

Case report

Solitary rectal neurofibroma in von Recklinghausen's disease

K.H. Katsanos, M. Economou, Sevasti Kamina¹, D.J. Papachristou¹, Marika Syrrou², I. Georgiou³, K. Massalas, G. V. Tsianos⁴, E.V. Tsianos

SUMMARY

Gastrointestinal involvement in von Recklinghausen disease (NF-1) is quite frequent but forms restricted to the colon are exceptional. A 36-year-old woman with von Recklinghausen disease (NF-1) presented at the outpatient gastroenterology clinic complaining of recurrent episodes of abdominal pain. The patient had one child, who was also diagnosed with von Recklinghausen disease with similar café au lait spots in a similar location to those of her mother. Genetic linkage analysis and identification of haplotypes in mother and child showed that the abnormal haplotype was 3-1-8 and that the 53ab/nf-ex 38 was the only polymorphism that could discriminate the normal from abnormal haplotype in this family. Colonoscopy revealed only a lean lesion of 2cm in diameter in the rectal mucosa. Furthermore, upper gastrointestinal tract endoscopy, enteroclysis and abdominal computed tomography were negative. Rectal biopsies were compatible with rectal solitary neurofibroma. The patient, as well as her children, was advised to follow a certain surveillance protocol. This case of solitary rectal neurofibroma may represent either the prelude to many intestinal neurofibromas which will appear in this patient or it may simply represent a distinct phenotype of colonic involvement within the NF-1 gene.

Key words: von Recklinghausen's disease, NF-1, intestinal neurofibromas, neurofibromatosis, bowel, colon.

INTRODUCTION

Neurofibromatosis (NF) is an autosomal dominant transmitted disease of the peripheral and central nervous system with 100% penetrance but variable phenotypic expression. The gene frequency is 1 per 3,000-4,000 births. In patients with NF benign and malignant tumors may occur in different organs.¹

There are several types of neurofibromatosis (NF). Neurofibromatosis type 1 (NF-1) or von Recklinghausen disease, NF type 2 (NF-2), NF-3, otherwise known as familial intestinal neurofibromatosis, and atypical types. Genetic linkage studies have localized the NF-1 gene to chromosome 17q, and cloning and characterization of the mutant gene has also been achieved.²

Cutaneous disease in NF-1 (von Recklinghausen's disease) comprises café au lait spots and neurofibromas, which can occasionally develop into sarcoma. Additional characteristics of NF-1 include multiple neurofibromas, axillary or inguinal freckling, optic gliomas, iris deformities and bony dysplasia.³

NF-1, when affecting the gastrointestinal tract, takes three main forms: ganglioneuromatosis/neurofibromatosis, stromal tumours and tumours in the duodenum and periampullar region. Frequently these patients present with gastrointestinal bleeding or obstruction.⁴

Herein we report a case of a 36-year old woman with von Recklinghausen's disease (NF-1) and gastrointestinal bleeding diagnosed with solitary rectal neurofibroma.

Division of Internal Medicine (Hepato-Gastroenterology Unit)
¹Department of Pathology, ²Laboratory of Biology, ³Department of Obstetrics/Gynecology (Clinical Genetics Unit) Medical School, University of Ioannina, 451 10 Ioannina and ⁴1st Department of Surgery, Trikala General Hospital, Greece.Greece

Author for correspondence:

Dr Epameinondas V. Tsianos, Professor of Internal Medicine, Department of Internal Medicine University of Ioannina, Medical School, Leoforos Panepistimiou, 45 110 Ioannina, Tel: 0030-26510-97501, Fax: 0030-26510-97016, e-mail: etsianos@cc.uoi.gr

CASE REPORT

A 36-year-old woman with von Recklinghausen disease (NF-1) presented at the outpatient gastroenterology clinic complaining of recurrent episodes of abdominal pain.

The patient was diagnosed with von Recklinghausen disease with eight cutaneous café au lait spots, which were located in the abdominal area and in the upper and lower extremities, and axillary freckling. The patient had one daughter, who was also diagnosed with von Recklinghausen disease with similar café au lait spots in a similar location to those of her mother. Peripheral blood and biochemical analysis did not show anything remarkable. Colonoscopy revealed a lean lesion of approximately 2 cm in diameter in the rectal mucosa, which was located 10 cm above the anal ring (Figure 1). This solitary lesion had no surface abnormalities and was soft when touched with the biopsy forceps. Many biopsies were taken from this lesion, which was not bleeding more than is expected in such instances. The rest of the bowel mucosa, including terminal ileum, was carefully examined, but no additional lesions were found. Furthermore, upper gastrointestinal tract endoscopy, enteroclysis and abdominal computed tomography were negative for any mass or abnormal lesion.

Histological study showed extensive neurofibromatous proliferation, involving the lamina propria (Figure 2a).

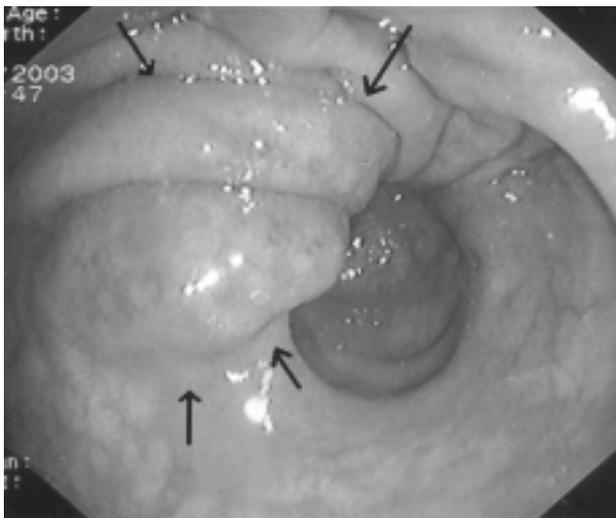


Figure 1. Solitary neurofibroma in the rectal mucosa located 10 cm above the anal ring in a patient with von Recklinghausen's disease.

Immunohistochemical study. Using the streptavidin-biotin method (Dako) rectal biopsies were immunohistochemically studied. Immunohistochemical staining for S-100 protein was strongly positive (Figure 2b), whereas expression for CD117 was not observed.

Molecular genetic analysis. Family molecular genetic analysis was performed with PCR after DNA extraction from all members of this family. This analysis showed the following haplotypes and genotypes for each family member; mother 3-1-2/3-1-8, father 1-1-3/3-1-7, daughter 1-1-3/3-1-8. The abnormal haplotype was the 3-1-8, which was identical in mother and child while the 1-1-3

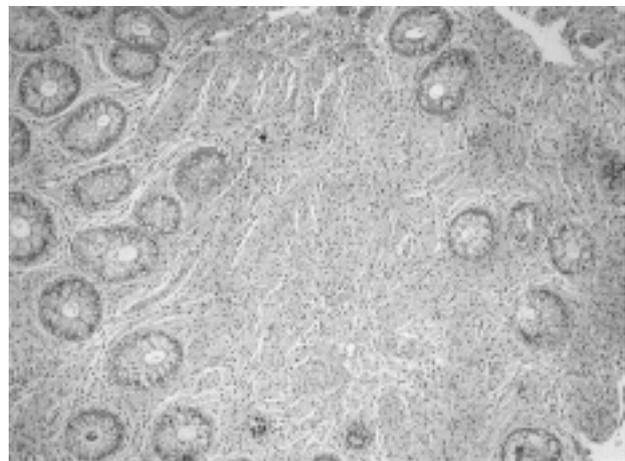


Figure 2a. Solitary rectal neurofibroma in a patient with von Recklinghausen's disease. Bundles of proliferating neurons, Schwann cells and myofibroblasts, located in the lamina propria (H+E, x200).

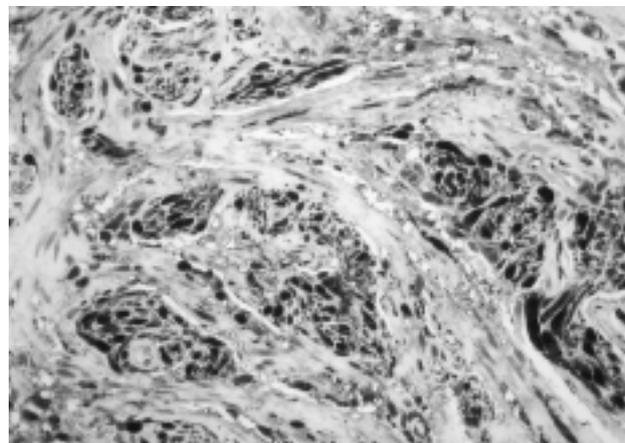


Figure 2b. Solitary rectal neurofibroma in a patient with von Recklinghausen's disease. Strong immunoreactivity for S-100 protein (x400).

haplotype was the normal, father's haplotype. In addition, in each family member three polymorphism loci were studied; Alu/nf-IVS19, 31.2/nf-ex.31 and 53ab/nf-ex 38. The 53ab/nf-ex 38 was the only polymorphism that could discriminate normal from abnormal haplotype in this family.

The patient, as well as her children, was advised to follow a certain surveillance protocol in order to early recognize and treat colorectal lesions suspicious for malignancy as early as possible.

DISCUSSION

We presented a case of a thirty-six-year-old patient diagnosed with NF-1 (von Recklinghausen disease) and relapsing episodes of abdominal pain in which we discovered the presence of a solitary rectal neurofibroma.

About 25% of individuals affected with NF-1 (von Recklinghausen disease) exhibit multiple intestinal polypoid neurofibromas or ganglioneuromas. Carcinoids, neurofibrosarcomas, leiomyomas and leiomyosarcomas have been also reported in von Recklinghausen disease (NF-1). The small bowel is most often affected, followed by the stomach. Occasionally the liver and gallbladder are also affected. Colonic involvement in von Recklinghausen disease is very infrequent and forms restricted to the colon are exceptional⁵. In fact, it seems that less than fifteen well-documented cases similar to ours have been reported to date.⁶

NF-3 as NF-1 can also be associated with gastrointestinal hemorrhage because of ulceration of neurofibromas in the bowel lumen. However, NF-3 patients have only intestinal neurofibromas and none of the other features seen in NF-1, which were evident in this patient.⁷

Furthermore, gastrointestinal tract stromal tumors (GISTS) associated with NF-1 should be considered in the current concept of the stromal tumours with reference to recent advances in immunohistochemistry.⁸

It is of interest that the upper and lower gastrointestinal tract of this patient had no additional lesions on careful endoscopic and radiological examination. However, the possible existence of several malignant and benign lesions all over the gastrointestinal tract in NF-1 patients has been suggested. If this is the case, there is a

real potential of malignancy, and surgical treatment is the main option.³

Thus, careful follow up of NF-1 patients is strongly advisable, as it has been shown that these patients have an increase incidence of mesenchymal tumours and other neoplasias.

In addition, the probability of malignant digestive disease associated with NF-1 should be kept in mind in any patient, regardless of age and neurofibromatosis characteristics of localization. For this reason, the patient and her children were strongly advised to follow a certain preventive surveillance programme.

This case of solitary rectal neurofibroma may represent either the prelude to many intestinal neurofibromas which will appear in this patient in the future, or it may simply represent a distinct phenotype of colonic involvement within the NF-1 gene.

REFERENCES

1. Miyoshi LM, Tamiya S, Iida M, et al. Primary jejunal malignant mixed tumor in a patient with von Recklinghausen neurofibromatosis. *Am J Gastroenterol* 1996; 91:795-797.
2. National Institutes of Health. Consensus development conference on neurofibromatosis report. *Neurofibromatosis* 1988; 1:172.
3. Scheuner M, Yang H, Rotter JI. Gastrointestinal manifestations of specific genetic disorders (Neurofibromatosis). In: T. Yamada ed, Philadelphia 1995, Lippincott J&B eds: 2395.
4. Artaza T, Garcia JF, Gonzalez C, et al. Simultaneous involvement of the jejunum and the colon by type-1 neurofibromatosis. *Scand J Gastroenterol* 1999; 34:331-334.
5. Baril A, Bayle JJ, Boucheron S, Dano P, Meley J. Colonic localization of pseudopolypoid type disclosing Recklinghausen's neurofibromatosis. *Sem Hop* 1982; 9:2665-2668.
6. Pinsk I, Dukhno O, Ovnat A, Levy I. Gastrointestinal complications of von Recklinghausens' disease: two case reports and a review of the literature. *Scand J Gastroenterol* 2003; 38:1275-1278.
7. Verhest A, Heimann R, Verschraegen J, Vamos E, Hecht F. Hereditary intestinal neurofibromatosis. Translocation between chromosomes 12 and 14. *Neurofibromatosis* 1988; 1:33-36.
8. Giuly J, Monges B, Picaud R, Giuly D, Leroux C, Cat RN. Recklinghausen's disease and gastrointestinal stromal tumors. *Ann Chir* 2002; 127:477-479.