EJCRIM
European Journal
of Case Reports
in Internal Medicine

ISOLATED RECTAL NEUROFIBROMA IN THE ABSENCE OF NEUROFIBROMATOSIS: REPORT AND REVIEW OF MOLECULAR IMPLICATIONS

Karam Karam[1], Kim Charro[1], Ariane Alirkilicarslan[2], Aurélien Morini[2], Jacquot Rakotobe[3], Emilien Brousset[1], Christophe Locher[1]

[1] Department of Gastroenterology and Hepatology, Grand Hôpital de l'Est Francilien, Meaux, France
[2] Department of Anatomical Pathology, Grand Hôpital de l'Est Francilien, Meaux, France
[3] Department of Radiology and Medical Imaging, Grand Hôpital de l'Est Francilien, Meaux, France

Corresponding author's e-mail: karamek7@gmail.com

Received: 04/03/2026
Accepted: 12/03/2026
Published: 15/05/2026

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: A signed informed consent was obtained.
This article is licensed under a CC Attribution-NonCommercial-NoDerivatives 4.0 License

How to cite this article: Karam K, Charro K, Alirkilicarslan A, Morini A, Rakotobe J, Brousset E, Locher C. Isolated rectal neurofibroma in the absence of neurofibromatosis: report and review of molecular implications. *EJCRIM* 2026;**13**:doi:10.12890/2026_006508

ABSTRACT

Neurofibromas are benign peripheral nerve sheath neoplasms composed of Schwann cells, fibroblasts, perineurial-like cells and axonal elements within a variably collagenous or myxoid stroma. They most commonly arise in the context of neurofibromatosis type 1 (NF1), an autosomal dominant tumour predisposition syndrome driven by inactivating mutations of the NF1 tumour suppressor gene. Isolated colorectal neurofibromas unassociated with syndromic disease are exceptionally rare, and their biological behaviour remains incompletely characterised.

We report a case of a 26-year-old man presenting with non-specific abdominal pain who was found to have a solitary rectal submucosal lesion. Endoscopic resection was performed, and histopathologic and immunophenotypic evaluation confirmed the diagnosis of an isolated rectal neurofibroma. This case underscores the diagnostic and management challenges posed by these rare lesions and highlights unresolved questions regarding their molecular underpinnings and malignant potential.

KEYWORDS

Rectal neurofibroma, neurofibromatosis

LEARNING POINTS

- Isolated rectal neurofibromas are extremely rare, particularly without evidence of neurofibromatosis.
- Gastrointestinal neurofibromas are usually linked to systemic syndromes, especially neurofibromatosis type 1. The lesion can mimic other rectal tumours such as gastrointestinal stromal tumour (GIST), schwannoma or rectal carcinoid tumour.
- Diagnosis usually requires histopathology and immunohistochemistry.
- This case highlights the importance of considering rare nerve sheath tumours in the differential diagnosis of rectal lesions.

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

INTRODUCTION

Neurofibromas are benign peripheral nerve sheath tumours characterised by a heterogeneous cellular composition that includes Schwann cells, perineurial-like cells, fibroblasts and entrapped axons[1]. They most frequently occur in association with neurofibromatosis type 1 (NF1), a tumour predisposition syndrome caused by germline mutations in the NF1 gene located on chromosome 17q11.2[1]. Loss of neurofibromin function results in constitutive activation of the ras/MAPK signalling pathway, promoting cellular proliferation and tumourigenesis[2].

Gastrointestinal involvement in NF1 is well recognised and may include neurofibromas, gastrointestinal stromal tumours (GISTs) and neuroendocrine neoplasms[3]. In contrast, sporadic, isolated colorectal neurofibromas in patients without clinical or genetic evidence of neurofibromatosis are exceedingly uncommon. Due to their rarity their natural history, molecular landscape and malignant potential remain poorly defined.

We report a case of an isolated rectal neurofibroma in a young adult without stigmata of neurofibromatosis and discuss its diagnostic, molecular and clinical implications.

CASE DESCRIPTION

A 26-year-old, previously healthy man presented with a three-month history of intermittent, non-specific abdominal pain refractory to conservative medical therapy. He denied haematochezia, melena, altered bowel habits, weight loss or constitutional symptoms. There was no personal or family history of gastrointestinal malignancy, neurocutaneous disease or hereditary cancer syndromes.

Laboratory evaluation, including complete blood count and metabolic panel, was unremarkable. Contrast-enhanced computed tomography of the abdomen and pelvis demonstrated focal circumferential rectal wall thickening *(Fig. 1)*. Subsequent pelvic magnetic resonance imaging (MRI) confirmed localised mural thickening without lymphadenopathy or evidence of extramural extension *(Fig. 2)*.

Colonoscopy revealed a 3 cm sessile, submucosal-appearing rectal lesion with intact overlying mucosa *(Fig. 3)*. Endoscopic mucosal resection was performed piecemeal using hot snare polypectomy, and prophylactic clip placement achieved haemostasis.

Histological examination demonstrated a spindle-cell proliferation composed of elongated cells with wavy nuclei embedded in a collagenous stroma containing scattered mast cells and entrapped axons. No cytologic atypia, increased mitotic activity or necrosis was identified *(Fig. 4A)*. Immunohistochemical analysis showed diffuse nuclear and cytoplasmic positivity for SOX10 and S100 protein, supporting Schwannian differentiation. The lesion was negative for CD117 (c-KIT) and DOG1, excluding GIST, desmin and smooth muscle actin, excluding smooth muscle neoplasms, and CD34. These findings established the diagnosis of rectal neurofibroma *(Fig. 4B)*.



Figure 1. Axial enhanced CT scan of the abdomen and pelvis revealing circumferential rectal wall thickening and enhancement (white arrow).

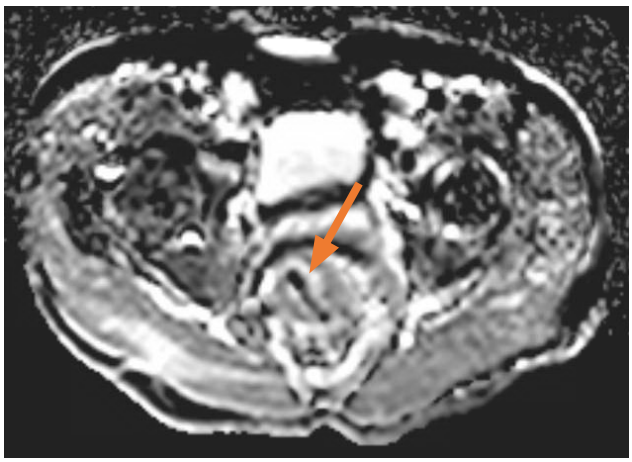


Figure 2. Axial MR sequence showing circumferential thickening of the rectal wall (orange arrow).

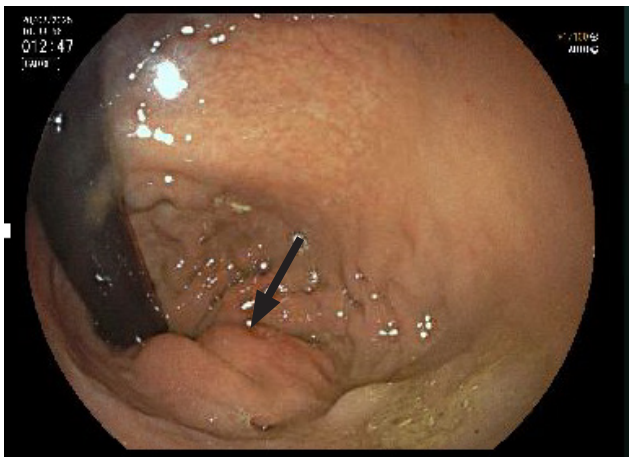


Figure 3. Colonoscopy revealing a 3 cm sessile, submucosal-appearing rectal lesion with intact overlying mucosa (black arrow).

Clinical evaluation revealed no café-au-lait macules, axillary freckling, cutaneous neurofibromas, Lisch nodules or other diagnostic criteria for NF1. The patient was scheduled for interval endoscopic surveillance.

Despite complete removal of the rectal lesion, the patient was scheduled for colonoscopy after one year as an endoscopic follow up, which revealed normal rectal mucosa and no disease recurrence. Physical examination revealed

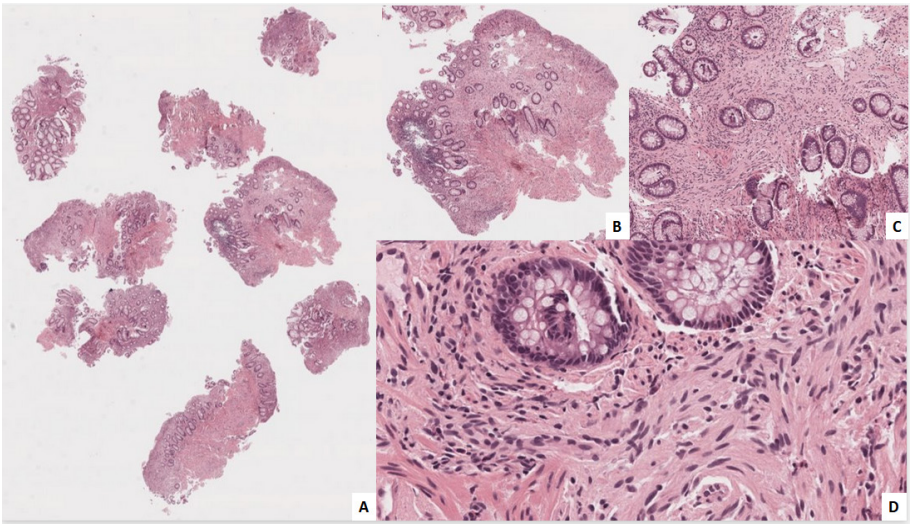


Figure 4A. Rectal neurofibroma, HES stain, ×1 magnification (A), ×5 magnification (B), ×15 magnification (C) and ×40 magnification (D).

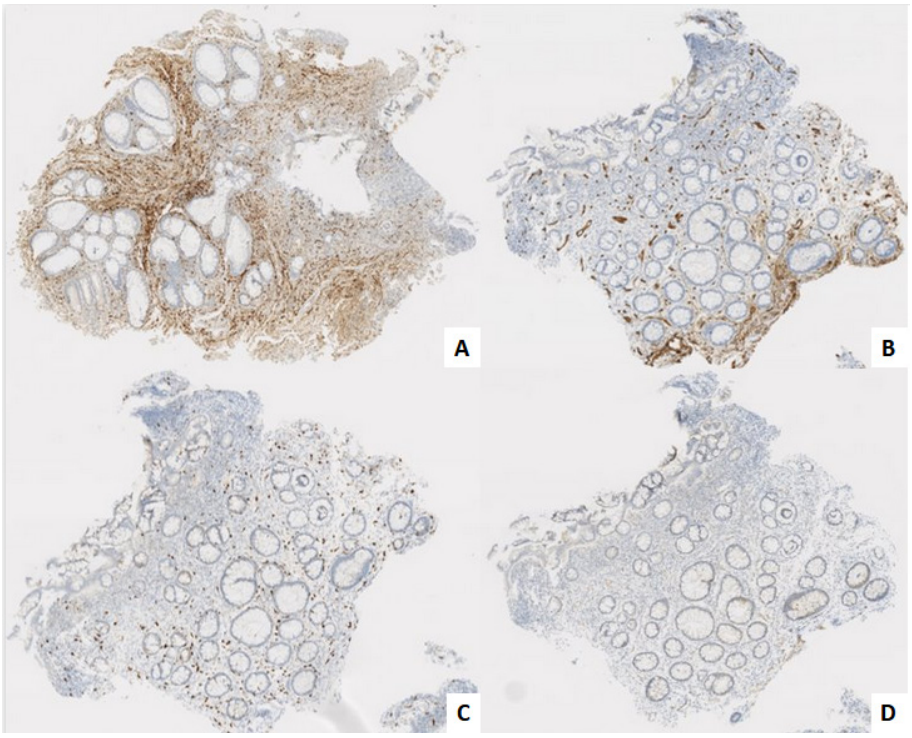


Figure 4B. Immunohistochemistry of neurofibroma staining positive with the S-100 protein (A), negative with CD 34 (B), negative with c-Kit (C) and negative with DOG-1 (D), with magnification ×10 for all figures.

no café-au-lait spots or skin neurofibromas. Pelvic MRI was performed and was unremarkable. The patient remains under regular follow up.

DISCUSSION

Neurofibromas represent benign peripheral nerve sheath neoplasms arising from a complex interplay of Schwann cells and stromal components. In NF1-associated tumours, biallelic inactivation of NF1 leads to loss of neurofibromin-mediated negative regulation of RAS signalling, resulting in hyperactivation of the Ras/Raf/MEK/ERK and PI3K/Akt/mTOR pathways[3]. This molecular dysregulation underlies tumour formation and confers a measurable lifetime risk (estimated 8–13%) of malignant transformation into malignant peripheral nerve sheath tumours[4].

In contrast, the molecular drivers of isolated, sporadic colorectal neurofibromas remain undefined. Whether these lesions harbour somatic NF1 mutations, alternative RAS pathway alterations or represent biologically distinct entities is unknown. Emerging genomic analyses of sporadic peripheral nerve sheath tumours suggest heterogeneity in MAPK pathway activation and variable involvement of additional tumour suppressors, including CDKN2A and components of polycomb repressive complex 2[5]. However, comparable molecular profiling data for isolated gastrointestinal neurofibromas are lacking.

From a diagnostic standpoint, colorectal spindle-cell lesions encompass a broad differential diagnosis including GIST, schwannoma, leiomyoma, inflammatory fibroid polyp and perineurioma. Immunohistochemistry is therefore essential. Neurofibromas typically demonstrate S100 and SOX10 positivity reflecting Schwannian differentiation, while lacking CD117 and DOG1 expression, which distinguishes them from GISTs[6].

The malignant potential of isolated colorectal neurofibromas remains speculative. Unlike plexiform

neurofibromas in NF1 – which carry well-established risk of progression to malignant peripheral nerve sheath tumours – the risk associated with solitary sporadic lesions is undefined due to limited case numbers and absence of long-term follow-up data[7]. Nonetheless, given the theoretical possibility of malignant transformation and the absence of consensus guidelines, complete excision with interval surveillance appears prudent.

This case is clinically important as it emphasises that isolated neurofibroma may be the first manifestation of underlying neurofibromatosis. Also, rectal neurofibroma can be misdiagnosed as a malignant rectal tumour, leading to unnecessary aggressive treatment. Early recognition allows appropriate surgical management and surveillance. Additionally, distinguishing it from other mesenchymal tumours such as a gastrointestinal stromal tumour is critical because management and prognosis differ significantly.

This case expands the limited literature on isolated colorectal neurofibromas and highlights the need for systematic molecular characterisation and longitudinal outcome studies. Clarifying whether these lesions share pathogenetic mechanisms with NF1-associated neurofibromas or represent distinct molecular entities will be critical in defining their biological behaviour and informing management strategies.

CONCLUSION

Isolated rectal neurofibroma is a rare entity that poses diagnostic and management challenges due to its infrequency and uncertain biological potential. Accurate histopathologic and immunophenotypic evaluation is essential to distinguish it from other colorectal spindle-cell neoplasms. Further genomic and longitudinal investigations are needed to elucidate the molecular drivers and true malignant risk of these uncommon lesions.

REFERENCES

1. Jett K, Friedman JM. Clinical and genetic aspects of neurofibromatosis 1. *Genet Med* 2010;**12**:1–11. doi: 10.1097/GIM.0b013e3181bf15e3
2. Razek AAKA. MR imaging of neoplastic and non-neoplastic lesions of the brain and spine in neurofibromatosis type I. *Neurol Sci* 2018;**39**:821–827. doi: 10.1007/s10072-018-3284-7
3. Ricci R, Martini M, Cenci T, Carbone A, Lanza P, Biondi A, et al. PDGFRA-mutant syndrome. *Mod Pathol* 2015;**28**:954–964. doi: 10.1038/modpathol.2015.56
4. Evans DG, Howard E, Giblin C, Clancy T, Spencer H, Huson SM, et al. Birth incidence and prevalence of tumor-prone syndromes: estimates from a UK family genetic register service. *Am J Med Genet A* 2010;**152A**:327–332. doi: 10.1002/ajmg.a.33139
5. Agaimy A, Vassos N, Croner RS. Gastrointestinal manifestations of neurofibromatosis type 1 (Recklinghausen's disease): clinicopathological spectrum with pathogenetic considerations. *Int J Clin Exp Pathol* 2012;**5**:852–862.
6. Basile U, Cavallaro G, Polistena A, Giustini S, Orlando G, Cotesta D, et al. Gastrointestinal and retroperitoneal manifestations of type 1 neurofibromatosis. *J Gastrointest Surg* 2010;**14**:186–194. doi: 10.1007/s11605-009-0940-5
7. Keith AR, Albert R. A case of neurofibroma of the rectal wall. *Tr Am Proct Soc* 1937;**38**:68.