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Gastrointestinal stromal tumors : About 21 cases

F. Mghyly, H.El Bacha, S. Mechhor, M. Cherkaoui, N.Benzzoubeir, I.Errabih
Hepato-Gastro-Enterology and Proctology Department "B " Ibn-Sina Hospital, Mohammed V University Rabat, Morocco.

Abstract :
GISTs are the most common sarcoma of the digestive tract, but represent only 0.2 % of all digestive malignancies. They occur in adults of all ages, but rarely before the age of 40. GISTs are generally located in the stomach or small intestine, and the diagnosis is initially made on the basis of endoscopic, echo-endoscopic or radiological features. Only anatomopathology can confirm the diagnosis. Surgical resection remains the only curative treatment for localized stromal tumors, and in the case of locally advanced or metastatic disease, or in the event of recurrence, the first-line treatment is imatinib, a tyrosine kinase inhibitor. In the light of literature data, we will study the epidemiological characteristics and endoscopic aspects of gastrointestinal stromal tumors through a series of 21 cases collected within the department of gastroenterology and proctology "Medicine B" Ibn Sina Hospital in rabat.

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I. Introduction

Gastrointestinal stromal tumors (GIST) are mesenchymal tumors arising in most cases in the stomach and small intestine, more rarely in the rectum, colon, esophagus or mesentery. They derive from Cajal's cells or one of their precursors in the wall of the digestive tract, and are exceptionally extradigestive. Although GISTs are the most common sarcomas of the digestive tract, they account for only 0.2% of digestive malignancies [1,2]. They are characterized by immunohistochemical overexpression of C-kit and by activating mutations of receptor tyrosine kinases. These tumors have a known malignant potential, and their prognosis is correlated with location, tumor size and mitotic index. Surgery is the standard treatment for localized forms. Targeted therapies, such as Imatinib followed by Sunitinib, have transformed the management and prognosis of advanced and metastatic forms.

The aim of our study is to analyze the epidemiological profile and endoscopic aspects of gastrointestinal stromal tumors through a series of 21 cases collected within the department of gastroenterology and proctology "Medicine B" Ibn Sina Hospital, Rabat.

II. Materials and methods:

This is a retrospective descriptive study, over an 18-year period between January 2005 and January 2023, including all patients followed up for GIST in our clinic. Epidemiological data, clinical symptomatology, endoscopic, radiological and anatomopathological aspects were collected.

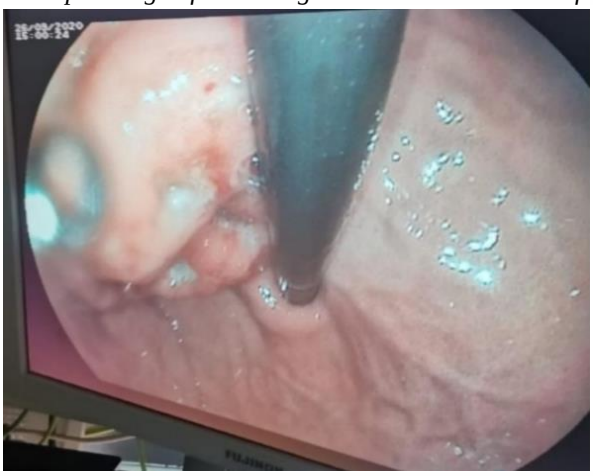
III. Results:

In our study 21 cases of gastrointestinal stromal tumors were reported. The mean age of our patients was 62 years, with extremes of 42 and 83 years, and the sex ratio was 1.1 (11 men and 10 women).

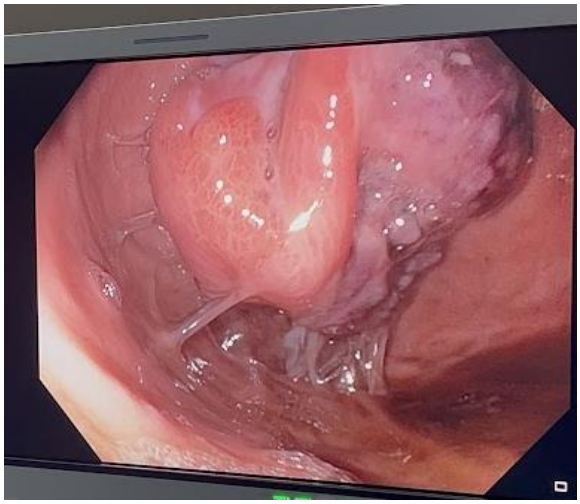
Clinically, abdominal pain predominated in 11 patients (52.4%), gastrointestinal bleeding in 4 patients (two cases of hematemesis and two cases of melena) (19%), discovery of an abdominal mass in 19% of patients (4) (including 2 epigastric masses and 2 hepatomegaly), proctalgia in one patient (4. 8%) and proctological examination revealed anal ulceration extending into the anal canal, while colonoscopy showed the presence of a submucosal formation bulging into the anal canal and extending into the rectum. Finally, the discovery of the tumour was fortuitous in one patient (4.8% of cases).

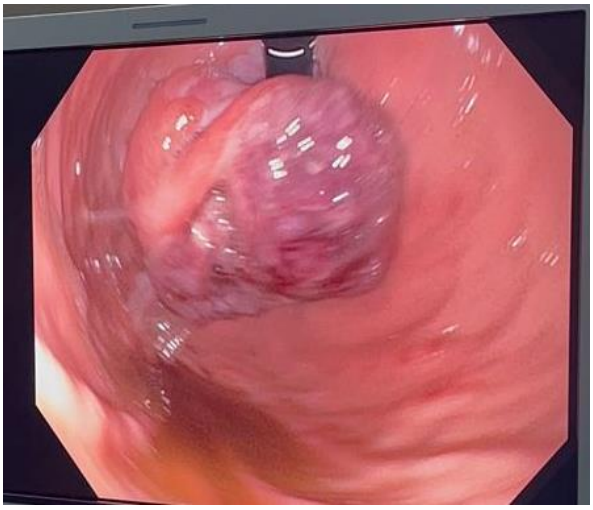
20 patients underwent oeso-gastroduodenal fibroscopy, with endoscopic findings dominated by : Surface ulcerated gastric formations in 11 patients and extrinsic compression in 6 patients (compression of the greater gastric curvature in 4 patients and of the duodenum in two patients), an appearance of large duodenal folds ulcerated on the surface and bleeding on contact in one patient, and FOGD was strictly normal in two patients. (Table 1)

Endoscopic image of a budding GIST with ulcerated surface



Endoscopic images of an ulcerative process with a submucosal part





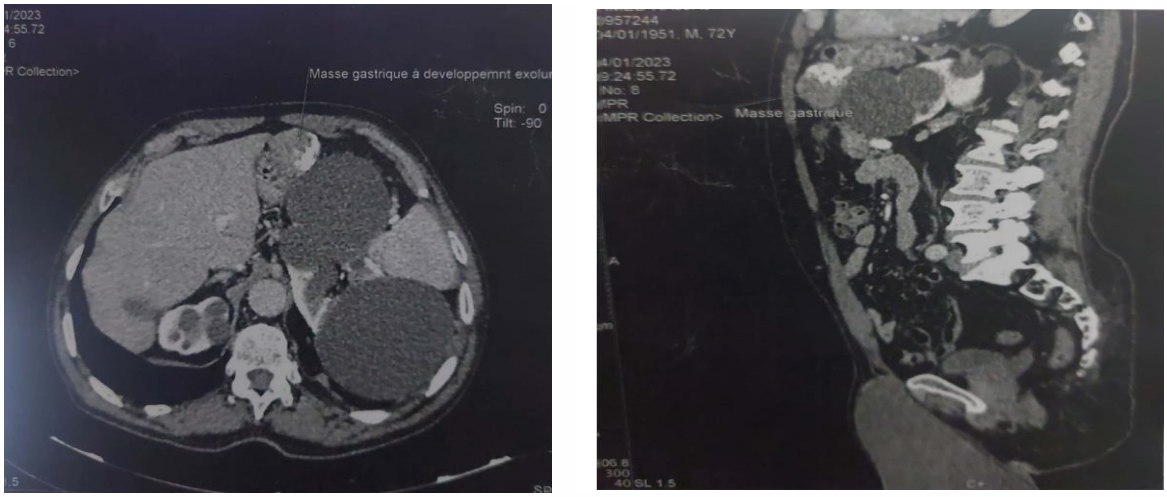
Endoscopic appearance	Number of cases
Surface ulcerated gastric formations	N=11 (52,4%)
Extrinsic compression	N= 6 (28,6%)
Large ulcerated duodenal folds	N= 1 (4,8%)
Normal FOGD	N=2 (9,5%)

Table 1 : Endoscopic appearance of GIST in our series

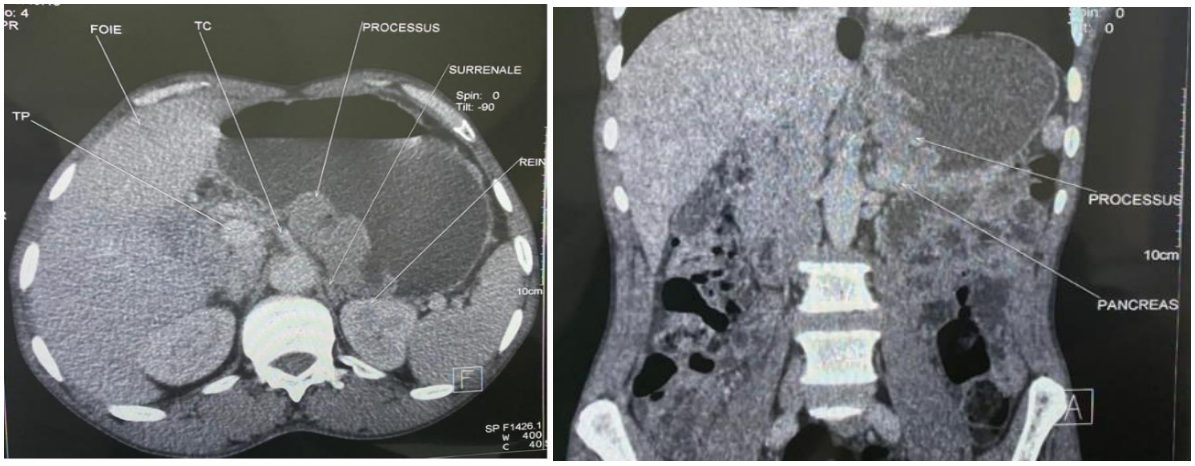
Histologically, anatomopathological study with immunohistochemistry (of endoscopic biopsies) led to a positive diagnosis of GIST in 12 patients (57%), whereas it was inconclusive in 8 patients (38%) whose echoendoscopic complement and CT scan appearance were pathognomonic of GIST.

For the anorectal location, the histological study of the per-endoscopic biopsies was inconclusive, but the anatomopathological study of the echoendoscopic biopsies was in favour of a high-grade stromal tumour.

CT scans were carried out in all our patients, enabling us to identify the primary tumour, which was dominated by gastric tumours in 16 patients (76.2%), 3 duodenal tumours (14.2%), one small bowel tumour and one anorectal tumour (4.8% each) (Table 2). CT scans revealed hepatic metastases in 4 patients (19%), and pancreatic invasion in one patient (4.8%).



CT aspects of gastric GIST.



CT aspects of gastric GIST invading the pancreatic body

Location of GISTs	Number of cases
Gastric	16 cases (76.2%)
Duodenal	3 cases (14.3%)
Small intestine	1 case (4.7%)
Anorectal	1 case (4.7%)

Table 2 : Location of GISTs in our series

Concerning therapeutic management, 1 patient underwent haemostasis gastrectomy, 11 patients (52.4%) underwent surgical excision adapted to the tumour location, including two patients who received adjuvant imatinib therapy.

The patient with anorectal GIST underwent abdominoperineal amputation. 4 patients received palliative treatment with imatinib. And 4 patients died prior to any therapeutic project, either as a result of metastases with AEG or extensive digestive haemorrhage.

IV. Discussion :

Although they are the most common mesenchymal tumours of the digestive tract, GISTs are thought to account for only around 1% of all digestive tumours. Several studies have estimated their incidence at between 10 and 15 cases per year and per million inhabitants, or around 600 to 900 new cases per year in France [3].

GISTs occur in adults at any age, but rarely before the age of 40, with a peak frequency around 50-60 years and a sex ratio close to 1.

Around 60% of GISTs are found in the stomach, 30% in the small intestine, and around 5% in the colon or rectum [3]. Other sites are very rare (esophagus, pancreas, omentum and mesentery).

GISTs remain asymptomatic for a long time, until they become very large or complicated. Their discovery may be fortuitous in around 20% of cases, notably during upper gastrointestinal endoscopy, imaging or

surgery. Digestive bleeding is the most frequent mode of revelation, either in the context of iron-deficiency anemia or externalized hemorrhage, when the tumor is ulcerated.

Other symptoms may include unspecific abdominal pain, a palpable mass, or complications such as perforation or occlusive syndrome, which can reveal GISTs in the bowel.

The diagnosis of GIST is initially made on the basis of endoscopic (particularly for gastric, duodenal or colorectal GIST), echo-endoscopic or radiological features [4,5].

The endoscopic appearance of GISTs is not very specific, generally that of a regular nodule, with a submucosal appearance because it is covered by normal mucosa. The tumour may also be ulcerated at the apex. Endoscopic biopsies are usually negative, as GISTs develop from the muscularis propria of the digestive tract.

Hence the importance of complementary echoendoscopy, which remains the best examination for characterizing lesions under the oesogastroduodenal or rectal mucosa. In fact, the tumor appears as a more or less hypoechoic round or oval mass located in the muscularis or submucosa, thus making it possible to differentiate submucosal tumors from extrinsic compressions.

Certain echoendoscopic criteria for GIST malignancy have been established by several retrospective studies: lesion size > 3 to 4 cm, existence of central necrosis, poorly defined contours, invasion of neighbouring organs, presence of intra-tumoral cystic zones.

CT is an indisputable tool both for the detection of primary tumours and for the assessment of GIST extension [6].

Primary lesions usually present as well-limited masses of variable size, isodense to muscular structures, attached to digestive structures. After contrast injection, their appearance varies according to size and lesion vascularization. The lesion is hyperdense or isodense, more or less homogeneous, with a wall that is usually hyperdense. Some lesions may remain hypodense due to extensive tumor necrosis and hemorrhagic remodeling [7], but certain examination characteristics and tumor presentation may vary according to location.

In addition to its role in characterizing primary tumors, CT is the key examination for studying locoregional and distant extension. GISTs progress locally, with distant extension mainly to the liver.

The diagnosis can only be confirmed by anatomical pathology, using either endoscopic or echoendoscopic biopsies. Histologically, the cells are spindle-shaped in 70% of cases, epithelioid in 20% and mixed or pleomorphic in rare cases. Even when clinical and histological findings are suggestive, the diagnosis of GIST must be confirmed by immunohistochemical study, which reveals KIT expression in tumour cells in 95% of cases.

In the vast majority of cases, KIT expression is strong and widespread throughout the tumor cells. In a few cases, the labeling is heterogeneous within the tumor, and only small tumor territories are positive; this can pose problems of false negatives on biopsies or microbiopsies. However, the near-constant presence of positive controls on slides, such as intra-mucosal or intra-tumoral mast cells and interstitial Cajal's cells in the muscularis, makes it easy to rule out a technical problem.

Conversely, false positives can occur when the antibody is too concentrated. Finally, it should be remembered that many other tumors may express KIT in the majority (seminoma, adenoid cystic carcinoma) or in a variable proportion of cases (melanoma, bronchial carcinoma, etc.). Around 5% of GISTs are KIT-negative, in which case diagnosis requires the identification of mutations in the KIT or PDGFRA genes within the tumour DNA [8].

The curative treatment of primary GISTs is complete surgical resection [1,2]. Lymph drainage is not routinely performed in GISTs [9,10] because, as with other sarcomas, GISTs are not very lymphophilic: the rate of lymph node invasion is usually less than 10%, and the risk of lymph node recurrence less than 5%. Surgical treatment of a gastrointestinal stromal tumour must be macroscopically complete, without tumour invasion and with healthy margins, while favouring functional exeresis. The edges of the resection must be free of tumour infiltration [9,10], but there is no consensus on the necessary safety distance between the edge of the tumour and the surgical section. However, a margin of 1 to 2 cm is generally considered sufficient.

Tyrosine kinase inhibitors (TKIs) have dramatically improved the prognosis of GIST, and imatinib is the only first-line treatment. The recommended dose of imatinib is 400 mg/day, except in the case of KIT exon 9 mutation (800 mg/day) [1,2].

The decision on adjuvant therapy should be based on the tumor's recurrence potential (very low, low, intermediate and high risk of recurrence) and potential sensitivity to imatinib [1,2]. Histological analysis of the surgical specimen is therefore essential, as is genotyping. Molecular biology testing for mutations in the KIT and PDGFRA genes is now standard practice in the management of GIST. Indeed, the type of mutation influences prognosis and treatment efficacy in adjuvant and metastatic settings. Genotyping of GISTs is recommended, with the exception of GISTs at very low risk of recurrence [1,2].

For metastatic forms (mainly peritoneal and hepatic), the only first-line treatment remains imatinib.

Surveillance of localized GIST There is no evidence to suggest that a specific surveillance protocol improves prognosis. It must be adapted to the risk of recurrence, the patient's condition and whether or not adjuvant treatment with imatinib is prescribed (fig 1).

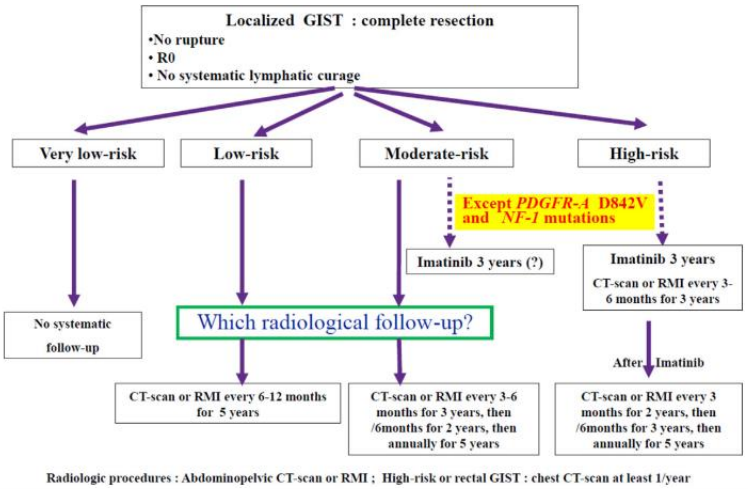


Figure 1: Algorithm for the management and monitoring of localized GIST [11].

V. Conclusion

Gastrointestinal stromal tumors (GIST) are rare connective tissue tumors, usually located in the stomach or small intestine.

The endoscopic appearance of GISTs is not very specific, and the anatomopathological study is often negative, hence the need for complementary echoendoscopy.

Surgical resection remains the only curative treatment for localized stromal tumors. In the case of locally advanced or metastatic disease, or in the event of recurrence, the first-line treatment is imatinib, a tyrosine kinase inhibitor that has completely changed the prognosis of these tumors.

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