English clinical literature

Ref.	Age	Sex	Location
Keith <i>et al</i> ^[8] , 1937	50	Female	Rectum
Woolf <i>et al</i> ^[9] , 1938	70	Male	Rectum
Butler and Hanna ^[10] , 1959	45	Female	Rectum
Suzuki and Yamashita ^[11] , 1966	NA	NA	Rectum
Geboes <i>et al</i> ^[12] , 1978	NA	NA	Rectum
Abramsone <i>et al</i> ^[13] , 1997	53	Male	Transverse colon
Bononi <i>et al</i> ^[14] , 2000	68	Female	Diffuse involvement
Panteris <i>et al</i> ^[15] , 2005	65	Female	Descending colon
Carter and Laurini ^[16] , 2008	52	Female	Rectum, transverse colon
Hindy <i>et al</i> ^[17] , 2012	59	Male	Transverse colon
Chelimilla <i>et al</i> ^[18] , 2013	70	Female	Ascending colon
Ahn <i>et al</i> ^[19] , 2016	26	Female	Sigmoid colon
Bilal <i>et al</i> ^[20] , 2016	52	Male	Descending colon
Adiou <i>et al</i> ^[21] , 2018	29	Female	Sigmoid colon
Miao <i>et al</i> ^[22] , 2018	24	Female	Ileocecal valve
Sun <i>et al</i> ^[23] , 2020	33	Female	Ascending colon

NA: Not applicable.

History of past illness

He had no significant past medical history or surgical history and was not taking any medications.

Personal and family history

Father had a history of hypertension. No family member had a history of cancer.

Physical examination upon admission

Temperature was 37 °C, heart rate was 75 beats per minute, respiratory rate was 18 breaths per minute, blood pressure was 129/72 mmHg and body mass index was 23.4 kg/m². Physical examination was normal. His abdomen was soft with no tenderness or palpable masses. He had no skin lesions, pigmented or hypopigmented spots.

Laboratory examinations

Laboratory testing including complete blood count, basic metabolic panel, liver function tests and coagulation profile were all within normal limits. Hepatic serology was also negative.

Imaging examinations

He underwent a screening colonoscopy and was found to have a 3-cm submucosal pedunculated polyp about 15 cm from anal verge adjacent to the second rectal fold (Figure 1). Mucosal biopsies were obtained during the procedure. The specimen included fragments of colonic mucosa and a spindle cell tumor. As the mucosal specimens were unrevealing, the patient underwent magnetic resonance imaging of the pelvis which showed a 2.3 cm × 1.4 cm lesion in the submucosa with no adenopathy. A subsequent endoscopic ultrasound revealed an ill-defined avascular lesion of mixed echogenicity measuring 2.8 cm × 15.2 cm in the submucosa with no communication with muscularis mucosa or propria (Figure 2). Fine needle biopsy, with 19G SharkCore™ needle (Covidien), was obtained for pathology assessment (Figures 2 and 3). The tumor showed bland spindle cell proliferation in a uniform fascicular pattern with edematous stroma (Figure 3). The cells were elongated, with oval/wavy nuclei. No mitotic figures, necrosis, or tumoral hemorrhage were seen. The tumor showed strong and diffuse S100 staining, with rare penetrating axons deep within the tumor (Figure 4). Tumor cells were negative for c-kit, desmin and had low Ki-67 index.

FINAL DIAGNOSIS

These findings were consistent with a colonic submucosal neurofibroma. A detailed

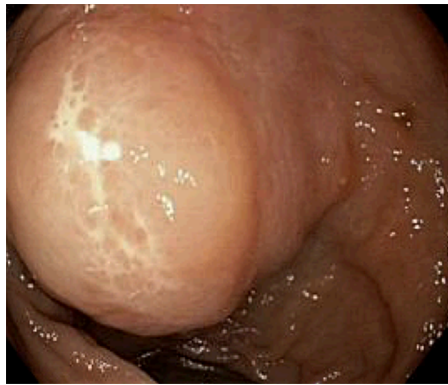


Figure 1 Findings at colonoscopy. A 3 cm submucosal pedunculated polyp is seen about 15 cm from anal verge.

history and physical examination did not reveal any evidence of extraintestinal manifestations.

TREATMENT

Our patient opted for transanal surgical resection.

OUTCOME AND FOLLOW-UP

The patient tolerated the procedure well without any complications. He will undergo a repeat colonoscopy in one year to evaluate for recurrence.

DISCUSSION

Our patient was diagnosed with a localized colonic neurofibroma without any clinical signs of NF1. The presence of such lesions in the intestinal tract without associated systemic manifestations is a rare finding.

Gastrointestinal involvement in NF1 has been reported in up to 25% of cases, with most lesions localizing to the upper gastrointestinal tract and rarely to the lower intestinal tract^[24,25]. The pathological forms seen in the gastrointestinal tract of patients with NF1 are characterized by hyperplasia and hypertrophy of the nerve plexus and ganglionic cells in the mucosa, submucosa, muscularis propria or even serosa^[20,26]. In addition to neurogenic tumors, patients may develop neuroendocrine and mesenchymal tumors such as gangliocytic paragangliomas, pheochromocytomas and gastrointestinal stromal tumors (GIST)^[2-4]. Intestinal neurofibromas predominately originate from the plexus of Meissner in the submucosa or the plexus of Auerbach^[9]. Dense growths known as plexiform neurofibromatosis may infiltrate the mesentery and lead to arterial compression or nerve injury^[25]. Endoscopically, neurofibromas are often sessile and wide-based or, as seen in this patient, pedunculated polyps^[23]. Clinically patients may present with abdominal pain, palpable masses, rectal bleeding, or obstruction due to intussusception or extra-luminal pressure, although most cases are found incidentally in asymptomatic patients.

Since there is no recommendation about modalities to explore these patients and because of the nonspecific clinical presentation of gastrointestinal lesion manifestations and limitations of endoscopic techniques, cross-sectional imaging may be used to aid in diagnosis. MR enterography is a non-invasive technique that has high sensitivity for detecting small bowel lesions and is more preferable than computed tomography (CT) enterography for follow up of these patients because of concerns over exposure to ionizing radiation^[24]. CT colonography (virtual colonoscopy) is a potential alternative to conventional colonoscopy for the detection of colorectal tumors especially in poor risk patients^[27]. It is a non-invasive technique that requires no sedation and is well tolerated by most patients. CT colonography allows for complete visualization of the entire large bowel in almost all patients even following incomplete endoscopy and for colorectal examination proximal to an obstructing lesion. The use of multidetector technology improves the detection of many colorectal lesions^[27]. Potential limitations of this modality include the inability to



Figure 2 Findings with endoscopic ultrasound. A 2.8 cm × 15.2 cm avascular lesion of mixed echogenicity seen in the submucosa with no communication with muscularis mucosa or propria.

obtain tissue biopsy and exposure to ionizing radiation^[27,28].

Tissue biopsy remains the gold standard for diagnosis^[26]. The differential diagnosis for neurofibroma of the abdomen includes schwannoma, myxoma, inflammatory fibroid polyp and GIST^[2,25]. Unlike myxomas, neurofibromas are diffusely positive for S-100^[2]. The absence of calretinin and a peripheral lymphoid cuff help distinguish these tumors from schwannomas and inflammatory fibroid polyps, respectively. In contrast to schwannomas, neurofibromas stain positively for CD34 and factor XIIIa^[2]. On the other hand, GIST stain positive for c-kit while neurofibromas do not^[2]. In our patient, histopathology revealed bland spindle cell proliferation in a fascicular pattern. Immunohistochemical staining was positive for S100, negative for c-kit and desmin. These features are consistent with a diagnosis of neurofibroma.

Malignant transformation of neurofibromas has been reported in patients with NF1^[3,27]. Malignant peripheral nerve sheath tumors are highly aggressive tumors associated with low survival rates (34%-52%)^[29-31]. The lifetime risk of these tumors in patients with NF1 is 8%-13%^[3]. Plexiform and larger neurofibromas are more likely to undergo malignant transformation^[30-32]. Malignant sheath peripheral nerve sheath tumors are often clinically silent when they arise in the abdomen and are often diagnosed at advanced stage. The prognosis remains poor and depends on the tumor size and location, resection margins, adjuvant chemotherapy, distant metastasis, stage and site^[29-32].

The clinical significance of solitary neurofibromas is currently unknown, hence a thorough search should be made to exclude the possibility of colonic neurofibromas presenting as initial sign of NF1. Unfortunately, due to the rarity of this condition there is no consensus regarding management of these patients. Given the low incidence, and very few cases reported, long term follow up and screening goals are also unknown but close follow up is recommended to exclude neurofibromatosis and the associated risk of malignant transformation^[29-32].

CONCLUSION

An isolated colonic neurofibroma without associated signs of neurofibromatosis or systemic disease is a rare pathological finding. The clinical significance lies in the need to follow these patients as bowel involvement might be the first systemic manifestation of syndromic diseases such as NF1.

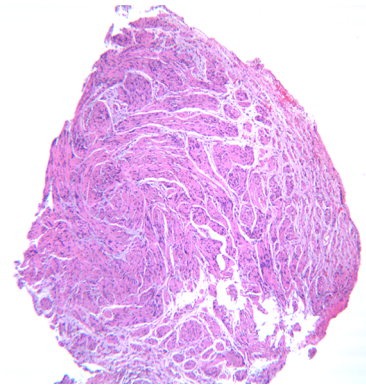


Figure 3 Histopathology of the tumor at low power $\times 10$ magnification. Bland spindle cell tumor is seen in a fascicular growth pattern.

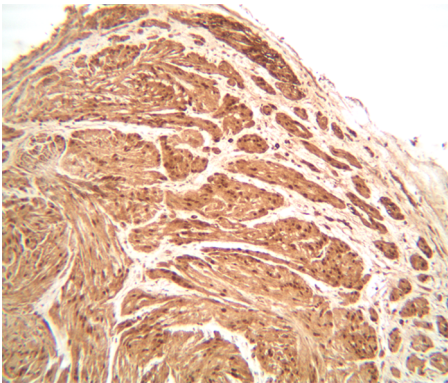


Figure 4 Immunohistochemistry of the lesion at $\times 50$ magnification. Tumor is diffusely positive for S100. Note the penetrating axons with neurofilament stain.

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