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Case report of a giant gastrointestinal stromal tumor and review of the literature

Reporte de caso clínico de un tumor del estroma gastrointestinal (GIST) gigante y revisión bibliográfica

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Palabras clave:
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ABSTRACT

Introduction: Gastrointestinal stromal tumors (GIST) represent a group of non-epithelial rare tumors with an estimated incidence of 10 to 20 per million persons. GISTs can present at any age but more commonly in persons between ages of 40 and 70 years. They arise more frequently from the stomach and have Kit gene mutation. **Material and methods:** We presented a case of a 39-year old male with a giant abdominal tumor with surgical resection and review of the literature of GIST. **Results:** A wedge resection of a GIST measuring 49 × 45 × 15 cm was performed. Microscopically, it was a spindle-shaped tumor cells GIST, low-grade histology (1), pT4 (more than 10 cm), with an intermediate risk (mitotic count less than 5 per 50 HPF and more than 10 cm) and complete resection (R0). **Conclusion:** In this case, we describe the clinical presentation and the diagnosis algorithm of a low grade giant gastric GIST. To our knowledge, this could represent the biggest GIST reported in the literature.

RESUMEN

Introducción: *Los tumores del estroma gastrointestinal (GIST) son tumores no epiteliales poco frecuentes con incidencia de 10-20 casos por millón de habitantes; se presenta en personas de 50 a 71 años de edad. Se presentan principalmente en estómago y tienen como característica mutaciones en el gen Kit.* ***Métodos:*** *Se describe el cuadro clínico de un paciente masculino de 39 años que presentó un tumor abdominal gigante con tratamiento quirúrgico y realizamos la revisión bibliográfica de los GIST.* ***Resultados:*** *Resección quirúrgica de un tumor del estroma gastrointestinal de bajo grado con dimensiones de 49 × 45 × 15 cm. Desde el punto de vista histopatológico se trató de un GIST de células fusiformes bien diferenciado, pT4 (de más de 10 cm), de riesgo intermedio (índice mitótico menor a 5 mitosis por 50 campos y mayor a 10 cm) y resección completa (R0).* ***Conclusiones:*** *En este caso describimos la presentación clínica y el protocolo de estudio de un GIST gástrico gigante de bajo grado. Este tumor podría representar el GIST más grande reportado en la literatura según nuestro conocimiento.*

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INTRODUCTION

Gastrointestinal stromal tumors (GIST) represent a group of non-epithelial rare tumors with an estimated incidence of 10 to 20 per million persons.[1,2] GISTs can present at any age but more commonly in persons between ages of 40 and 70 and do not show gender predilection.[3] They are the most common mesenchymal tumors of the gastrointestinal tract (stomach, small intestine, mesentery, liver, retroperitenum and omentum), arising more frequently from the stomach (50-60%) followed by the small intestine (30-40%).[4]

The great majority of GISTs harbour activating mutations in the tyrosine kinase KIT gene and Platelet Derived Growth Factor Receptor Alpha (PDGFRA) gene members of the type III transmembrane receptor tyrosine kinase family; less commonly, GISTs have also been reported to display mutations

elsewhere, including BRAF, NF1 and SDH-complex genes and EGFR gene.[5] Since the integration of molecular features, targeted therapy with tyrosine kinase inhibitors (TKIs) (imatinib) has been introduced for the management of high risk advanced and metastatic tumors.

Gastric GISTs are clinically asymptomatic until they reach a significant size; in most cases, they are incidentally diagnosed. Surgical resection has been the mainstay of GIST management as it stands as the only potentially curative treatment.[3] Appropriate oncologic outcome is challenging since complete resection should be performed in every case. We present a case report of a giant GIST tumor according to the SCARE criteria.[6]

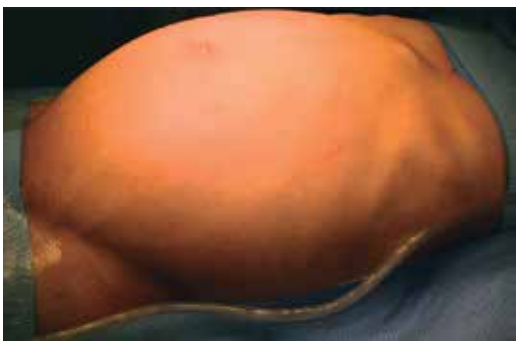

Figure 1: *The patient presented abdominal distension and enlarged abdomen.*

CASE PRESENTATION

A 39 years-old male patient presented to our service complaining of abdominal pain along with a giant, painless and palpable mass. He had a history of 3-4 kg weight loss over 2-3 months, with progressive abdominal distension *(Figure 1)*, normal bowel movements with no blood or mucous in the stools. He complained of asthenia, adynamia and general malaise. His vital signs: TA 100/60, HR 76x', RR, 16x', temperature 36.0 ºC. On physical exam, he looked pale and cachectic, his habitus externus showed enlargement and visual asymmetry of the abdomen, a solid mass to palpation, concurrent with a gigantic mass that was well defined with asymmetrical borders occupying all quadrants.

Contrast-enhanced computed tomography (CT) reported a big 38 × 24 × 32 cm tumor *(Figure 2)*, probably of mesenteric origin. The mass demonstrated heterogeneous contrast uptake and internal low-density components. The vascular structures around the lesion were pushed back and up of the peritoneum. An ultrasound-guided biopsy was performed, and reported a GIST with spindle-shaped tumor cells, with a mitotic count 2 per 50 high-power fields; Ki-67 proliferation index was 4-6%.

The tumor was removed through a midline, xiphoid-pubis incision. A wedge resection of the stomach using a linear stapler, following identification and ligation

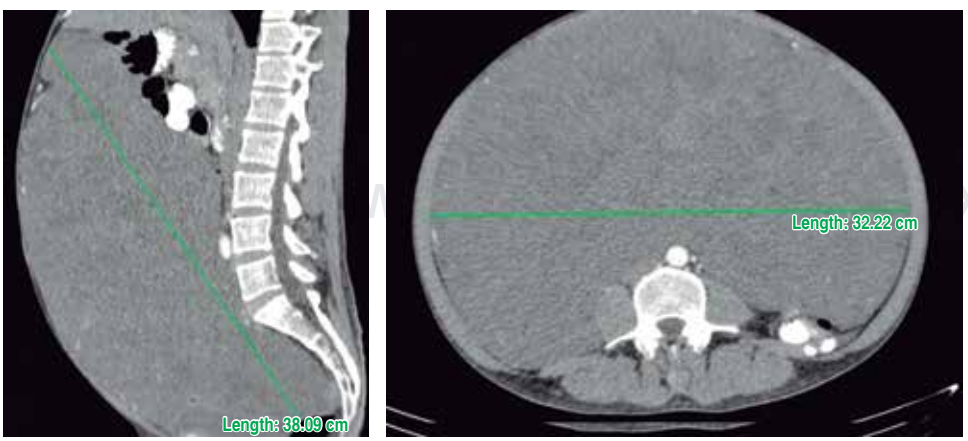

Figure 2:

Computed tomography reported a 38 × 24 × 32 cm intraperitoneal tumor.

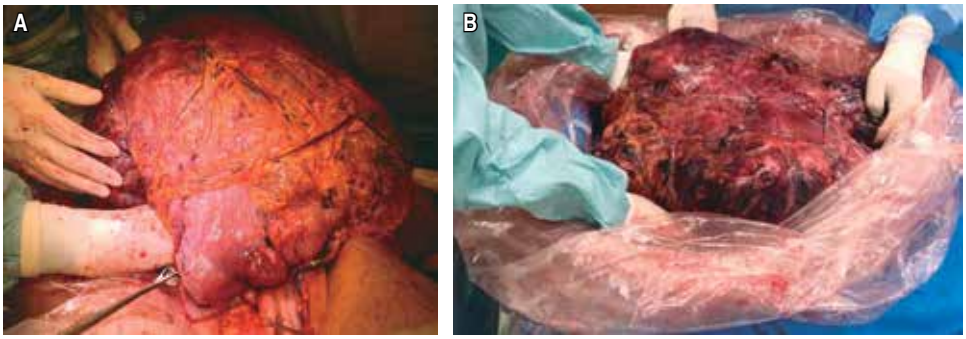

Figure 3:

*A laparotomy was performed with a wedge gastric resection of the tumor **(A** and **B)**.*

of multiple vessels supplying the mass *(Figure 3)* was performed. There was no rupture nor spillage of the tumor, as a large plastic bag was utilized to wrap the big mas as it was fully mobilized and resected. The specimen consisted of a tumor with irregular borders, weighting 13 kg and measuring 49 × 45 × 15 cm. Microscopically, it was a spindle-shaped tumor cells GIST, low-grade histology1, pT4 (more than 10 cm), with an intermediate risk (mitotic count less than 5 per 50 HPF and more than 10 cm) and complete resection *(Figure 4 A, B, C)*.

The patient had not postoperative complications and is currently fifteen months out disease-free with no evidence of recurrence.

DISCUSSION

GIST are a group of rare tumors with an estimated incidence of 10 to 20 per million persons in America.[1,2] These tumors represent the most common mesenchymal neoplasms of the gastrointestinal tract.[1] The term stromal tumor was introduced by Mazur and Clark in 1983.[7] Nowadays, it is hypothesized that GISTs originated from interstitial cells of Cajal, also known as the intestinal pacemaker cell.[3]

GIST is characterized by activating mutations in KIT and PDGFRA genes coding for receptor tyrosine kinases. KIT mutations are found in 60-85% of GIST tumors while PDGFRA mutations are found in 10-15%. However, 10-15% of GIST do not have detectable mutations in any of these receptors, in these tumors BRAF, NF1, SDH-complex

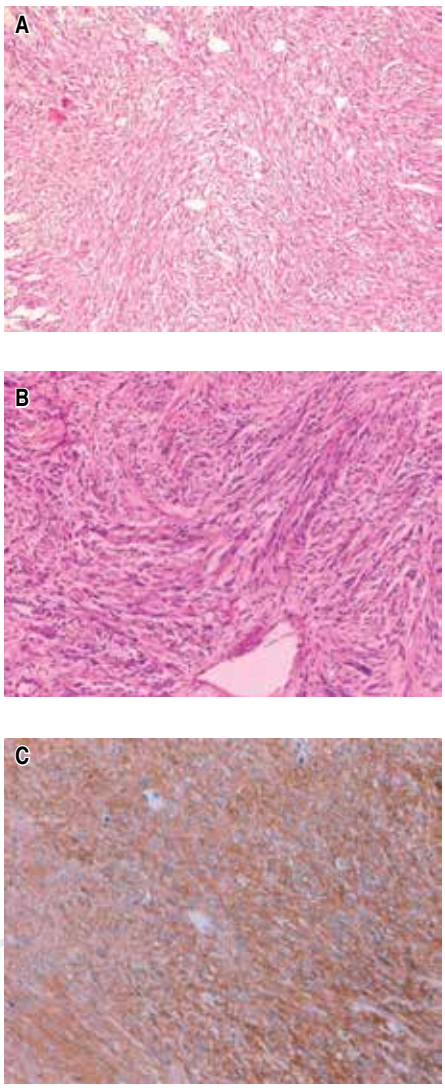

***Figure 4:** Mitoses per 50 HPF (40x fields), foci of necrosis are observed.*

genes and EGFR gene mutations have been described.[5] Zeng et al[8] have described that the Wnt/β-catenin signalling is involved in disease progression and imatinib-resistance. Meanwhile, Geddert et al reported that the cancer stem cell marker CD133 low DNA methylation level and high abundance of the protein were significantly associated with larger tumors and shorter disease-free survival.[9] These evidences suggest others molecular pathways involved in the pathogenesis of these tumors. Is strongly recommended including a molecular systematic analysis in the diagnosis of all GIST, given the type of relevant predictive and prognostic information provided and required in cases of GIST without CD117 expression.[5]

The clinical presentation is variable and dependant on the tumor size and its localization. The symptoms are often unspecific.[3,4] The most frequent symptoms are anemia, weight loss, gastrointestinal bleeding and abdominal pain.[3] At least, 10 to 30% are discovered incidentally, while 70% of patients present a broad range of clinical manifestations. Fifteen to 50% of these patients have metastasic disease.[10] There is no physical finding that specifically suggest the presence of a GIST. The first-choice imaging techniques are CT scan or magnetic resonance imaging (MRI). The CT-scan with IV contrast allows for identification of haemorrhage or intratumoral calcification and hypervascular hepatic lesions, while the MRI is useful for tumors in pelvic area and the study of the mesenteric and peritoneal extension. Although these imaging alternatives are helpful in establishing a presumptive diagnosis, none of them is highly specific[5], and the ultimate diagnosis is provided by histopathological examination of a biopsy sample. GIST histology allows to classified them as: spindle cell type (70%), predominantly epithelioid cell type (20%), or a mixture of both spindle and epithelioid cells.[11] The immunohystochemical marker most widely used in diagnosis is CD117 with positive staining being recorded in > 95% of cases with an intense staining in 75% of cases. Another markers used are CD34 (positive expression in 70-90% of cases), actin (20-30%), S-100 (10%) and desmin (2-4%).[5] Despite these markers, the factors necessary to classify patients' recurrence risk depends on: tumor size, mitotic index and location of the tumor. If the tumor is less than 2 cm and mitotic index lower than five HPF the risk is very low. Additionally, gastric GISTs have better prognosis.[5]

GISTs are usually radioresistant and insensitive to chemotherapeutic agents. This is why surgery remains as the main therapy for the patients without evidence of metastasis.[12] However, the presence of metastatic disease does not contraindicate surgery but infiltration of the celiac trunk, superior mesenteric artery or mesenteric-portal confluence does. Laparoscopic surgery is acceptable in tumors less than 5 cm in diameter. Lymphadenectomy should not be performed due to low frequency of lymphatic metastasis in these tumors.[5] Prior to the incorporation of adjuvant therapy, the global 5-year survival rate in patients with surgically treated localized tumors was approximately 70%. Before the administration of TKIs, the median overall survival of patients with advanced disease was around 20 months. The introductions of TKIs has notably modified the natural history of this disease, and the median overall survival in patients with metastatic GIST now exceeds 5 years.[12] The role of imatinib as adyuvant treatment has been assessed in several clinical trials. For low-risk patients adyuvant therapy is not indicated; for intermediate risk patients there is not enough evidence to support adyuvant treatment, while high-risk patients must be submitted to imatinib therapy of 400 mg/day over 3 years.[5]

Tumors over 10 cm were reported by Misawa et al (10 cm),[13] by Bara et al (12 cm),[14] Sun et al (13 cm),[15] Dal Corso et al and Vinagreiro et al (17 cm),[16,17] and Schneider et al (19 cm).[18] Masses reaching 20-30 cm have been reported in several cases. Zhou et al (21 cm),[11] Fukuda et al (22 cm),[19] Miyazaki et al (23 cm)[2] and Patil et al[10] reported 4 cases and reviewed 21 GISTs' cases while Sorour et al[3] reported 90 cases, both authors reporting tumors of 30 cm. GIST larger than 30 cm have been reported by Navarrete et al[20] –who reported a 32 cm tumor– similar to Schmieder et al in a 558 patient cohort.[21]

Wang et al reported a 34 cm tumor[1] and Cappellani et al reported a 37 cm and 8.5 kg tumor,[22] this last one representing the largest tumor reported we found in the literature. To our knowledge, we presented a case of a giant GIST which was presented as unspecific systemic and gastrointestinal symptoms. A 49 cm and 13 kg tumor could represent, to our knowledge, the largest ever GIST reported so far, and in fact this is the first report of a GIST bigger than 40 cm.

CONCLUSION

In conclusion, GIST are rare tumors. Most patients are asymptomatic and incidentally diagnosed. The management has significantly changed over the last few decades. We present a case of 49 cm and 13 kg tumor, and to our knowledge this tumor could represent the biggest GIST reported so far in the literature.

Acknowledges

Authors declare no conflicts of interest.

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