Gastrointestinal Stromal Tumors: Update and Therapeutic Strategies

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Abstract

Gastrointestinal Stromal Tumors (GISTs) represent a significant clinical challenge due to their resistance to conventional chemotherapy. This study aims to provide an update on the clinical, morphological, pathological, and therapeutic aspects of GISTs treated at our institution over an 11-year period. We highlight the efficacy of Imatinib as a targeted therapy and emphasize the importance of complete surgical resection. Additionally, we present a case of concomitant gastric adenocarcinoma and duodenal GIST, underscoring the need for comprehensive clinical evaluation in these cases.

Key words: Gastrointestinal Stromal Tumors

Introduction

Gastrointestinal Stromal Tumors (GISTs) are rare neoplasms, likely arising from Cajal cells, with an estimated annual incidence of 15 million worldwide.(1) Predominantly found in the stomach (60%) and small intestine (30%), they pose a challenge due to their chemoresistance.(2) In 1998, the discovery of the KIT receptor and activating mutations in the KIT gene marked a significant milestone. Subsequently, Imatinib emerged in 2001 as a major therapeutic breakthrough. By 2010, GISTs became the most prevalent sarcoma, accounting for 18% of cases.(3)

Materials and Methods

Patient Selection:

Inclusion criteria encompassed all cases of GISTs diagnosed through comprehensive paraclinical investigations, including histological examination. Exclusion criteria involved incomplete data pertaining to major variables such as histological findings, operative reports, and follow-up assessments.

Study Objective:

This retrospective descriptive study analyzed 35 cases of GISTs treated in our department from January 2010 to June 2022. We aimed to investigate their clinical, morphological, anatomopathological, and therapeutic characteristics.

Results:

In our study, a slight female predominance was observed, reflected by a male-to-female ratio of 0.75. Regarding the presenting symptoms, abdominal pain was the most common, reported in 65.71% of cases, followed by digestive bleeding (25.71%), digestive stenosis (17.14%), and the presence of an abdominal mass (15%).

Morphological evaluation was conducted through various exploratory procedures, with abdominopelvic CT scans being the most frequently utilized (30%), followed by upper GI endoscopy (17%), abdominal ultrasound (11%), lower GI series (2%), MRI (2%), endoscopic ultrasound (2%), enteroclysis (1%), and colonoscopy (1%).

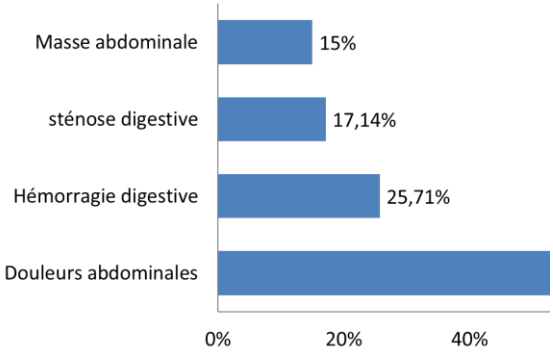

Figure 01: Revealing Functional Signs of the Tumor

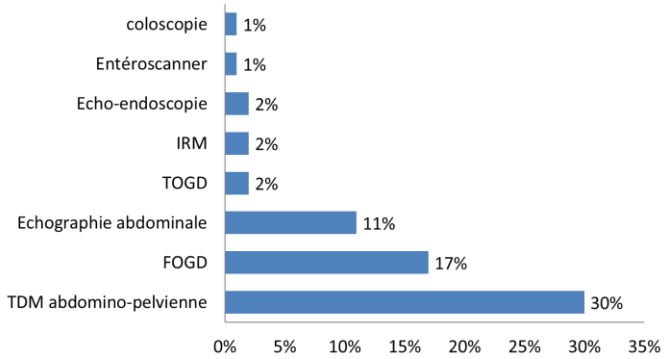

Figure 02: Digestive and radiological explorations carried out in our patients

Regarding tumor localization, the majority of cases were found in the gastric region (60%), followed by the small intestine (34%) and the duodenum (6%). Preoperative biopsies were performed in 20 cases, yielding diagnostic insights in 45% of instances. Surgical interventions adhered to the principle of macroscopically complete (R0) en bloc resection, with a focus on avoiding tumor rupture and eschewing lymph node dissection. Minimally invasive techniques were preferred to optimize patient outcomes. Pathological classification according to Miettinen's Histo-prognostic system revealed diverse tumor sizes, with 13 cases below 5 cm, 13 cases between 5 and 10 cm, and 9 cases exceeding 10 cm. The mitotic index, a critical prognostic factor, ranged from less than 5 mitoses per 50 fields in 10 cases, to 5-10 mitoses in 14 cases, and more than 10 mitoses in 11 cases. Resection status was predominantly R0, achieved in 34 cases, while one case had R1 resection and none had R2 resection.

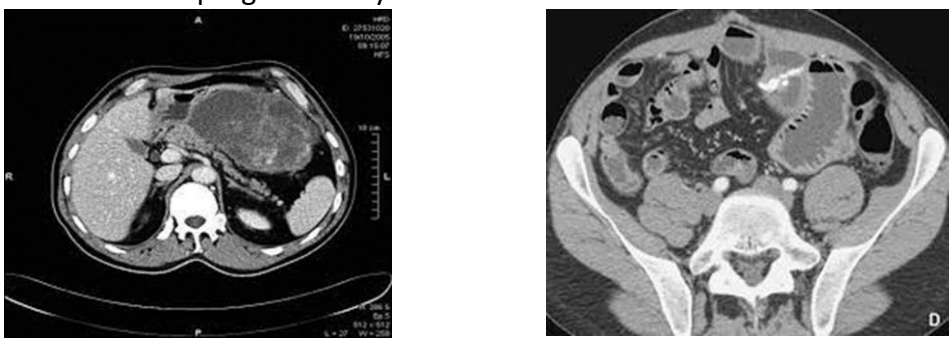

Figure 03: abdominal CT scan

Immunohistochemistry played a pivotal role in confirming the diagnosis, employing various markers. Specifically, C kit (CD 117) was assessed in 35 cases, with 31 cases testing positive (88.57%). CD 34, another crucial marker, was examined in 35 cases, revealing positivity in 29 instances (82.85%). PS100, a marker of neural differentiation, was studied in 17 cases, with 4 cases displaying positivity (23.53%). Dog1, a reliable GIST marker, was assessed in 15 cases, all of which tested positive (100%). Desmine, indicative of muscle differentiation, showed negative results in all 6 cases.

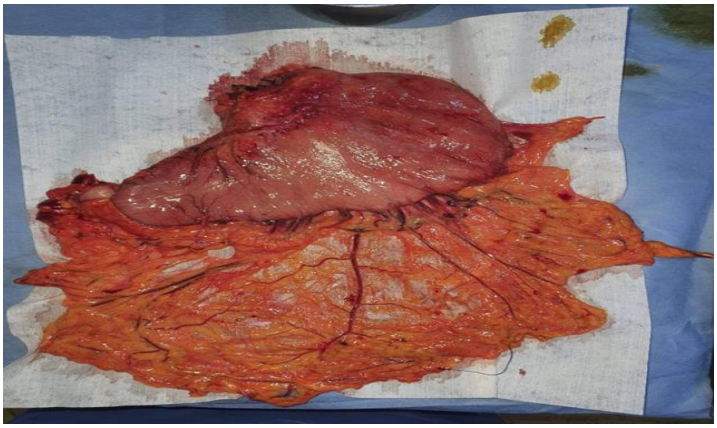

Figure 04: GIST, gastrectomy, general surgery department, Benimessous Hospital

Furthermore, risk stratification according to the National Institute of Health classification categorized tumors as low risk in 12 cases, intermediate risk in 8 cases, and high risk in 15 cases. These findings collectively provide comprehensive insights into the clinical and pathological characteristics of GISTs in our cohort, informing future therapeutic strategies and clinical management decisions.

Of the 35 patients, 23 are currently under follow-up, with a mean follow-up period of 54 months (range: 10-124).Overall Survival (77%) and Recurrence-Free Survival (86%).

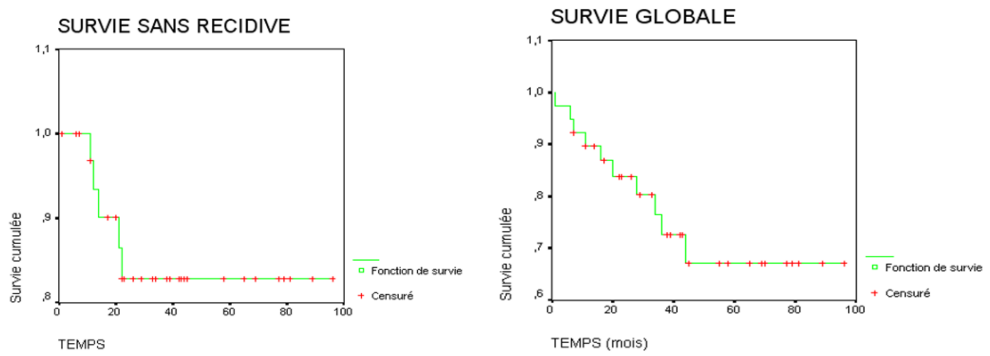

Figure 05: A: recurrence free survival *B: overall survival*

Discussion:

The observed slight female predominance in our study aligns with previously reported trends in GIST epidemiology. This finding may be attributed to hormonal influences or genetic predispositions, warranting further investigation. The male-to-female ratio of 0.75 underscores the need for gender-specific considerations in the clinical management of GIST patients.

Notably, the presenting symptoms exhibited a diverse spectrum, with abdominal pain being the most prevalent complaint. This aligns with established literature, where abdominal discomfort often serves as the initial clinical manifestation of GISTs.(4) The substantial proportion of cases presenting with digestive bleeding and stenosis highlights the potential for complications and underscores the necessity for prompt diagnosis and intervention.(5)

Morphologilical evaluation played a pivotal role in characterizing GISTs. Abdominopelvic CT scans were the most frequently employed imaging modality, offering a comprehensive assessment of tumor size, location, and potential involvement of adjacent structures. The utilization of upper GI endoscopy provided valuable insights, particularly in cases with gastric localization, aiding in accurate diagnosis and surgical planning.(6)

Our study revealed a significant representation of GISTs in the gastric region, consistent with the existing literature. The relatively high prevalence of small intestinal GISTs underscores the importance of comprehensive assessment of the entire gastrointestinal tract in clinical practice. The relatively lower incidence of duodenal GISTs, though less common, emphasizes the need for vigilant evaluation of this anatomical site, given its unique surgical considerations.

Preoperative biopsies, while contributing diagnostically in 45% of cases, presented a diagnostic challenge in the remaining cases. This highlights the intricate nature of GIST diagnosis and underscores the need for

multidisciplinary approaches, including thorough clinical, radiological, and immunohistochemical assessments.

Surgical intervention adhered to meticulous principles, aiming for macroscopically complete resection(7). The emphasis on avoiding tumor rupture and minimizing lymph node dissection aligns with established guidelines, prioritizing oncologically sound practices. The preference for minimally invasive techniques is a noteworthy advancement, offering potential benefits in terms of reduced postoperative morbidity and shorter hospital stays(8).

Pathological classification according to Miettinen's Histo-prognostic system provided valuable insights into tumor characteristics. The observed distribution of tumor sizes and mitotic indices underlines the heterogeneity within our cohort. These factors, alongside resection status, are pivotal determinants of patient prognosis, guiding subsequent therapeutic decisions(2,5).

Immunohistochemistry emerged as a critical tool in confirming GIST diagnoses. The high positivity rates of C kit (CD 117) and CD 34 affirm their established roles as reliable markers for GIST identification. The absence of Desmine expression in our cases reinforces its limited utility in GIST diagnosis.

Finally, risk stratification according to the National Institute of Health classification offers a framework for prognostic assessment and therapeutic decision-making. The distribution of cases across low, intermediate, and high-risk categories underscores the clinical heterogeneity within our cohort, emphasizing the need for individualized treatment approaches(5,9,10).

Conclusion

Complete surgical resection remains paramount and computed tomography remains the primary diagnostic and post-therapeutic follow-up modality.

Neoadjuvant treatment is not indicated if R0 resection is feasible.

Adjuvant Imatinib therapy is recommended for 3 years in high-risk or perforated GISTs, Prolonged surveillance is imperative due to the late recurrence of tumors, even with reduced malignant potential. Survival is contingent on complete surgery and other prognostic factors. Molecular biology has made remarkable strides in GIST research.

Acknowledgments

The authors express their gratitude to the patients and the medical staff of the General and Oncological Surgery Department, Beni-Messous, for their invaluable contributions to this study.

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