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A rare case of giant gastrointestinal stromal tumor of the stomach involving the serosal surface

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ABSTRACT

INTRODUCTION: Although rare, gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors affecting the gastrointestinal tract.

PRESENTATION OF CASE: Here we report the case of a 43-year-old man complaining of abdominal pain along with a painless and palpable mass, which was confirmed on magnetic resonance and multi-slice computed tomography. Laparotomy revealed a nodular grayish-white firm noninfiltrative mass (39 × 27 × 14 cm, 6109 g) that was well localized within the extramuscular and peritoneal surface of the anterior wall of the stomach; complete tumor resection was performed. Histopathological examination revealed features typical of GIST, including increased cellularity, increased mitotic activity, and spindle shaped cells as well as positive immunoreactivity for KIT, CD34, and vimentin.

DISCUSSION: A review of literature revealed that GISTs of the size and weight similar to the present case has been rarely reported. GIST most frequently involves the stomach. Although the etiopathogenesis of this disease remains unclear, few well-documented familial cases have been associated with GIST syndromes.

CONCLUSION: The primary treatment preferred is complete surgical excision of the tumor.

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1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most frequent mesenchymal neoplasms of the gastrointestinal tract [1]. They are rare, accounting for approximately 0.1–3% of all gastrointestinal tumors [2]. Most GISTs occur in patients aged >50 years at the time of diagnosis [3]. The etiological factors of GIST have not been determined so far [4], with the stomach being the most frequently (60%) affected site [5]. Clinically, most patients present with asymptomatic tumors are detected incidentally [6]. Generally, GISTs are thought to originate from interstitial cells of Cajal or their precursors [3]. These tumors are usually positive for KIT (CD117), and the combination of characteristic histopathological features and KIT (CD117) positivity is observed in 95% of cases [2,7]. GISTs have been associated with molecular alterations and mutations in platelet-derived growth factor receptor alpha (PDGFRA) [7]. The size of these tumors ranges from a few millimeters to several centimeters in diameter [6]. GISTs >10 cm in diameter are referred to as giant GISTs. To the best of our knowledge, giant GISTs of

this size and weight have been rarely reported in the literature (Table 1).

2. Presentation of case

A 43-year-old male arrived at the emergency department of a state hospital with nonspecific systemic symptoms, abdominal pain and weakness, and local examination was detected to have a painless, palpable abdominal mass. Patient also gave a no history of trauma or mass in the abdomen. Abdominal ultrasonography, computed tomography (CT), and magnetic resonance (MR) imaging revealed the presence of a solid cystic mass in the intra-abdominal region, which was clinically considered as a tumor and was resected completely (Fig. 1).

The tumor measured 39 × 27 × 14 cm in diameter and weighed 6109 g. Serial sections of the surgical specimen did not reveal tumor infiltration to the any major organ compartment. Gross findings of the nonperitonealized perimuscular or mesentery tissues included the presence of a nodular, grayish-white, firm, well-localized and well-demarcated, smooth mass. The cut surface of the tumor revealed ill-defined solid areas that were diffuse gray, with focally hemorrhagic, myxoid, and cystic degeneration (Fig. 2). Macroscopically, tumor perforation and ulceration were not observed and the tumor margins were negative and focally surgical margins close.

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Table 1
Anatomic location, age, gender, size (cm) and weight (kg) distributions of gastrointestinal stromal tumor

References	Year	Anatomic location	Age (year)	Gender	Size (cm)	Weight (kg)
Kitabayashi et al. [25]	2001	Stomach	75	M	15 × 11 × 4.4	
Kimura et al. [26]	2004	Stomach**	84	F	20	
Mehta et al. [22]	2005	Stomach	75	M	13 × 10	
Dal Corso et al. [27]	2007	Stomach	88	F	17 × 13 × 9	1.630
Cruz Jr et al. [14]	2008	Stomach	37	M	32 × 25 × 21	3.750
Funahashi et al. [28]	2008	Stomach**	65	F	25 × 18 × 11	
Alder et al. [29]	2013	Rectum	70	M	10 × 8.5	
Cappellani et al. [30]	2013	Stomach	67	M	37 × 24 × 13	8.5
Colović et al. [31]	2013	Stomach	52	F	20.5 × 16	
Notani et al. [32]	2013	Stomach	58	M	22	
Skandalos et al. [2]	2013	Stomach ^a	79	F	10.77 × 9.67	
Misawa et al. [33]	2014	Jejunum	70	M	10 × 10	
Mu et al. [34]	2014	Esophagus	29	M	13 × 12 × 5	
Nakano et al. [35]	2014	Esophagus	65	F	18	
Schneider et al. [36]	2014	Stomach	71	M	19 × 18 × 16	2.6
In our case	This	Stomach ^b	43	M	39 × 27 × 14	6.109

kg: kilogram, cm: centimetre, M: male, F: female.

^a Lesser curvature.

^b Extragastric growth.

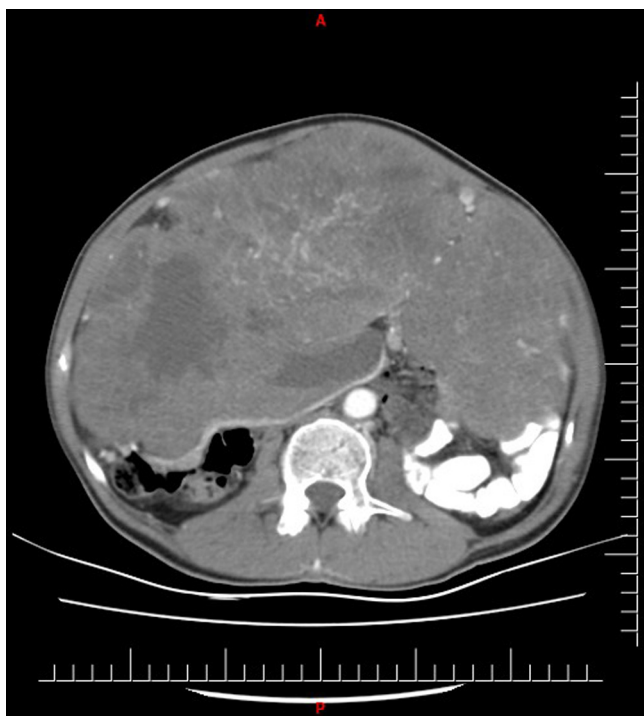


Fig. 1. Computed tomography (CT) scan of the abdominal showed tumors fulfilling.

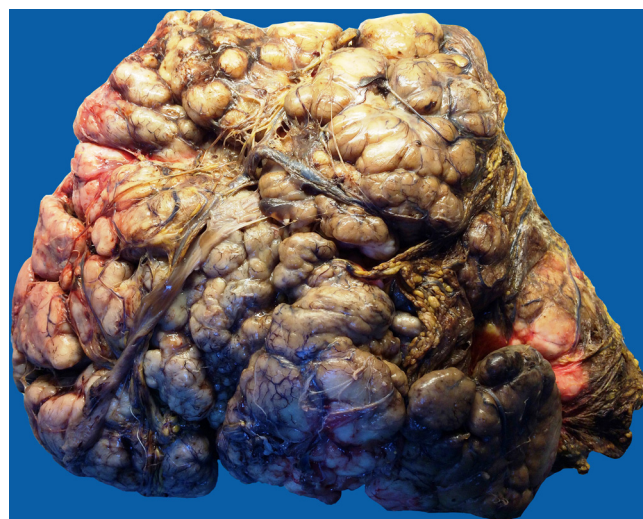


Fig. 2. Gross morphology: the macroscopic appearance of gastrointestinal stromal tumors (GIST), multinodular features and gray-white firm, peritoneal surface intact.

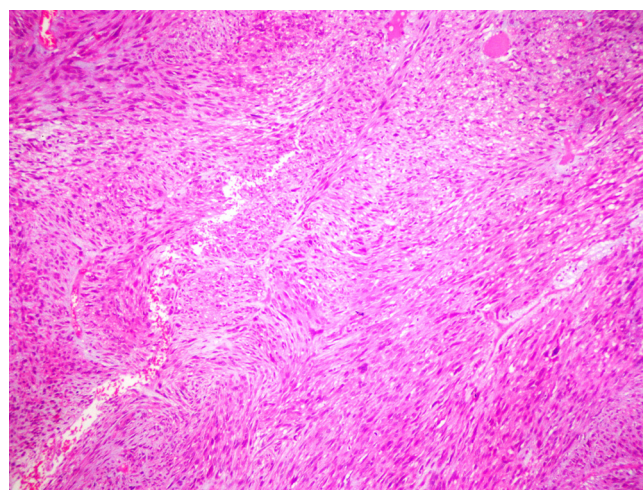


Fig. 3. GIST low power view demonstrating prominent fascicular pattern, predominantly spindle cell cytomorphology (hematoxylin–eosin, original magnification × 40 objective).

Histologically, the tumor appeared to consist predominantly of spindle cells and multinucleated giant cells along with low-moderate levels of cytological pleomorphism. The cells were arranged in a prominent fascicular pattern with areas of collagenization and mitosis [mitotic rate; 30 per 50 high-power fields (HPF)]. In addition, focal necrosis and a myxoid stroma were also present. The histopathological features of the lesion in the present case were similar to those seen in high-risk tumors (Fig. 3). Therefore, it was classified as a high-grade (grade 2) tumor. Lymphovascular invasion and calcifications were not observed. However, the tumor cells were diffusely and strongly positive for KIT (CD117, cytoplasmic and membranous), CD34 (Figs. 4 and 5) and vimentin. The cells were focally positive for S-100 and neuron-specific enolase, but negative for desmin, smooth muscle actin, epithelial membrane antigen, synaptophysin, calretinin, and CK5/6.

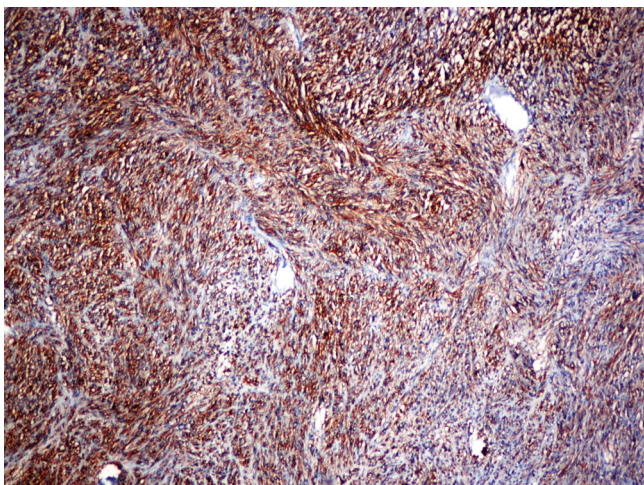


Fig. 4. Immunohistochemical stain, CD117 (KIT), The tumor cells are diffuse and strong positive($\times 40$ objective).

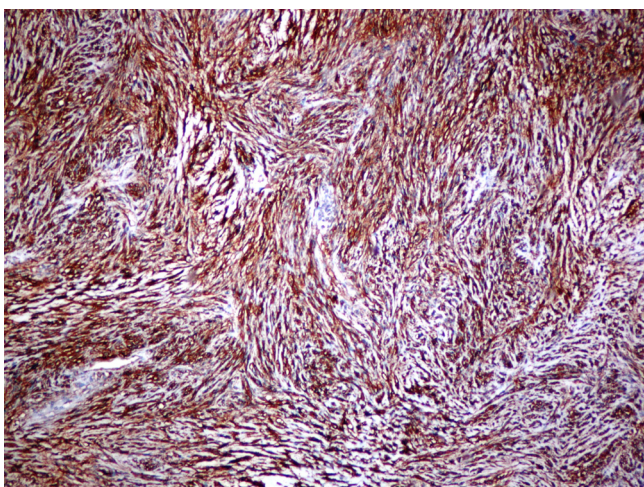


Fig. 5. Immunohistochemical stain, CD34, diffuse and strong positive($\times 40$ objective).

3. Discussion

Gastrointestinal stromal tumor is the terminology employed for mesenchymal tumors of the gastrointestinal tract that are positive for the antigen KIT (CD117). GISTs originate from interstitial cells of Cajal, which are known to originate from mesodermal precursors as opposed to those overlying the smooth muscle cells [8]. A high percentage of GISTs is associated with PDGFRA gene mutations, with several of them positively immunoreactive for KIT (approximately 85% cases) [9]. By contrast, the KIT-negative GIST is stomach or extragastrointestinal GIST that is positive PDGFRA mutation [13]. The incidence of GIST is currently estimated at about 4000 new cases per year in the United States [5]. The tumor shows no sex predilection and usually occurs in adults [5], with a mean reported age of 50.6 years [10]. GIST is extremely uncommon in children and adolescents [11]. Some instances of GISTs show a pattern of familial incidence suggestive of genetic predisposition, whereas others are associated with neurofibromatosis and Carney's triad [5]. The most common sites of occurrence are the gastrointestinal tract of the stomach, and less frequently, the small bowel, large bowel, and esophagus. These tumors, are also known as extragastrointestinal GISTs (EGISTs), as they arise from

the omentum, mesentery, and retroperitoneum [10]. Gastrointestinal bleeding, illness, anemia, and the presence of an abdominal mass are the most common features of this disease [4]. Most tumors arise as the submucosa or the muscularis propria growths on the gastrointestinal wall, and some tumors arise from extramural growths [5]. In the present case, the tumor presented as a large protruding mass on the extramucosal and peritoneal surface of the anterior wall of the stomach. The most significant risk factors for GISTs are site (anatomical region), size, and mitotic rate [4]. Orosz et al. have reported that tumor size can range from 0.5 to 30 cm, with a mean size of approximately 8.3 cm. Patients with high-risk tumors present with tumors up to 8 cm in diameter [12]. In the present study, the tumor was large enough to almost completely occupy abdominal cavity. So far, to our knowledge, no case with such a large tumor size and weight have been previously reported in the literature. The histopathological presentation of GIST includes predominance of spindle cells, whereas epithelioid cells are less commonly seen in some cases. In addition, other features, such as growth of cells in the form of fascicles, palisade, and whorls, presence of skenoid fibers, increased cellularity, bizarre cell shapes, palisading, and myxoid matrix, may also be present. [8]. Epithelioid type of stromal tumors occurs most frequently in the stomach. As with other types of densely spindle cells [5]. The criteria of GIST as recommended by the College of American Pathologists for detecting high-risk cases of gastric GISTs are as follows: mitotic rate; >5 per 50HPF, size; 5–10 cm, or >10 cm [13]. Essentially, tumors >10 cm in diameter present the risk of widespread metastasis [14]. The tumor described in the present study was classified as a high-grade tumor (grade 2) with a mitotic rate of $>5/50$ HPF. Anatomical location in the stomach acts as a favorable prognostic factor, and patients with small-bowel involvement usually experience progressive or higher risk behavior [13]. Gastrointestinal stromal tumors metastasize most commonly to the hepatic or peritoneal surfaces presenting as innumerable metastatic nodules all over the abdominal cavity wall [4]. In the present case, there were no metastases lymph node or liver. Most GIST patients exhibit mutations in KIT exon 11 (70%), whereas KIT exon 9 mutations are less common in GISTs (10–15%) [15]. The differential diagnosis of GIST involves an immunohistochemical panel composed of KIT, DOG1, S-100, desmin [4], smooth muscle actin, and CD34 [16]. Espinosa et al. reported positive staining for DOG1, CD117, and CD34 in 87%, 74%, and 59% cases of GIST, respectively [17], whereas other studies have reported 100% and 89% positive immunoreactivity for CD117 and CD34, respectively [18]. Recently, Ríos-Moreno et al. evaluated 99 cases and concluded that immunohistochemically, GISTs often stain for CD117, DOG1, a total of 93.5% positive [19]. The differential diagnosis of GIST includes benign and malignant lesions consisting mostly of spindle cells, such as retroperitoneal leiomyosarcomas. Retroperitoneal leiomyosarcomas are composed of cells that consistently express smooth muscle actin and desmin, but they are negative for CD34 and CD117 [20]. Greenson, in addition, benign inflammatory fibroid polyps, fibromatoses, schwannomas, and leiomyomas must also be included in the differential diagnosis of GIST [21].

Mehta et al. Complete surgical excision is the treatment of choice, and the projected 5-year survival rate of patients undergoing surgical resection GISTs is 20–80% [22].

Quezada et al., on the other hand, more aggressive treatments have been recommended for metastatic and unresectable tumors [23], such as, the use of selective receptor tyrosine kinase inhibitors. In the present study, we did not perform a biopsy in order to reach a pathological diagnosis and, the patient did not receive neoadjuvant (preoperative) therapy. Singer et al. [24] reported that patients with spindle cell and epithelioid or mixed cell histology had 5-year disease recurrence-free survival rates of $49\% \pm 7\%$ and $23\% \pm 11\%$, respectively. Singer et al., the same study also demon-

strated prognostic relations with KIT mutations where the disease free survival rates in patients with exon 11 type mutations and other mutation types was $89\% \pm 11\%$ and $40\% \pm 8\%$, respectively [24].

4. Conclusion

In conclusion, large sized, heavy tumors are rare in the case of GISTs, which generally present with varying duration of symptoms before surgery. These tumors may be difficult to distinguish from a number of other benign or malignant spindle cell lesions. Complete surgical resection of the tumor along with adjuvant therapy involving selective receptor tyrosine kinase inhibitors is effective, and should be considered as primary modalities of treatment in high-risk group GIST patients. Because the present case belongs to the high-risk category, it is assumed to have a poor prognosis.

Conflict of interest

No financial competing interests.

Ethical Approval

A copy of the written consent is available for review by the Editor-in Chief of this journal upon request.

Consent

Written informed consent was obtained from the patient for publication of this case report and its accompanying images.

Author contribution

AK conceived, designed and supervised the case report, and provided final editing of the article. LG and AVK collected and analyzed the data and drafted the manuscript. All authors read and approved the final manuscript.

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