

STROMAL TUMOR IN VON-RECKLINGHAUSEN DISEASE

BENSETTI HOUARI Amina Karima

university of medicine, Algeria

Abstract

Summary :

The association of digestive stromal tumors and Von Recklinghausen's disease is of the order of 25% of cases in autopsic studies and only 5% with clinical manifestation; our observation focused on a particular mode of revelation in a table of acute intestinal obstruction, remains a diagnosis to be evoked given the frequency of the association and to be taken into consideration given the potential of malignancy of stromal tumors.

Observation:

63-year-old man with a history of VON RECKLINGHAUSEN's disease, treated for a subocclusive syndrome, Clinical examination found multiple neurofibromas disseminated on all the trunk with coffee milk spots.

Palpation perceives a sub-umbilical mass of imprecise limits, Morphological examination (CT, ECHO): Grelic tissue formation measuring 92mm × 52mm heterogeneous with grelic distension upstream; Normal tumor markers (CA 19 9, ACE); Normal rectosigmoidoscopy up to 55cm from the anal margin, the diagnosis of a secondary localization of a neurofibroma was suspected, a laparotomy is indicated due to the table of occlusion on an obstructive gel mass, exploration after laborious viscerolysis highlights evidence of two formations of ileal seat, one voluminous extraluminal one of 100 × 40mm invading the sigmoid colon as well as a second location of 20mm surgical resection removing the masses with a safety margin of 05cm with double anastomosis, post-suites The anatomopathological study returned in favor of a low-grade spindle-shaped cell tumor with dual localization evoking a GIST or others supplemented by immunohistochemistry confirming the low-grade stromal nature. Patient referred to oncology for further treatment. His follow-up patient

did not present with tumor recurrence until the last CT scan in May 2015.

Conclusion: in a patient with Recklinghausen's disease with an occlusive syndrome, do not rule out the possibility of association with stromal tumors given the frequency of the association of Recklinghausen, GIST with multiple characters.

Keyword: *stromal tumor - neurofibromatosis - occlusion*

1.INTRODUCTION

The neurofibromatose 1 (NF1) or von Recklinghausen's disease is a disease that is manifested by coffee and milk spots on the skin and tumors located along the nerves, called neurofibromas. Depending on the size, number and location of these neurofibromas, complications can occur. It is one of the most common genetic diseases. Its manifestations are extremely variable from one patient to another, ranging from minor forms which can almost go unnoticed to severe forms. There are two types of neurofibromatosis: The neurofibromatosis type I, which alone concerns us here, also called peripheral or Recklinghausen disease, concerns one birth in 3000, the result of an autosomal dominant, can be sporadic, and implicates an anomaly on chromosome 17. Type II neurofibromatosis, also called central, rarer (1 in 50,000 births) involves an anomaly on chromosome 22. The most common manifestations are cutaneous and neurological but other organs can be affected like the eye, the bones... Arterial hypertension is more frequent there than in the general population, as are certain cancers. This disease has been known for a long time. It was described in 1793 by Tisellius then in 1882 by Von Recklinghausen

Digestive damage from Recklinghausen's disease occurs in middle age, usually much later than skin damage, and can be divided into four categories: damage to the intrinsic digestive nervous system and its supporting tissues; stromal tumors; endocrine tumors of the

duodenum and the peri-ampullary region; and tumors various non-classifiable in the preceding categories, Digestive with the disease is present in 12-60% of cases. Along the digestive tract that is a cancer born, liver and pancreas also be achieved tumors stromal gastrointestinal are rare tumors of the tract digestive, of mesenchymal origin and of unknown etiology. Their clinical presentation is polymorphic and their diagnosis is based on the pathological and immunohistochemical study of the lesion. the c-kit mutation at the origin of these tumors has enabled a better understanding of their physiopathological mechanisms, with, as a result, important advances in their diagnostic and therapeutic management . Any GIST is potentially malignant. The association of digestive stromal tumors and Von Recklinghausen's disease is in the order of 25% of cases in autoptic studies and only 5% in clinical manifestation.

2. MATERIALS AND METHODS

Our observation focused on a particular mode of revelation in a picture of an acute intestinal obstruction , remains a diagnosis to be evoked given the frequency of the association and to be taken into consideration given the potential for malignancy of stromal tumors .

3. RESULTS

Mr XY aged of 63 years, the previous history of disease recklinghausen , chronic smoking; married with 03

children admitted for diagnostic management and treatment of a syndrome sub occlusive .a notion of diffuse abdominal pain , nausea, vomiting, hematemesis and melena then transit disorders for two months . A e CONSIDERATION clinic found a patient with é tat g eneral altered , of a thoracic deformation with depression of the sternum. , multiple neurofibromas scattered all over the body predominantly on the trunk with café au lait spots. (photo n ° 1) the abdomen slightly distended. with a mass occupying the entire region under the umbilicus of imprecise boundaries . In addition, the free hernial orifices.



Photo n ° 1
ASP from the front standing and profile (Right - Left)



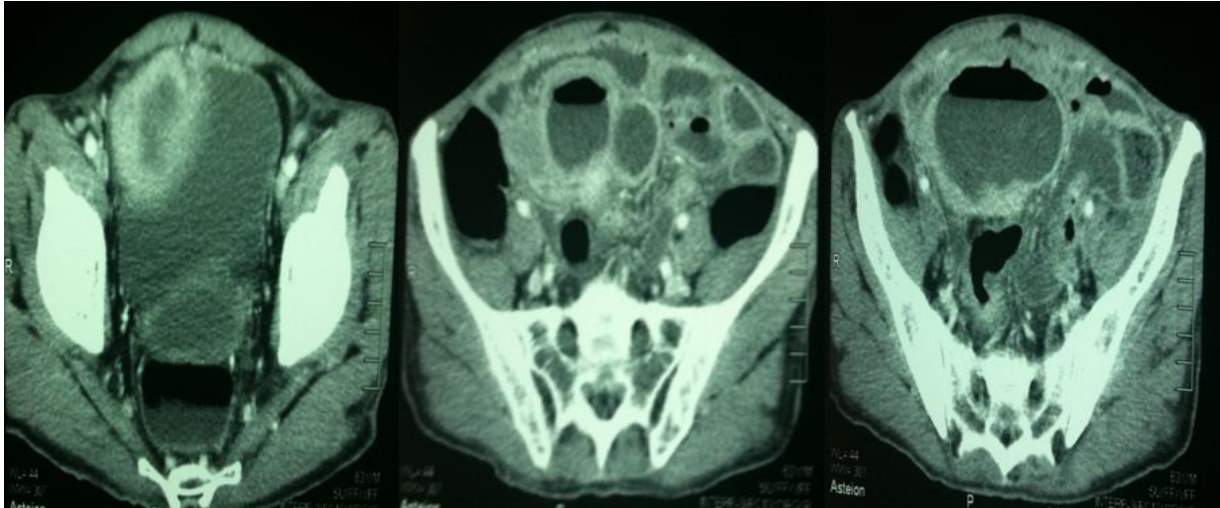
The radiology of the abdomen without preparation finds the p resence of some hydro-areal images in projection of the left sacrum and sacroiliac .

The e ultrasound abdominal pelvic allows i dentification extra vesical lateralized right of tissue formation measuring 92 × 52,2mm heterogeneous belonging

probably the hinge recto sigmoid and prostate is increased volume contours reguliers of echostructure heterogeneous by calcification.

Scanner abdominal pelvic objective of a distension small bowel with stasis and ectasia marked with a bight which

has a épaissement pariétal at the right iliac fossa and distension aeric colic , otherwise the liver is of normal size by heterogeneous density presence of multiple biliary cysts, the largest of which measures 17mm , No ADP



Biological assessment: TP: 73% ; GB18000elts / mm , HB: 10.7g / dl , plq: 468000 / mm , Vs : 115mm 1H 123mm 2H Gly, urea and creat correct . Tumor markers : normal, i.e. CA 1 9-9: 2U / ml CA 15-3: 7U / ml ACE: 2.16ng / ml

The patient was operated .we do laparotomy is indicated because of the occlusal table on mass small bowel obstructive exploration after viscerolysis laborious highlights two formations small bowel ileal seat the voluminous training extraluminal 100 × 40mm adhering

sigmoid colon with the presence of an abscess collection being evacuated after practice p raising cytobacteriological to study; and a second location small bowel 20mm long axis, surgical resection small bowel carrying the two masses small bowel with a margin of safety of 02cm followed by a double anastomosis and confection of a colostomy on a rod at the sigmoid level . Abundant toilet , installation of a drain in the douglas cul de sac. Parietal closure.



The anatomopathological study was in favor of a spect for a low grade spindle cell tumor with double

localization which makes us suggest either a GIST or other, hence the interest of an immunostaining . The immunohistochemical study shows an i mmunolabeling carried out with DAKO product

CKIT: strong expression therefore appearance of a low grade GIST confirming the histopathology.

The postoperative follow-ups were simple patient referred to oncology, then the patient was taken again three months later to reestablish digestive continuity.

The follow up : After one year, one notes no clinical recurrence or radiologique photo

3. DISCUSSION

3.1. On the epidemiological level

GIST 3% of all tumors of the digestive tract; 80% of tumors mesenchymal are seated throughout the digestive tract, from the esophagus to the anus. In neurofibromatosis, GISTs occur at a younger age, less than 40 years old. slight female predominance. Experts in the field agree that GIST-associated neurofibromatosis is a separate entity from sporadic GIST; GISTs develop in 7% of patients with neurofibromatosis, while in the general population where the prevalence of GIST is 0.013%(1)

3.2. On the diagnostic level

There are associations with the GIST [1] [2]

- Type 1 neurofibromatosis
- Familial forms of multiple stromal tumors (exceptional)
- Carney 's triad (very rare): multiple gastric stromal tumors , pulmonary chondroma and extra-adrenal paraganglioma
- Diade of Stratakis-Carney (very rare): tumor stromal gastric multiple paraganglioma extra-adrenal (but no pulmonary chondroma).

In these cases, an oncogenetics consultation is recommended after patient information and agreement (expert agreement) . an annual clinical examination for patients with NF1 except in the event of complications (Pinson 2002).

3.3. On the anatomopathological level

- From a macroscopic point of view:
- tumors appearing well limited , lobulated , white or pink when cut, with a very characteristic

encephaloid appearance. Necrotic, hemorrhagic or cystic changes are sometimes observed in the largest tumors, which can reach (30 to 40 cm in diameter).

- The histological presentation of GISTs is very varied: The cells either spindle- [3] shaped , conjunctive- like (70%), or rounded, epithelioid (20%), or intermediate in appearance (<10%).

3.4. On the immunohistochemical level

The demonstration of CD117 is the key element in the diagnosis of GIST and the differential diagnosis of other tumors (leiomyoma, leiomyosarcoma, leiomyoblastoma, etc.) and in the treatment of therapy [4] [5].

- the demonstration of smooth muscle actin and desmin in the absence of CD117 (30 to 40% of GISTs also express smooth muscle actin), the presence of the S-100 protein will be favor of a digestive schwannoma . ; c-kit / CD117 + in 95% of cases ; CD34 + in 70% of cases ; H- caldesmone + in 80% of cases ; DOG .1+ in 98% ; Molecular biology ; kit mutation: exon 11 (70%), exon 9 (10%), exon 13 (1%), exon 17 (1%) ; PDGFR alpha mutation: exon 18 (6%), exon 12 (0.7%), exon 14 (0.2%) (Reference centers: in the North-East region, Besançon and Strasbourg are reference centers for molecular biology. Other sites on www.gist-france.org cases.) [6]

3.5. On the therapeutic level:

Complete mono-block surgical resection of the tumor (R0 resection) with a margin of 1 to 2 cm is the treatment of choice. Les enucleations "simple" are burdened with significantly higher risk of recurrence than segmental resections. The surgical procedure depends on the site of the tumor. Lymph node dissection is not systematic. The efficacy of imatinib (a tyrosine kinase inhibitor molecule including KI T and PDGFRA) in locally advanced or metastatic stromal tumors is well established. (recommendation level: grade A)

In neoadjuvant situation : proposed after discussion in multidisciplinary consultation . It is based on imatinib (Glivec ®) for 6 to 12 months. in the form hardly are resectable at the outset due to their anatomical location , in the forms using the functional threatening , in the forms where surgery poses a significant risk of morbidity . In adjuvant situation . Optional in moderate and high

risk forms or in case of tumor break-in . It is based on imatinib . The optimal duration of treatment is not known. A period of 12 months is currently recommended [7] [8].

3.5. On the plane prognosis

All stages, the survival after resection of tumors stromal malignant gastrointestinal is 35% at 5 years. For an isolated primary tumor, survival is 50 to 56% at 5 years and 35 to 43% at 10 years with a more favorable prognosis for the stomach than for the small intestine. The treatment of an isolated tumor is essentially surgical .

• In the event of metastasis, the chemotherapy was deemed ineffective. All stages combined, survival after

resection of malignant gastrointestinal stromal tumors is 35% at 5 years. For an isolated primary tumor, survival is 50 to 56% at 5 years and 35 to 43% at 10 years with a more favorable prognosis for the stomach than for the small intestine.

- The treatment of an isolated tumor is essentially surgical.
- In the event of metastases, the chemotherapy was considered ineffective

The AFIP classifications of Miettinen and NIH modified by Joensuu (Tables 1 and 2) are the most used in Europe [4]. A TNM classification is available (UICC TNM8), but is still little used in practice.

Maximum tumor diameter (cm)	Mitotic index **	Gastric GIST	GIST jejuno -iléale	Duodenal GIST	Rectal GIST
≤ 2	≤ 5	0	0	0	0
> 2 -5	≤ 5	1.9% (very weak)	4.3% (low)	8.3% (low)	8.5% (low)
> 5 -10	≤ 5	3.6% (low)	24% (intermediate)	- *	- *
> 10	≤ 5	12% (intermediate)	52% (High)	34% (High)	57% (High)
≤ 2	> 5	0	50% (High)	- *	54% (High)
> 2 -5	> 5	16% (intermediate)	73% (High)	50% (High)	52% (High)
> 5 -10	> 5	55%	85%	- *	- *

		(High)	(High)		
> 10	> 5	86% (High)	90% (High)	86% (High)	71% (High)

* number of patients insufficient for estimation.

** the mitotic index is evaluated by Miettinen on an overall surface area of 5 mm², estimation of 50 conventional high magnification fields in order to limit the variability depending on the microscopes (this corresponds in fact to only 20-25 high magnification fields on recent microscopes).

Table 1. Estimated risk of disease-related recurrence or death in localized GISTs resected in groups defined by size, mitotic index and tumor site (AFIP: Armed Forces Institute of Pathology) (d ' after Miettinen)the figures are based on the long-term

monitoring studies on 1055 gastric GIST 629 jejuno -iléales, duodenal GIST 144 and 111 rectal GIST. To this should be added the perforation which is associated with a high risk of recurrence.

Risk of relapse	Cut	Mitotic index	Location
Very weak	≤ 2 cm	≤ 5	Indifferent
Low	> 2 - 5 cm	≤ 5	Indifferent
Intermediate	≤ 5 cm	6-10	Gastric Gastric
	> 5 - 10 cm	≤ 5	
High	Indifferent	Indifferent	Tumor rupture
	10 cm	Indifferent	Indifferent
	Indifferent	10	Indifferent
	5 cm	5	Indifferent
	≤ 5 cm	5	Non gastric
	> 5 - 10 cm	≤ 5	Non gastric

Table 2. Estimation of the risk of recurrence in localized GIST resected in the Joensuu classification derived from that of the NIH [4]

It aims in particular to better separate intermediate and high risk GISTs, and incorporates the pejorative nature of perforation

Conclusion

Patient with Recklinghausen's disease with an occlusive syndrome, do not rule out the possibility of association with stromal tumors given the frequency of the association of Recklinghausen, GIST with multiple characters.

The prognosis is influenced by the fact that usually there are low grade tumors, the survival is relatively good and at the same time the effectiveness of imatinib treatment is far worse than the excellent results obtained. in patients with sporadic GIST.

BIBLIOGRAPHIE

- [1] Boudet MJ, Demestier P. Les tumeurs stromales du tube digestif. *J Chir* 2001;138:104—8..
- [2] Dewailly A, Yasdanparrah Y, Renou C, Paris JC. Urgences abdomi-nales et neurofibromatose de Von Recklinghausen. *GastroenterolClin Biol* 1997;21:227—8..
- [3] Fuller CE, Williams GT. Gastrointestinal manifestations of type I neurofibromatosis (von Recklinghausen disease). *Histopathology* 1991;19:1—11.
- [4] Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stro-male tumors: recent advances in understanding of their biology. *Hum Pathol* 1999;10:1213—9.
- [5] Kramer SC, Gorich J, Rilinger N, Siech M, Aschoff AJ, Vogel G, et al. Embolization for gastrointestinal hemorrhage. *Eur Radiol* 2000;10:802—5.
- [6] Balaton AJ, Coindre JM. Tumeurs stromales digestives. *Gas-troenterol Clin Biol* 2001;25:473—82..
- [7] Joensuu H, Roberts PJ, Sarlomo-Rikala M, et al. Effect of the tyrosine-Kinase inhibitor STI571 in a patient with a metastatic gastro-intestinal stromal tumor. *N Engl J Med* 2001;344:1052—6*.
- [8] Barrier A, Huguier M, Levard H, Montariol T, Fagniez PL, Sauva-net A. Tumeurs gastriques

conjonctives. Résultats d'une étude multicentrique. *Chirurgie* 1999;124:494—502.