

# Intestinal neurofibromatosis and small-bowel adenocarcinoma: a single case study

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**Intestinal neurofibromatosis and small-bowel adenocarcinoma: a single case study**

**Objective:** Patients with Von Recklinghausen's disease (neurofibromatosis type 1) are at increased risk of developing various tumours. However, the coexistence of neurofibromatosis with small-bowel adenocarcinoma is exceedingly rare. We present an uncommon case of neurofibromatosis type 1, involving the small bowel in a 73-year-old man, who was admitted to our department with signs of acute abdomen. At laparotomy, multiple mesenteric and intramural nodules were seen in the distal ileum. These nodules obstructed ileal lumen, while the intestine wall was perforated in one point. A wide resection of the affected ileum together with all visible nodules in the adjacent mesentery was performed. Histology revealed neurofibromatosis type 1 with malignant transformation to small-bowel adenocarcinoma. The patient had no additional therapy. In a follow-up of 2 years, the patient is very well and there was no recurrence of the disease. We suggest that adenocarcinoma of small bowel should be considered in the evaluation of acute abdominal pain in neurofibromatosis patients.

**Keywords:** Von Recklinghausen's disease, neurofibromatosis 1, small-bowel adenocarcinoma.

## INTRODUCTION

Intestinal neurofibromatosis is well known but it is extremely rare when it is associated with a coexisting small-bowel adenocarcinoma. We herein report a rare case of adenocarcinoma of the ileum complicating neurofibro-

matosis type 1 (NF1) that presented with signs of acute abdomen.

## METHODS

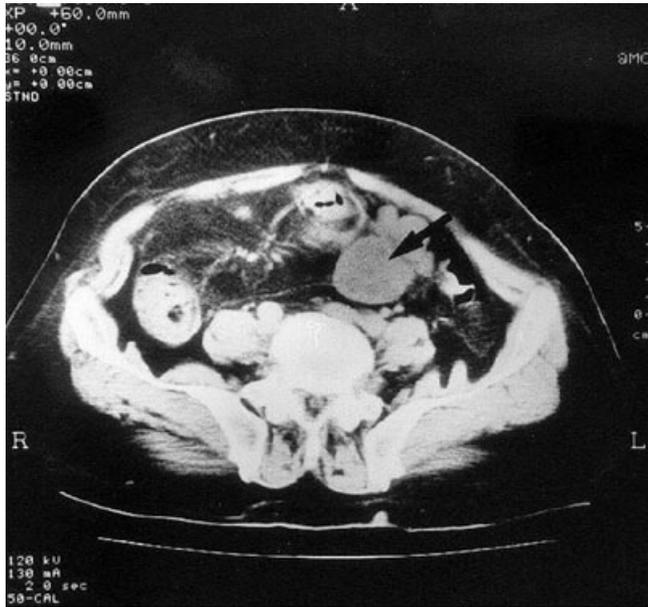
A 73-year-old man with known neurofibromatosis since childhood was admitted to our department complaining of acute severe abdominal pain and vomiting. On admission, the patient was febrile (38.6°C). Physical examination revealed multiple café au lait spots larger than 1.5 cm in diameter scattered over his trunk, multiple soft subcutaneous nodules and axillary freckling (diagnostic features of Von Recklinghausen's disease – 'six spot' criterion)

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**Figure 1.** Computed tomography abdomen scan demonstrated a solid round mass of 4 cm diameter in the ileum.

(Lukash *et al.* 1970). Abdomen was distended with decreased bowel sounds. Rebound tenderness and guarding were present over the lower abdomen. Laboratory tests showed only neutrophil leucocytosis (WCC 19 580/mm<sup>3</sup>, 85.4% neutrophils). Abdominal computed tomography (CT) scan demonstrated a solid round mass of 4 cm diameter in the ileum (Fig. 1).

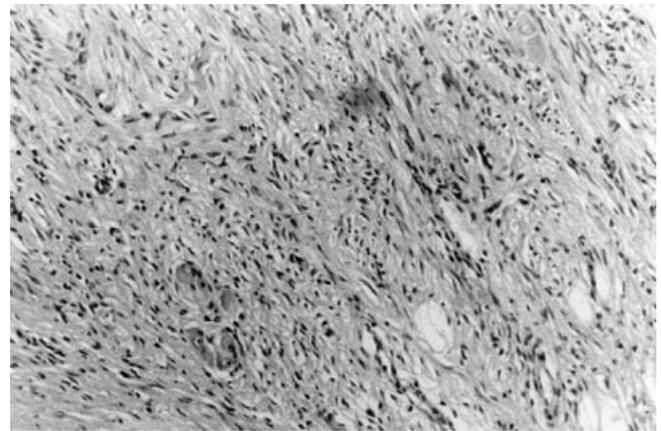
## RESULTS

Exploratory laparotomy was performed. Multiple, mesenteric and intramural nodules of 0.5 cm to 5 cm diameter were found in the distal ileum. The nodules obstructed the ileal lumen, while the intestinal wall was perforated at one point. A wide resection of a 65 cm segment of ileum with all visible nodules in the adjacent mesentery was performed and the continuity was restored with an end-to-end anastomosis.

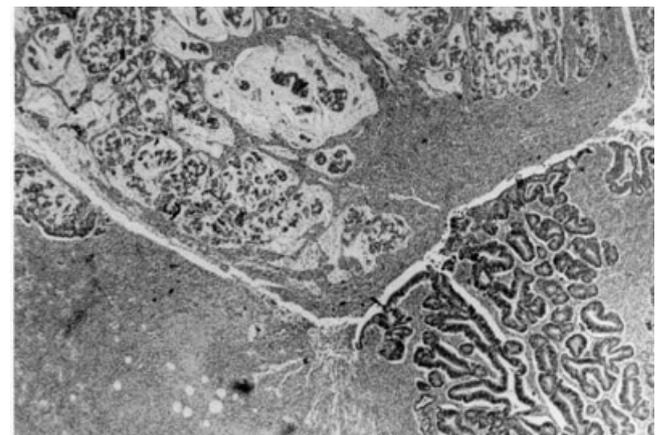
Histological examination of the resected part of the bowel showed:

- 1 Type 1 nodular and diffuse neurofibromatosis with local ganglioneurofibromatous elements (Fig. 2), and
- 2 Small-bowel adenocarcinoma of 4 cm in diameter of moderate and locally low differentiation with presence of mucous lakes and signet cells (Fig. 3). The carcinoma infiltrated the intestinal wall. Metastatic infiltration of two out of seven local lymph nodes was noted.

Patient's postoperative course was uneventful and the patient was discharged 2 weeks later. The patient denied



**Figure 2.** Intestinal neurofibroma (H&E ×200).



**Figure 3.** Small-bowel adenocarcinoma with mucous lakes (H&E ×100).

receiving adjuvant chemotherapy. The patient is doing well 2 years after the operation with no evidence of recurrence on follow-up imaging studies (CT scan, colonoscopy).

## DISCUSSION

Neurofibromatosis type 1 is a familial disease first described by Von Recklinghausen in 1882 and it is characterized by multiple soft, sessile or pedunculated skin nodules of varying size and areas of cutaneous pigmentation (café au lait spots). It is one of the most common autosomal dominant traits with an estimated frequency of one in 3000 births and has been mapped to 17q11.2 (Glover *et al.* 1991). The frequency of involvement of gastrointestinal tract in neurofibromatosis varies from 10% to 25% (Davis & Berk 1973; Benharroch *et al.* 1992), but only a small number of patients have symptoms. Gas-

**Table 1.** Reported cases of small-bowel adenocarcinoma in patients with neurofibromatosis

No.	Author	Age (years)/sex	Symptoms	Location	Neurofibromata	Treatment	Outcome
1	Albores-Saavedra <i>et al.</i>	48/m	Pain	Ileum	Small bowel	Resection	Died
2	Ho <i>et al.</i>	75/m	Anorexia	Duodenum	Skin	Bypass	Died
3	Nelson <i>et al.</i>	72/f	Anasarca	Ileum	Skin	Resection	Unknown
4	McGunchey <i>et al.</i>	29/m	Jaundice	Duodenum	Skin	Resection	Died
5	Jones and Marshall	59/m	Pain	Ileum	Skin	Resection	Unknown
6	Benharroch <i>et al.</i>	73/m	Pain	Ileum	Skin	Resection	Unknown
7	Joo <i>et al.</i>	49/f	Pain	Duodenum	Skin	None	Unknown
8	Present case	73/m	Pain	Ileum	Skin, small bowel	Resection	Alive

f, female; m, male.

trointestinal tumours in NF1 can present clinically with pain, haemorrhage or intussusception but most cases have been diagnosed as incidental findings at laparotomy or post mortem or on barium studies. The majority of these lesions are neurofibromas, but other tumours of neural-crest and non-neural-crest origin are known to occur. Much more rare is the development of epithelial malignancies, and here an oncogenic relationship is not apparent. The prevalence of malignant tumours is reportedly four times higher in NF1 patients than in the general population (Zoller *et al.* 1995). Besides, the incidence of adenocarcinoma of small bowel in general population is very low (0.5/100.000) (Jones & Marshall 1987). Although an estimation of adenocarcinoma incidence in patients with neurofibromatosis cannot accurately be made, this association appears to be more than coincidental.

Transit time of the fecal flow in the small intestine may be protracted due to neurofibromatosis and this has been implicated for the malignant transformation to small-bowel adenocarcinoma (Benharroch *et al.* 1992). Neurofibromatosis type 1 patients have mutations of the NF1 gene on chromosome 17. Neurofibromatosis type 1 gene protein, neurofibromin, acts as a tumour suppressor by turning the active form of Ras into an inactive form. This molecular switch has an important role in the control of the cell cycle and differentiation, and changes in Ras activity are present in many different cancers. Recently, it has been suggested that NF1 gene may play a role in the development and progression of colon cancer (Cacev *et al.* 2005). This possible mechanism could also be involved in the development of small-bowel adenocarcinoma in NF1 patients.

The coexistence of neurofibromatosis with small-bowel adenocarcinoma is exceedingly rare (Table 1) (Albores-Saavedra *et al.* 1974; Ho *et al.* 1980; McGunchey *et al.* 1982; Nelson 1982; Jones *et al.* 1987; Benharroch *et al.* 1992; Joo *et al.* 2002). A review of the English-language literature disclosed seven reported cases of adenocarcinoma of the small bowel in patients with neurofibromatosis. The patients were aged 29–75 years, and consisted of

six men and one woman. Five cases of adenocarcinoma were located in the ileum, and two in the duodenum. Almost all patients complained of gastrointestinal symptoms. The adenocarcinoma in our patient was located in the ileum, and he presented with abdominal pain. In our case, the patient underwent a wide resection of the involved ileum together with all visible nodules in the adjacent mesentery. The patient denied other adjuvant treatment; he is alive 2 years after the operation with no recurrence of the disease or sign of metastases.

In conclusion, because epithelial malignancies of the small bowel are relatively uncommon, we propose that the association between small-bowel adenocarcinoma and neurofibromatosis may not be coincidental, and we suggest that adenocarcinoma of small bowel should be considered, in particular, in the differential diagnosis of symptoms of acute abdomen in neurofibromatosis patients.

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