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GASTROINTESTINAL STROMAL TUMORS : Retrospective study of 5 cases

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ABSTRACT

Gastrointestinal stromal tumors are the most common mesenchymal tumors of the digestive tract. These tumors are mostly localized in the stomach and small intestine. The particularity of these tumors is related to the discovery on the surface of its cells of the expression of a growth receptor with Tyrosine Kinase activity called C-kit. Our retrospective study focused on 5 cases of digestive stromal tumors diagnosed, treated and followed in the department of visceral surgery (Wing 3) of CHU IBN ROCHD of Casablanca. The aim of this work is to illustrate the clinical, paraclinical, histopathological, prognostic, evolutionary and therapeutic characteristics of these tumors using 5 clinical observations and a general review of the literature.

Keywords: Gastric Gastrointestinal Stromal Tumors- GIST- Epidemiology- Diagnosis- Treatment- Evolution

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INTRODUCTION

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract. These tumors are localized most often in the stomach and the small intestine. They derive from Cajal cells and are well characterized histopathologically and molecularly. The positive diagnosis is based on anatomopathological examination: fusiform or epithelioid morphology and positive immunohistochemical staining for cKit and CD34. However, even if recommendations are published for the management of these tumors, they still raise many problems for the clinician, both diagnostic and therapeutic.

MATERIAL AND METHODS

This is a retrospective study of 5 digestive stromal tumors treated at the visceral surgery department

(Wing 3) at IBN ROCHD CHU Casablanca. The average age of our patients was 60 years with extremes ranging from 31 to 65 years with a sex ratio of 0.6. The tumor localization was mainly concerned with the stomach (2 cases) and the small intestine (3 cases). Functional symptomatology leading to the diagnosis was dominated by pain (2 cases), gastrointestinal haemorrhage (3 cases), and deterioration of the general condition (4 cases). The clinical examination objectified an abdominal mass in 2 patients. Abdominal CT and endoscopy constituted the 2 main complementary examinations to characterize the tumor. The means of diagnostic confirmation was biopsy in 2 cases and surgery in 3 cases. The fusiform form was found in all samples. The stromal tumors of our patients were C-Kit positive in 3 cases and C-Kit negative in 2 cases. Surgery was the initial treatment for all our patients followed by Imatinib adjuvant therapy in one patient. Monitoring was based primarily on clinical examination and abdominal CT. The course was marked by complete remission in all patients.

RESULT AND DISCUSSION

Gastrointestinal stromal tumors are mesenchymal tumors that most commonly develop from the lining of the stomach and small intestine [14], more rarely from the colon, rectum or esophagus. The extra digestive locations remain exceptional. These tumors are derived from intestinal Cajal cells. These Cajal cells are responsible for digestive peristalsis and express the KIT in the normal state [14]. Histopathologically, stromal tumors of the digestive tract (TSD) are currently defined as fusiform and / or epithelioid conjunctive tumors with uncertain evolutionary potential and expressing the CD 117 antibody (c-kit) [24,30]. The incidence of these tumors is often underestimated because some tumor forms are asymptomatic and therefore undiagnosed. They represent less than 1% of malignant tumors of the digestive tract and 20% of malignant tumors of the small intestine [23,33]. The average age of diagnosis is between 50 and 70 years. As for the distribution by sex, some studies have shown that there is no predominance of sex [16]. The most frequently encountered locations are: stomach (60%), small intestine and colon (30%). They are rarely observed in the esophagus and the anus. The concomitant metastases are seen in 25 to 30% of cases with frequent location of the liver and mesentery. They are often associated with poor prognosis [13, 33]. GISTs are asymptomatic for a long time until they become bulky or causing a complication, their discovery can be fortuitous, all the more often as their size is smaller. The 2 most common symptoms are: externalized or occult digestive bleeding (when the tumor is ulcerated) and nonspecific abdominal pain or discomfort. Stromal tumors of the intestingrel can become acute with an obstructive syndrome, more rarely a hemoperitoneum. Biology is not contributive. Chronic anemia and a biological inflammatory syndrome can be observed [35]. Since GISTs are asymptomatic for a long time, their discovery is fortuitous, especially during upper digestive endoscopy, in about 25% of cases [25]. The tests that are useful for diagnosis depend on the size and location of the tumor. For tumors less than 5 cm in diameter, the diagnosis of gastric or colorectal GIST is usually evoked during endoscopy. Endoscopic examinations of the effective small intestine are now available. The endoscopic video capsule can detect small tumors [28]. The use of preoperative enteroscopy is now exceptional [20]. Echo-endoscopy is the best test for characterizing oeso-gastroduodenal or rectal mucosal lesions when they are small [27, 29]. Indeed, the echoendoscopic aspect of GIST is often typical: oval hypoechoic lesion, often homogeneous with regular limits, developing from the fourth hypoechoic layer (corresponding to the muscularis) [5]. Some endoscopic ultrasound criteria predictive of GIST malignancy have been established by several retrospective studies [5]: the size of the lesion (> 4 cm), the existence of a central necrosis, poorly limited contours, the invasion of neighboring organs and the presence of cystic areas intra TSD is most often a rounded mass of the digestive wall, poorly limited, multiple, endophytic or polypoid [12]. Ultrasound allows the assessment of local and regional extension in search of

metastases. It also guides biopsy punctures to confirm the diagnosis [22]. CT is the exam of choice in the assessment of these tumors. It makes it possible to suggest the diagnosis in the case of typically showing a mass of variable size often exceeding 5 cm, well limited in relation to a digestive wall, heterogeneous due to the presence of areas of necrosis, haemorrhage or calcification. [2,3]. When a very early assessment of tumor response to Imatinib is required, PET is recommended by the experts. On the other hand, performing PET is not recommended in patients with localized stromal tumor before or after complete tumor resection. The high cost and low accessibility of PET have been mentioned as arguments for not systematically proposing this technique for therapeutic evaluation [4,18]. Endoscopic biopsies are often too superficial, therefore non-contributory because the tumor develops in the sub-serous and usually spares the mucosa. In a study by Colon et al. [36], only 49% of the biopsies were positive, before the histological diagnosis of certainty of the surgical resection room. In view of these disappointing results, fine needle aspiration biopsy guided by ultrasound, CT or endoscopy was proposed preoperatively. Ando et al. Have shown in their study of 23 cases, which compared the anatomopathological results of needle aspiration and those of the operative specimen, that this technique with the immunohistochemical study has a place more and more important for a diagnostic contribution. before the surgical act [7,17]. The GIST certainty diagnosis is based essentially on the immunohistochemical study of the specimen, showing a strong expression of the tumor cells of the C-Kit and CD34 markers. GISTs express CD 117 or C-Kit in 90 to 95% of cases, H caldesmone in 50 to 80% of cases, actin in 40% of cases, S100 in 5 to 15% of cases. Recently, 2 markers have been developed: DOG-1 and PKC theta. The search for mutations has a double interest, prognostic and therapeutic, is recommended in cases of strong suspicion of GIST despite a negative immunohistochemistry [6, 9, 13, 33]. The macroscopic aspect of GIST is that of a nodular mass well limited, unencapsulated, developed in the digestive wall and often extending towards the serous slope. Necrotic, haemorrhagic or cystic changes are common when they are bulky [15]. There are several histological types, the main ones being: fusiform, epithelioid and mixed, of which the fusiform variant represents 70% of the cases [15]. It is the immunohistochemistry of gastrointestinal stromal tumors that currently allows the differential diagnosis with other tumors of the mesenchyme [16,32]. Several prognostic classifications exist, but the most important ones are those of Fletcher and Miettinien. The Fletcher classification (2002) divides patients into four groups based on maximum tumor diameter and mitotic index [19]. The Miettinian classification (2006) is based on tumor size and the mitotic index, on the site of the tumor [15]. It seems that the gastric localization is associated with a good prognosis. Complete surgical resection in monobloc is the only potentially curative treatment of GIST. Preoperative perforation results in peritoneal dissemination with similar survival to patients with incomplete excision. There is no consensus on optimal resection margins, however a margin of 1 to 2 cm is generally considered sufficient [33]. The efficacy of Imatinib in locally advanced or metastatic GISTs is now well established [11,34]. The recommended dose is one 400 mg tablet once a day in the middle of a meal. The dose of 800 mg / day is recommended if it is known to be a tumor with a KIT exon 9 mutation [8,21]. Resistance to treatment may be primary (in the first few months) about 10%, or secondary. This resistance must be checked for histological diagnosis and compliance. The efficacy of Glivec treatment has been reported in several Phase I studies (EORTC 62001), II (EORTC 62001, B2222) and III (EORTC 62005, S0033) [31]. The advent of Imatinib in GISTs makes it possible to establish recommendations to optimize the management of patients with GIST, given the current knowledge on Imatinib, based on the experience of investigators in this field. , and the wide variety of clinical presentations of GISTs. Regarding the follow-up of patients with stromal tumors, there is no formal guideline, mainly because of difficulties in defining the malignant potential of GISTs. Complete remission can be achieved by surgery or to a lesser extent by Imatinib alone (5% of Imatinib-treated cases) [10]. Tumor recurrence may appear either at the initial site of resection or remotely [1]. In the Mudan study [26], local recurrence was associated in

half of the cases with metastases.

CONCLUSION

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract. These tumors are localized most often in the stomach and the small intestine. The peculiarity of these tumors is related to the discovery on the surface of its cells, the expression of a growth receptor with tyrosine kinase activity called C-Kit. The positive diagnosis is based on the pathological examination. surgery is the reference treatment in localized forms. Imatinib is the standard first line treatment for metastatic gastrointestinal stromal tumors and adjuvant after surgery. The prognosis of GIST is excellent for benign tumors completely resected. GISTs are one of the best examples of the value of current research in molecular biology.

Conflict of interests

The authors do not declare any conflicts of interest.

Contributions of the authors

All authors contributed to carry out this study and they read and approved the final manuscript.

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