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GASTRIC STROMAL TUMORS: ABOUT THREE CASES

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ABSTRACT

Gastrointestinal stromal tumors (GISTs) are the most frequent mesenchymal tumors of the digestive tract. These tumors were the object of numerous controversies in terms of histogenesis and of classification. They become integrated now into a frame (specific) precise nosologic since the discovery of the expression by the tumoral cells of the protein c-kit. Their malignant potential is often difficult to estimate. The diagnosis is confirmed by the anatomopathologic study completed by the immunohistochimic study. The treatment is essentially surgical, radiotherapy and chemotherapy being little effective. These tumors are particularly topical since the discovery of a treatment for the locally advanced, aggressive malignant forms, inoperable and/or metastatic by an inhibitor of the tyrosine kinase (STI571 or Glivec®).

KEYWORDS: Gastrointestinal stromal tumors; C-kit; Cells of Cajal; STI 571; Diagnosis and treatment,

INTRODUCTION

Digestive stromal tumors are mesenchymal tumors the most frequent of the digestive tract. These tumors have been the subject of much controversy in terms of histogenesis and classification. They integrate now within a precise nosological framework since the discovery of expression by the tumor cells of the protein c-kit. We report three cases of stromal tumors of gastric localization collected within the general surgery of the avicenne military hospital at marrakech, Morocco.

STUDY MATERIALS

We report a study with three observations of gastric stromal tumors collected at the surgery service of the 5th Military Hospital in Guelmim, Morocco. The patients' age was 43, 48 and 64 years, with a predominantly male. The time elapsed between onset of symptomatology and radiological exploration ranged from six months to two years.

The discovery of an abdominal mass was the main clinical manifestation associated with hemorrhage digestive tract in two patients with anemia. Slimming unencrypted was noted in one case.

The abdominal CT showed a tumor at the expense of the stomach in all cases (Figure 1). Surgical treatment has been introduced in all case. We performed a partial gastrectomy in one case and an enlarged total gastrectomy with splenectomy in two cases (Figs 2, 3 and 4). The anatomopathological report supplemented by a histochemical study was in favor of a stromal tumor in all cases.

Legendes

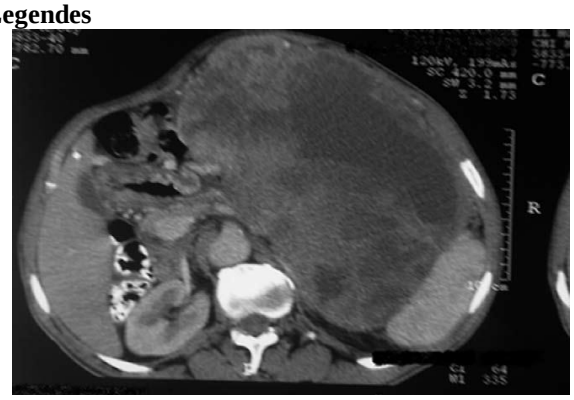

Fig. 1: Abdominal scan showing a huge tumor gastric.

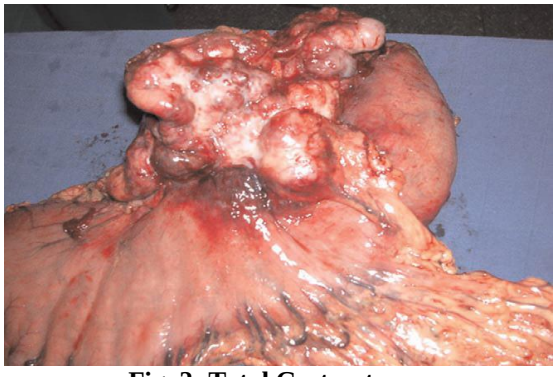

Fig. 2: Total Gastrectomy.

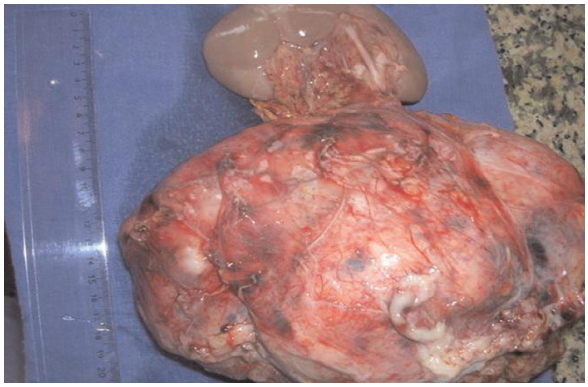

Fig. 3: Operative part of total gastrectomy extended to the spleen.

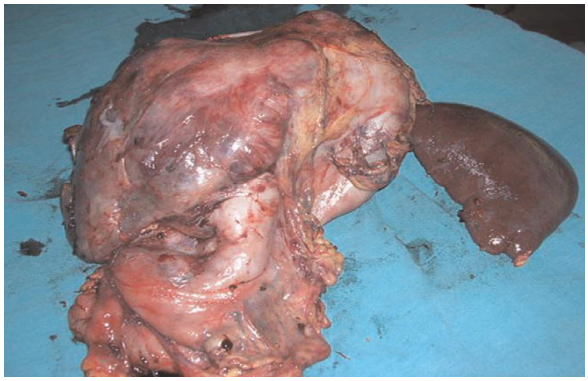

Fig. 4: Total gastrectomy with splenectomy.

Multiple unresectable hepatic metastases were discovered in the patient operated by a polar gastrectomy less than one year after surgery, a Glivec®-based treatment was introduced with good clinical and radiological evolution; the patient died 18 months after discontinuation of treatment. Both patients with total gastrectomy are still alive without any sign of recurrence on a three-year decline.

DISCUSSION

Gastrointestinal stromal tumors (gastrointestinal stromal tumor, GIST) are a very rare form of cancer digestive. They are the most common mesenchymal tumors of the digestive tract, the origin of which Cajal cells or their precursors, named after the neurologist who described them in 1893.[1] They correspond to nerve cells responsible for autonomic motor skills digestive.

They represent about 1% of digestive tumors And about 10% of sarcomas.[2] The impact of Stromal tumors would be between 7 and 15 per million inhabitants. An estimated 120 to 1,200 new cases year in France (2 to 20 per 100,000 / year). It is 5,000 year in the United States.[1,3,4] They occur in adults of any age, most often after 50 years, with a sex ratio Close to 1.[1,4] The most frequent localization of GIST Is the stomach, 60 to 70% of the cases, followed in order of frequency decreased by the small intestine (20-30% of cases), colon and rectum (5% of cases), mesentery (5% of cases) and the esophagus (less than 5% of cases).[2,5]

Mesenchymal tumors of the digestive tract has been, for long time, considered as tumoral musclar cell, leiomyomas, leiomyosarcoma or leiomyoblastomas or as nervous tumors, schwannomes on purely morphological criteria when examining the tissues under a microscope. This classification has been profoundly altered by the development of new cellular marking techniques.

These methods have shown that the majority of mesenchymal tumors of the digestive tract expresses, at their surface, a particular protein, CD34 (CD = cluster of differentiation). The term of GIST has imposed itself in the first place to designate any gastrointestinal mesenchymal tumor CD34 +, whatever its degree of differentiation. Subsequently, the GIST has become an entity in their own right since the discovery, in 1998, of a new marker, the Kit protein (CD117).

From the anatomical point of view, macroscopically the stromal tumors develop mainly from of the digestive tract muscle.[2,5,6] Their size varies from a few millimeters to more than 30 cm. The degrees of differentiation are variable. In case of digestive tumor macroscopic and histological appearance compatible with diagnosis of stromal tumor, CD34 immunoblotting (positive in 50-80% of cases) and CD117 (c-kit) should be sought after.[4,7] The expression of CD117 in the tumor is typically cytoplasmic, is generally present in the majority of cells. Spindle cell tumors CD117 can be positive for desmin or the S-100 protein, arguments in favor of diagnosis of leiomyoma and nervous tumor. These two markers are usually negative in tumors stromal.

Digestive stromal tumors have the particularity of having a malignant potential that is not always easy to be determined. A stromal tumor even of very low malignancy may relapse until 20 years after initial diagnosis. Like any sarcoma, the prognosis is correlated with the size tumor and the aggressiveness of the cells that compose it, specified by the measurement of the mitotic index.

The initial location of GISTs would also be a prognostic factor, favorable for proximal tumors (stomach) and unfavorable for distal sites (small intestine) (Table 1). Survival at five years after diagnosis initial all stages combined is 45%.[3,8,9] The mode of relapse for tumors whose resection may have been complete in 60% of cases in the form of locoregional relapses, in 25% of the locoregional and metastatic liver cases and in 15% of cases only intrahepatic. The invasion lymph node is exceptional (2%).[3,6,10] The median survival of a metastatic patient is 9 to 15 months[5,9] (Table 1). GIST symptoms are in function of size and location. They are rather small and asymptomatic in the tract digestive (30% of the cases) making their discovery often casual.[3,7,8,10,11] The most common frequent are digestive bleeding or abdominal pain non-specific, and more rarely a palpable mass.

Table 1: GIST prognostic factors.

Risk level (GIST workshop 2002)	Tumor (T)	Number of mitoses/50 fields to strong Magnification (IM)
	T < 2 cm	IM < 5
Very low risk	T = 2–5 cm	IM< 5
Low Risk	T = 5–6 cm	IM = 10
Risk	T = 5–10 cm	IM < 5
intermediate	T > 5 cm	IM > 5
High Risk	T > 10 cm	All IM values
	All values of T	IM > 10

Other possible symptoms are anorexia, dysphagia, obstructive syndrome, perforation, fever or obstructive jaundice.[11,12] Pathological associations have been described. In Carney's triad, there are classically multiple gastric stromal tumors, a pulmonary chondroma and an extrasurrenal paraganglioma, or more often in fact two of these tumors.[4,10,13] It is of interest to adolescent girls and young women. In the neurofibromatosis, 5% of patients develop tumors often symptomatic digestive stromal often multiple. Finally, cases of familial forms of stromal tumors multiples have been reported.[5,8,12,14]

In gastric localizations, the diagnosis can be evoked during an endoscopy before a tumor of pace submucosal ulceration. The abdominal scanner can be used to tumors, a possible invasion of neighboring organs or the presence of metastasis hepatic cells.[2,6,9,13]

Only the histological analysis will confirm the diagnosis of stromal tumor. Endoscopic biopsies, too superficial, are indeed generally negative. The sensitivity of ultrasound endosonography for diagnosis of malignancy of submucosal lesions is disappointing.[9,11,15]

A preoperative percutaneous biopsy is rarely discussed. It involves a theoretical risk peritoneal swarming in cases of malignant form. Its is not in the case of an inextricable tumor or, in doubt about the histological nature of the tumor which might to discuss a non-surgical approach, in particular a lymphoma.[2,7]

The cornerstone of GIST treatment has always rested until now on a wide and optimal surgery. The nature of the surgical procedure depends of course on the initial location of the tumor, its degree of extension and the presence or absence of synchronous metastases. In the case of a gastric tumor with malignancy, laparoscopic resection is increasingly practiced. Nevertheless, the pericardial or pre-pyloric localization are obstacles to this type of intervention. Extensive lymph node dissection is not indicated because of the scarcity of ganglion metastases. Survival is linked to the complete character of the resection.[6,16]

In more advanced forms, treatments of the type resection of peritoneal carcinoma with chemotherapy intraperitoneal or resection of liver metastases have been evaluated in small series; their profit is not established. Endosonography has an interest in monitoring patients not undergoing surgery.

Due to the high recurrence rate after resection, adjuvant treatment may be useful in cases of tumors with histological criteria for poor prognosis. There is no however, no evidence of efficacy of radiotherapy or of adjuvant chemotherapy.[5,7,15,17] The little data available in the literature shows that the radiotherapy is ineffective for palliative purposes. Chemotherapy Palliative is not very active in stromal tumors Malignant digestive tract, with response rates of less than 10%.[2,4,16,18]

In the case of resectable metastases, metastasis surgery should be undertaken, followed by supervision. In case locoregional recurrences or non-resectable metastases, treatment of stromal tumors resembled treatments of soft tissue sarcomas with chemotherapy whose monotherapy response rates do not exceed not in these stromal tumors 15% response (doxorubicin: 14%, DTIC: 10%, gemcitabine: 7%). Polychemotherapy (MAID: adriamycin, holoxan, deticene to high doses) have response rates of less than 35% and have no impact on the survival of patients.[2,4,8,15]

Since August 2000, the use of imatinib has revolutionized the management of stromal tumors. Imatinib form of mesilate, formerly STI 571) is an inhibitor selective protein tyrosine kinases, in particular c-kit, Cabl, bcr-al and the PDGF receptor at their level ATP binding site. This has led to the use of first in the treatment of chronic myeloid leukemia with high response rates. The justification for the use of imatinib in digestive stromal tumors is linked to its inhibitory action of the activated c-kit protein independently of its ligand. Imatinib is administered (96% bioavailability) in one dose daily because of a long half-life (18 hours). The capsules are dosed at 100 mg. Its metabolism is Hepatic and its essentially biliary elimination. The Low resectability rates of recurrences, including medians survival, even in complete resection, are less than 18 months, and the fact that purely local recidivism only one-third of patients refer to treatment with glivec® as first-line therapy in situations.[15,19]

In August 2000 the two phase I and II trials started. The results of this study were presented to the Congress American Oncology Society in 2001.[8,16,20] In february 2002, More than 2,000 patients had been included in

trials. On 2 february 2002, the Glivec® marketing authorization was given to United States for GIST.

Questions are still pending, such as the optimal daily and the interest of STI571 as adjuvant or neoadjuvant. Clinical trials will try to answer to these issues. A multicenter study coordinated by EORTC, and to include 600 patients, compares the dose from 400 mg / day to 800 mg / day. A phase II study must be carried out in the United States in order to test the STI571 in adjuvant treatment after resection of tumors with a high risk of recurrence in patients metastatic.

In a case of multiple hepatic metastatic recurrence and not resectable in a patient operated by a gastrectomy treatment, a Glivec®-based treatment has been established with a good clinical and radiological evolution. Unfortunately, the patient died 18 months after stopping treatment.

CONCLUSION

Histological diagnosis of digestive stromal tumors has been improved by demonstrating the expression of c-kit. The malignancy potential of these tumors remains often difficult to assess. Surgical resection is the curative treatment of localized tumors. After resection of a digestive stromal tumor, prolonged period is necessary because of the possibility of recidivism. The new therapeutic approach based on Glivec® has revolutionized the prognosis of patients with tumors metastatic stromal or nonresectable stromal.

No conflit of interest

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