ANNALI ITALIANI DI CHIRURGIA

Digital Edition
e-publish on-line
ISSN 2239-253X
Direttore Nicola Picardi

Gastrointestinal stromal tumor. A case report with over 5 years follow-up

Ann Ital Chir, 2022; 11 - July 18
pii: S2239253X22037021
Online Epub

Andrei Părău*/**, Ovidiu Ghirlea*/**, Sonia Rațiu*, Cosmin Dragomir*/**, Sorin Olariu*/**

**First Clinic of Surgery, The County Emergency Hospital "Pius Branzeu", Timisoara, Romania*
***University of Medicines and Pharmacy "Victor Babes", Timsoara, Romania*

Gastrointestinal stromal tumor. A case report with over 5 years follow-up

Gastro-intestinal stromal tumors (GIST) represent a type of mesenchymal tumors, located in the digestive tract wall, with the possibility of alternate locations such as the caul or the mesentery.
The relapse prognosis is closely corelated with the dimensions of the tumor, the rate at which tumor cells divide, the cellularity of the tumor and the nuclear pleomorphism.
The definitive treatment for these types of tumors is surgical resection, associated with tyrosine- kinase inhibitors.The largest gastro-intestinal stromal tumor ever recorded in medical literature measured 42/31/23 cm and weighed in at 18.5 kg. The following case presentation is of a patient aged 65 at his first admission, who received tyrosine-kinase inhibitors of different generations, associated with multiple surgical interventions for tumor cytoreduction. The case presented, according to specialty literature, is the second one as far as volume and weight of the tumor go, the tumor invading the peritoneal cavity and weighing in at approximatively 15 kg.

KEY WORDS: Gist, Second largest tumor, Tyrosine-kinase inhibitors, Nuclear pleomorphism

Introduction

Gastro-intestinal stromal tumors represent a rare digestive tract pathology, that come with a reserved prognosis, especially for advanced cases. The origin of a GIST consists of interstitial Caial cells, located in the muscular tunic of the digestive tract. The highest rate of occurrence takes place at a gastric level, although these tumors can be found within any part of the digestive tract, including the mesentery or the caul. GISTs are a type of mesenchymal tumors and they represent less than 1% out of the total neoplasms of the digestive tract, being set apart by a mutation of the c-KIT gene, which maintains tumor growth by activating tyrosine-kinase receptors [1-13].

The relapse prognosis is closely corelated with the dimensions of the tumor, the rate at which tumor cells divide, the cellularity of the tumor and the nuclear pleomorphism.
GISTs that develop from the stomach have a better prognosis as opposed to those located within the intestine, mesentery or caul.
Gastro-intestinal stromal tumors are frequent enough in the medical practice, with having different locations, dimensions, regional invasion, treatment methods (surgical ablation, immunotherapy, endoscopic ablation) [15].
The largest gastro-intestinal stromal tumor ever recorded in medical literature measured 42/31/23 cm and weighed in at 18.5 kg.
This case presentation is about a 65-year-old patient, who presented himself in the hospital clinic, in February 2015, with the following ailments: postprandial epigastric pain, heartburn, nausea, vomiting and severe weight loss (10 kg within 6 months).
Initial clinical examination uncovers abdominal distension, alargetumor mass located in the hypogastrium and mesogastrium, painful during palpatory exploration.

Pervenuto in Redazione Agosto 2021. Accettato per la pubblicazione Settembre 2021
Correspondence to: A. Părău, MD (e-mail: parau.andrei@gmail.com)

Biological values denote a slight anemia (Hb 12,6 g/dL; 4.30 10^6/uL), the rest of the parameters being within normal range. Therefore, an abdominal echography is performed, showing us a tumor mass of great dimensions, in the lower abdomen, also confirmed later by a CT scan (Figs. 1, 2).

During the exploratory laparotomy, there are multiple tumor masses found in the caul, the small intestine, the entire large intestine and peritoneum, with the appearance of peritoneal carcinomatosis and a pelvic tumoral block, with an extension in the Retzius space, having an apparent homogeneous structure.

The surgical intervention consisted of excising the pelvic tumoral block, cytoreduction of the many abdominal tumors, lavage and multiple drainage.

Histopathological examination concurs that this was indeed a gastro-intestinal stromal tumor (GIST) with a mixt cellularity, epithelioid and fusiform, with a high potential for malignant development (>5/50 atypical mitosis, CD34+, CD117+, vimentin+) (Figs. 3, 4).

The pacient is transferred to the Oncology clinic, where he begins treatment with Imatinib, having a favorable response, with tumor size reduction and also a lower tumor count being seen on multiple subsequent imag-

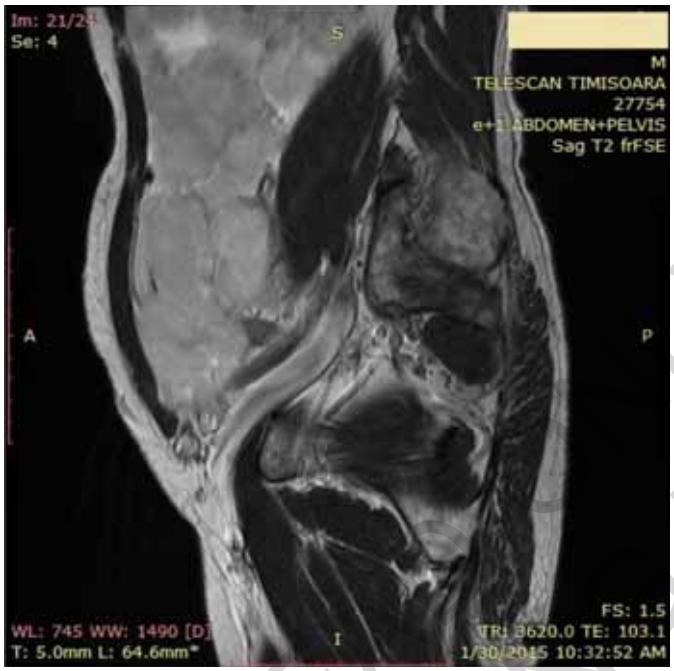

Fig. 1: Frontal and sagital view.

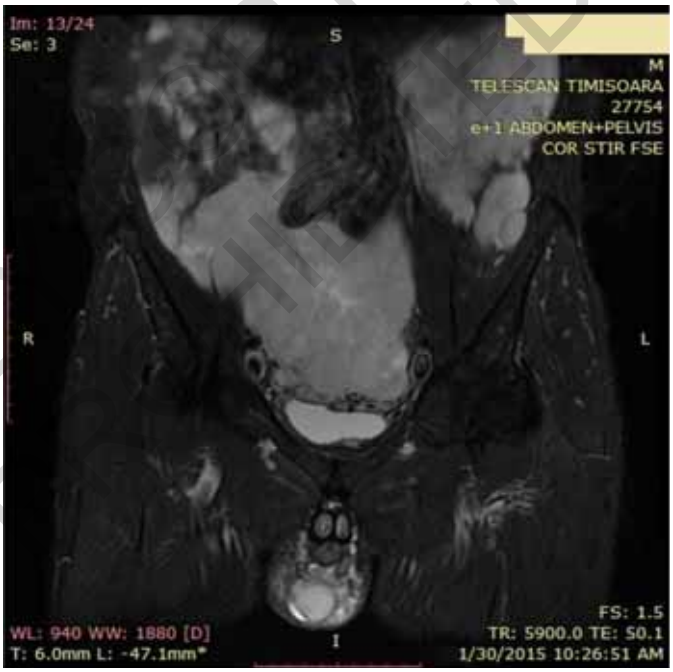

Fig. 2: Pelvic Tumor and peritoneal carcinomatosis.

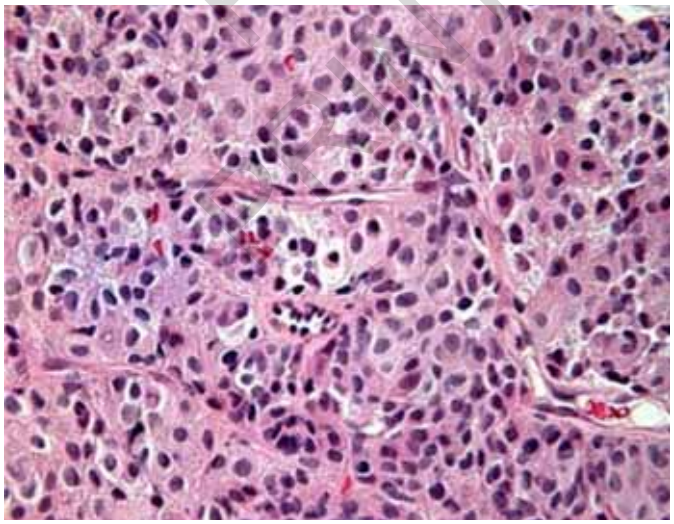

Fig. 3: Epitheliod cells GIST.

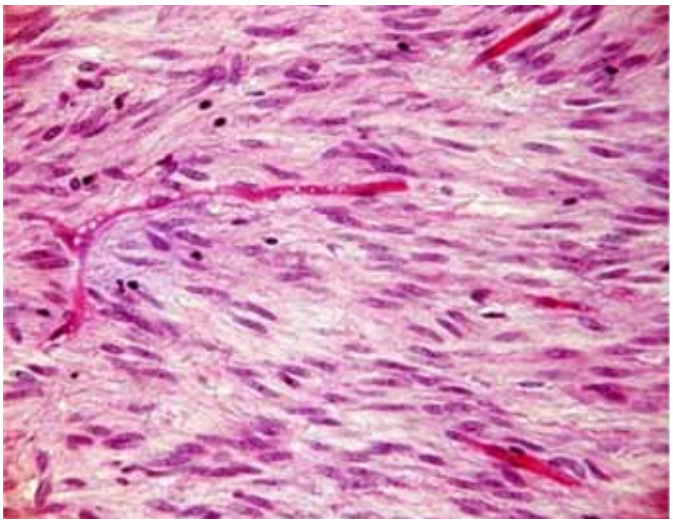

Fig. 4: Fusiform cell GIST.

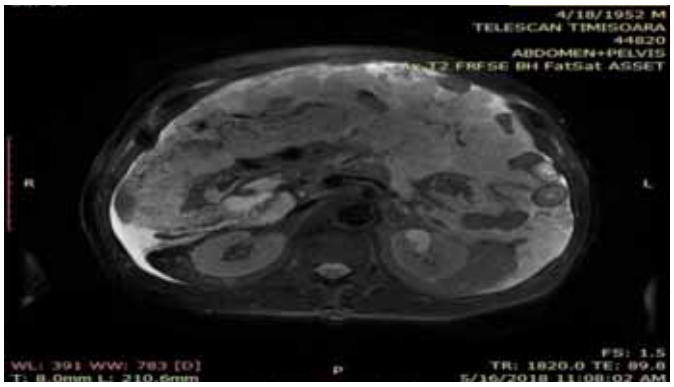

Fig. 5: Intraabdominal tumor recurrence.

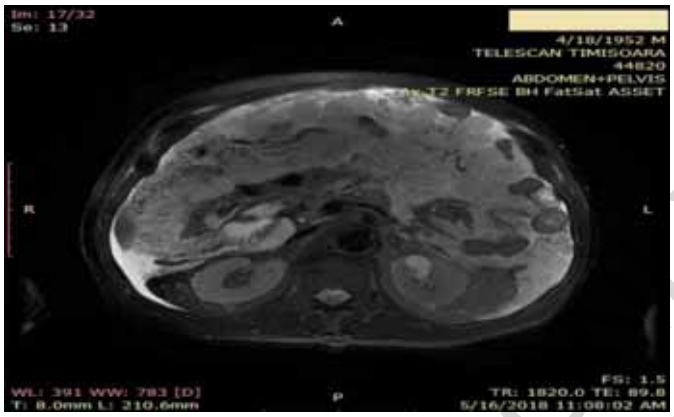

Fig. 6: Tumor recurrence small intestine.

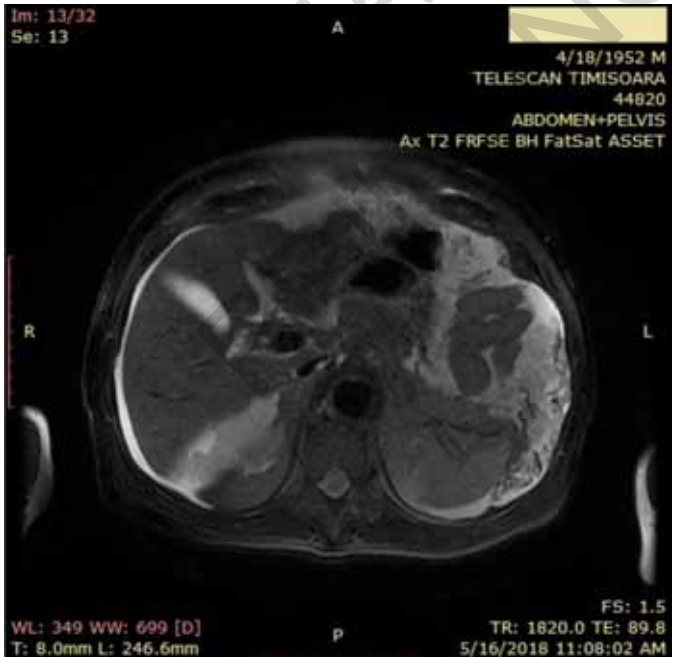

Fig. 7: Tumor recurrence mesentery, colon.

ing investigations. Due to immediate therapeutic succes, the patient discontinues his tyrosine-kinase inhibitor treatment, despite medical indications.

The pacient returns for a routine check-up in November 2017, without any apparent ailments, but with hints of a continuos development of the tumors on the CT scan, therefore it is decided to send the patient for an oncological reevaluation and initiate the treatment with a second generation tyrosine-kinase inhibitor (Sunitinib).

In June 2018, the patient returns for another check-up, this time with intense abdominal pain and fatigue. A clinical examination denotes abdominal distension and pain during palpatory exploration. Biologically all of the evaluated parameters are well within normal range. MRI imaging underlines an abdominal tumor relapse through multiple tumor masses which engulf the entire digestive tract, also invading the caul and peritoneum, with high quantities of ascites fluid (Figs. 5-7).

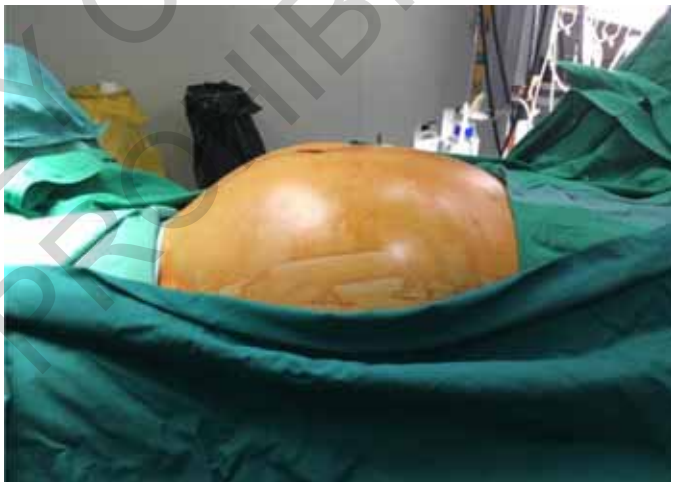

Fig. 8: Preoperative view.

Fig. 9: Itraabdominal tumor.

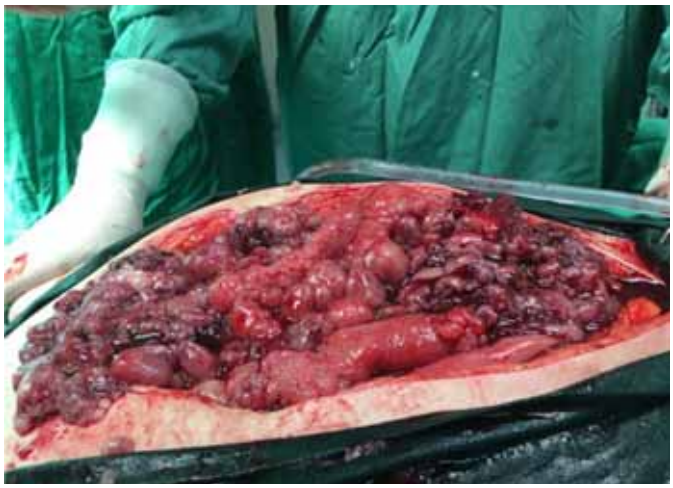

Fig. 10: Intraoperative view of GIST.

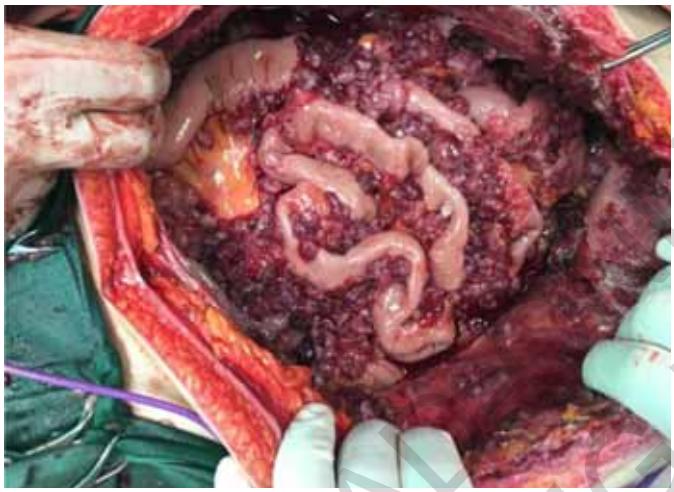

Fig. 11 Intraoperative view of GIST.

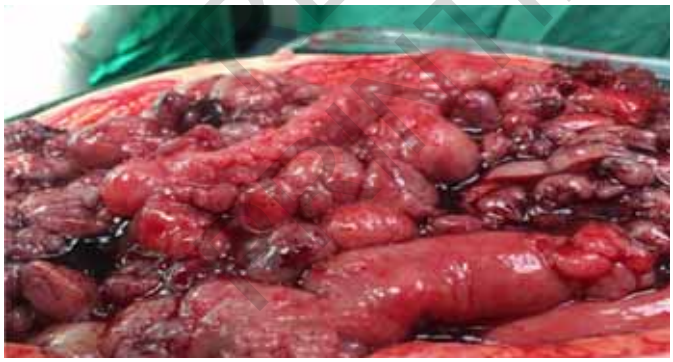

Fig. 12: Small intestine, mesentery tumor recurrency.

Due to the MRI result and clinical symptoms, the pacient is admited in the Surgical clinic, where after undergoing major surgery, aproximately 15 kg of solid tumor mass were removed (Figs. 8-14).

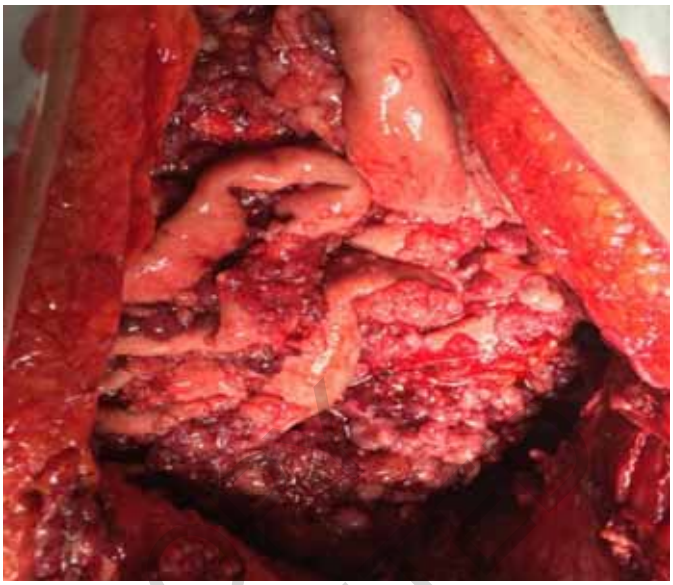

Fig. 13: intestine, mesentery tumor recurrency.

Fig. 14: Aproximately 15 kg of solid tumor mass were removed.

After aproximately three weeks postoperatively, the hystopathological result confirms the relapse of the gastro-intestinal stromal tumor.
The pacient reinitiates chemotherapy with Imatinib.
In October 2019, the patient comes in for anoter check-up, with imagistic documentation hinting at tumor relapse.
Another MRI is performed and it shows a tumor mass of 7/6 cm localized in the right parieto-colic cleft and six more in the adjacent mesentery with dimmensions in between 7 and 20 mm (Figs. 15-16).
Clinical examination does not convey anything pathological, the pacient not having any ailments or symptoms that would indicate tumor relapse.
A surgical intervention is performed and intraoperative it is obvious that it is a minimal local relapse, that engulf aproximately 5 cm or small intestine, which is removed,

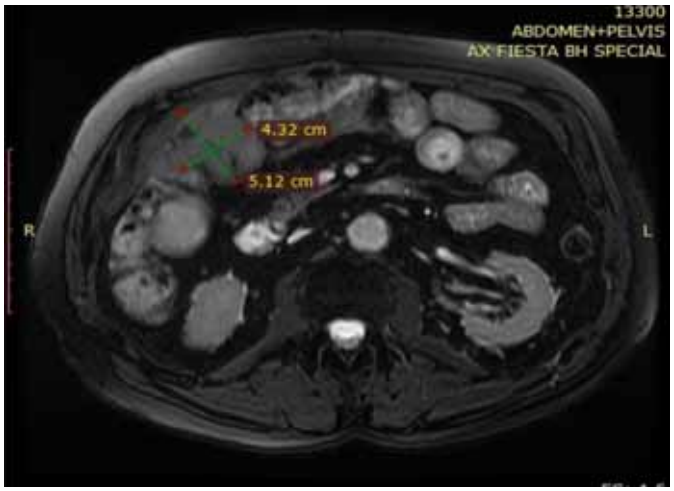

Fig. 15 Tumor relapse-right parieto-colic cleft.

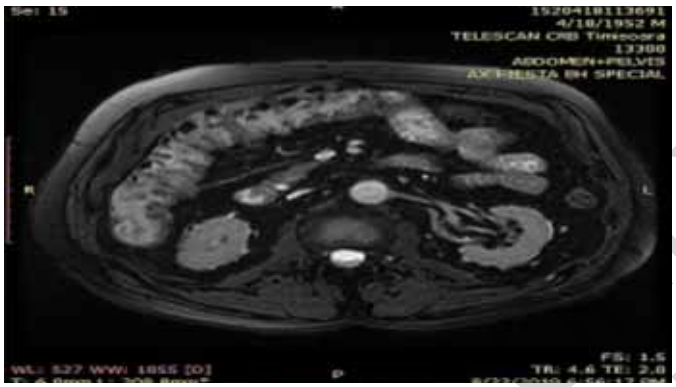

Fig.16: Tumor relapse

with assuring the continuity of the digestive tract through a side-to-side anastomosis (Figs. 17, 18).
Postoperative progress is favorable, the patient being discharged 10 days after the surgery.

Discussions

The term GIST was first introduced in the year 1983 by Mazur and Clark [1]. These types of tumors contain a a group of mesenchymal tumors, which can be fusiform or epithelioid [3,10]. They can be located anywhere in the digestive tract, including the stomach (Figs. 19).
Common symptoms in GISTs are bleeding, dyspepsia or discomfort, nausea and even palpable mass. Most patients are symptomatic. In a retrospective study presented and published by M. Di Vita et all,in 2019,in Ann. Ital. Chir., 90, 1, 92% of patients suffered from at least one of the above mentioned disorders [16].
These types of tumors can be discovered by chance, during imaging investigations or even during a surgical intervention. Data from literature can vary from 8% to

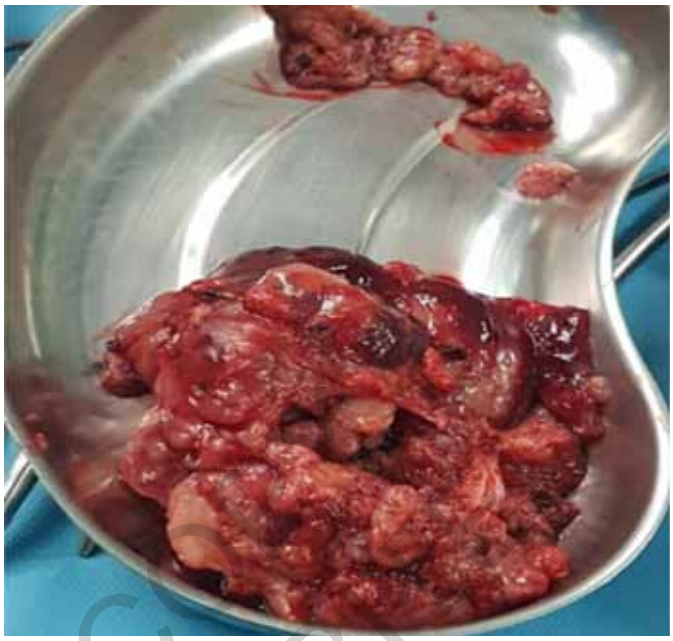

Fig. 17: Intraoperative view of minimal relapse.

Fig. 18: Side-toside anastomosis.

43,3% of incidental diagnosis. A recent study has shown even higher rate of asymptomatic cases up to 60% [16].
Their morpho-pathological character is diverse, with low, moderate or high chances of malignancy being present, or they can take a benign form, but with a high potential for malignancy or relapse [14].

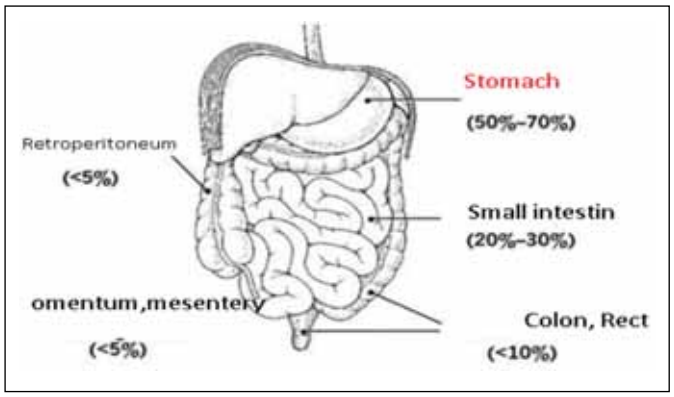

Fig. 19: Prognostic factors for GIST.

Characteristics	Low risk	High Risk
Tumor size	<5 cm	>5 cm
Cellularity	reduced	Increased
Necrosis	Absent-minimal	Extended
Mitosis	<5/50 HPF	>5/50 HPF
Growth pattern	No infiltration	Possible infiltration in adjacent structure
c-Kit mutation	Absent	Frequency

Fig. 20: Gastrointestinal stromal tumors workshop, Helsinki, 2002.

It is considered that 65% of stromal tumors are malignant. Gastro-intestinal stromal tumors are frequent enough in the medical practice, with having different locations, dimensions, regional invasion, treatment methods (surgical ablation, immunotherapy, endoscopic ablation) [7].
Investigative imaging represents a key part in placing a diagnosis preoperatively and establishing the right therapeutic conduit.
The final diagnosis is given by a histopathological and immunohistochemistry.
The immunohistochemistry diagnosis determines specific tumor markers such as: c-KIT (glycoprotein from tyrosine-kinase receptors, with a 95% positive rate for GIST cases), CD34 (specific marker for the mesenchymal cell, with a 70% positive rate for GIST cases), actin specific for smooth muscle, Ki67 (a cell division marker that gives data on prognosis and is useful for monitoring the patients) [5,10].
Tumour rupture, can causes disemination of malignant cells into the peritoneal cavity. It is considered a negative prognostic factor.Unidentify peritoneal lesions can be assumed to exist. Therefore patients should be treated with imatinib. The duration of the treatment varies as it is still unclear if tumour rupture patient should be considered metastatic [16].
The relapse prognosis is closely corelated with the dimensions of the tumor, the rate at which tumor cells divide, the cellularity of the tumor and the nuclear pleomorphism.
For relapse prevention it is considered that the best treatment is the Imatinib [16] targeted treatment. Imatinib is a tyrosine-kinase inhibitor which targets the c-Kit receptors. American oncology guides sustain the idea of administering Imatinib for 12 months in all patients with a high risk or relapse [2].
For patients that develop resistance to Imatinib (just as the aforementioned patient) the substitute treatment is with Desatinib or Sunitinib (Fig. 20).
The definitive treatment for these types of tumors is surgical resection, associated with tyrosine- kinase inhibitors. GISTs that develop from the stomach have a better prognosis as opposed to those located within the intestine, mesentery or caul.
Prognosis is more reserved if intraoperative the tumor is deteriorated. Lymphadenectomy is not necessary because metastasis does not take place through lymphatic pathway but tumoral invasion takes place through contiguity.
Excision of the invaded peritoneum is necessary because metastases are frequent at this level [5].
The largest gastro-intestinal stromal tumor ever recorded in medical literature measured 42/31/23 cm and weighed in at 18.5 kg.
The case presented, according to specialty literature, is the second one as far as volume and weight of the tumor go, the tumor invading the peritoneal cavity and weighing in at approximatively 15 kg.
Surgical ablation and corelating it with Protein-Kinase inhibitors (Sumatinib), make this case a remarkable medical success, all the more reason for which I had chosen to present this case.
The particularity of this case is the impressive dimension of the abdominal tumor (second as far as dimension goes, described in specialty literature), the treatment response and the limited relapse of the tumor, 2 years after the main surgery took place.

References

1. Mohamed A, Botros Y, Hanna P, Lee S, Baddoura W, Zuberi J, Damani T: *Gigantic GIST: A Case of the Largest Gastrointestinal Stromal Tumor Found to Date.* 2018; ID 6170861 | https://doi.org/10.1155/2018/6170861.

2. Rubin BP, Heinrich MC, Corless CL: *Gastrointestinal stromal tumour.* The Lancet, 2007; 369:9574, 1731-741.

3. Olariu S, Ruhmann C, Bloancă V, Shekhda J, Străin MA: *Tumoră intestinală stromală, cauză rară de hemoragie digestive inferioară. Caz clinic.* Dema Chirurgia, 2010; 105:5, 721-26.

4. Choti MA, Handelsman JC, Hueman M: *Gastric.* Gastrointestinal Tumors, e medicine (http://emedicine. medscape. com/article/278845-print), 2009.

5. Popescu I, Andrei S: *Gastrointestinal stromal tumors.* Chirurgia (Bucur), 2008; 103(2):155-70.

6. Bădulescu A, Bădulescu F, Constantinoiu S, Popescu C, Schenker M: *Gastrointestinal stromal tumors (GIST) - A newdiagnostic and therapeutic paradigm.* Chirurgia (Bucur), 2006; 101(1):87-99. [Article in Romanian].

7. Andrei S, Andrei A, Tonea A, Andronesi D, Becheanu G, Dumbravă M, et al.: *Risk factors for malignant evolution ofgastrointestinal stromal tumors.* Chirurgia (Bucur), 2007; 102(6):641-50. [Article in Romanian].

8. Andrei S, Andrei A, Tonea A, Andronesi D, Becheanu G, Dumbravă M, et al.: *Risk factors for malignant evolution of gastrointestinal stromal tumors.* Chirurgia (Bucur), 2007; 102(6):641-50. [Article in Romanian].

9. Savage Dg, Antman Kh: *Imatinibmesylate. A new oral targetedtherapy.* N Engl J Med, 2002; 346(9):683-93. Comment in: N Engl J Med, 2002; 347(1):67-8.

10. Schittenhelm MM, Shiraga S, Schroeder A, Corbin AS, Griffith D, Lee FY, et al.: *Desatinib (BMS-354825), a dualSRC-ABL kinase inhibitor, inhibits the kinase activity ofwild-type, juxtamembrane, and activation loop mutant KITisoforms associated with human malignancies.* Cancer Res, 2006; 66(1):473-78.

11. Eisenberg BL, Harris J, Blanke CD, et al.: *Phase II trial of neoadjuvant/adjuvant imatinibmesylate (IM) for advanced primary and metastatic/recurrent operable gastrointestinal stromal tumor (GIST): early results of RTOG 0132/ACRIN 6665*. Journal of Surgical Oncology, 2009; 99:42-47.

12. Singer S, Rubin BP, Lux ML, Chen CJ, Demetri GD, Fletcher CD, Fletcher JA: *Prognostic value of kit mutation type, mitotic activity and histologic subtype in gastrointestinal stromal tumors.* J Clin Oncol, 2002; 20:3898.

13. Miettinen M, Lasota J: *Gastrointestinal stromal tumors (GISTs): Definition, occurrence, pathology, differential diagnosis and molecular genetics.* Pol J Pathol, 2003; 54:3-24.

14. Stamatakos M, Douzinas E, Stefanaki C, Safioleas P, Polyzou E, Levidou G, Safioleas M: *Gastrointestinal stromal tumor.* World J Surg Oncol, 2009; 7: 61.

15. Popescu I, Andrei S: *Gastrointestinal stromal tumors.* Chirurgia, 103 (2): 155-70.

16. Di Vita M, et al: *Gastric GIST and prognostic models. Which is the best to predict survival after surgery?* Ann Ital Chir, 90, 1, 2019.