

Extra-gastrointestinal stromal tumor of the omentum: a rare case report and review of the literature

Dimitris Fagkrezos,¹ Zisis Touloumis,² Maria Giannila,¹ Charalampos Penlidis,¹ Kleo Papaparaskeva,³ Charikleia Triantopoulou¹

¹Radiology Department, Konstantopouleio General Hospital, Aghias Olgas; ²Surgery Department of Chalkida's General Hospital; ³Histopathology Department of Konstantopouleio General Hospital, Aghias Olgas, Greece

Abstract

Gastrointestinal stromal tumors (GIST) are uncommon mesenchymal spindle-cell or epithelioid neoplasms, located mainly with higher frequency in the stomach and small bowel. GISTs represent the majority of primary non-epithelial neoplasms of the digestive tract, most frequently expressing the KIT protein a transmembrane tyrosine kinase receptor for stem cell factor. Extra-gastrointestinal stromal tumors tend to present in fewer than 5% of cases; they originate primarily from the mesentery, omentum or peritoneum. Furthermore, these extra-gastrointestinal tumors (EGIST) tend to be more common in patients over the age of 50 years. EGISTs are neoplasms with overlapping immunohistological features, occurring in the abdomen outside the gastrointestinal tract with no connection to the gastric or intestinal wall. We describe here a rare case of EGIST of the lesser omentum and report the clinical, macroscopic, immunohistological and radiological features of an EGIST arising in the lesser omentum of a 63-year old man. Clinical course and the prognostic factors of such lesions will also be discussed. EGISTs in the lesser omentum can grow slowly and remain silent despite a large tumor size. In most cases, a pre-operative diagnosis is not possible, and the patient undergoes a surgical operation for the generic diagnosis of *abdominal mass*. During the intervention it is important to achieve a complete removal of the mass and to examine every possible adhesion to the gastrointestinal wall.

Introduction

Gastrointestinal stromal tumors (GISTs) are mesenchymal spindle-cell or epithelioid neoplasms that arise mainly in the stomach and small intestine; they are rarely located in the colon, rectum and esophagus. They also rarely originate from other intraabdominal tissues such as the omentum and mesentery.

They are characterized by the expression of KIT (CD117), a transmembrane tyrosine kinase receptor for stem cell factor. It has become apparent that some GISTs have myogenic features (smooth muscle GISTs), neural attributes (gastrointestinal autonomic nerve tumors), characteristics of both muscle and nerve (mixed GISTs), or lack differentiation.

Their presumed cell of origin is the interstitial cell of Cajal, a pace-maker cell that controls gastrointestinal (GI) tract peristalsis and is the only GI tract cell that exhibits the CD117+/CD34+ immunophenotype, which is the diagnostic hallmark of GIST.¹ The molecular pathogenesis of GISTs is usually driven by activating mutations of the *KIT* gene that encodes the CD117 oncoprotein.²

The clinical behavior of GISTs is variable, with tumor size and mitotic activity being the most useful parameters of metastatic risk stratification.^{3,4}

GISTs are rarely found as primary tumors in extragastrointestinal intra-abdominal tissues such as the omentum and the mesentery (EGISTs). The origin of EGISTs is uncertain but, as a rule, their histological appearance and immunophenotype are identical to those of classical GISTs. They are, therefore, thought to represent either GISTs that have separated from the GI tract wall,⁵ or independent growths of mesenchymal cells of the omentum and mesentery from which they originate. Accumulating molecular genetic data may lead to improved prognostic classification and patient management.

Only 5 cases of lesser omental GISTs have been reported.^{6,9} Furthermore, the median age at diagnosis is about 60 years and the diagnosis is slightly more prevalent in males than in females. Currently, only 3% of GIST cases are diagnosed in patients under the age of 21 years.¹⁰⁻¹²

Our knowledge about EGISTs is based on accumulated data from individual case reports. In this paper, we describe the radiological and pathological findings in a case of EGIST while a literature review is also made.

Case Report

A male, 63-year old patient presented to the emergency department in septic condition, complaining of abdominal distention, discomfort, high fever up to 39.5°C over the previous few days. On clinical examination, there was diffuse peritonism with a palpable mass on the epigastrium.

Blood tests revealed a severe leukocytosis (white blood cell 37300/86.2%), jaundice (Tbil 7.14 mg/dL, Dbil 6.75 mg/dL) and abnormal values of APTT (55.8 sec, INR: 1.71). Ultrasonography showed a hypoechoic mass located between the stomach and the pancreas, adjacent to the left liver lobe, and also diffuse dilatation of the intrahepatic biliary ducts and the common bile duct. Contrast-enhanced computed tomography (CT) was performed for initial staging. CT showed a large mass (16x16x12 cm) with solid and cystic components (Figure 1). The adjacent structures

Correspondence: Dimitris Fagkrezos, Radiology Department, Konstantopouleio General Hospital, Aghias Olgas 25, Miaouli street 173, 42 Aghios Dimitrios Athens, Greece. Tel. +30.210.992.6896. E-mail fdb1@ath.forthnet.gr

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including the mesenteric fat plane, the gastrohepatic ligament and the duodenum were displaced, and the mass was in contact with the stomach. The central area of the mass was of low density corresponding to cystic and necrotic components (Figure 2).

The patient underwent an emergency explorative laparotomy due to worsening of his clinical condition. A large mass was found in the lesser omentum in contact with the stomach. The mass could not be surgically detached from the stomach. Therefore, an enucleation of the mass was performed with simultaneous sphenoid gastrectomy of the posterior wall of the stomach in proximity to the stomach's lesser curvature using a TA 60 mm stapler. This type of resection was considered safer in terms of acquiring clear resections margins.

Postoperatively, the jaundice decreased till normalization.

Unfortunately, the patient presented peritonitis on post-surgery Day 5. An exploratory laparotomy was performed and a failure of the staplers' line of the stomach was found due to ischemic necrosis. The stomach was sutured again and a prophylactic gastro-enteroanastomosis was performed. The following postoperative period was uneventful and the patient is in good health one year after.

A macroscopic examination showed a clearly defined tumor with a white curt surface. No hem-

orrhage or necrosis was observed (Figure 3).

Microscopically, the tumor was composed of spindle to ovoid cells arranged in broad fascicles. The nuclei were ovoid and focally elongated, and showed mild to moderate atypia. The mitotic figures were fewer than 5 per 50 high power fields (HPF) (Figure 4). The MIB-1 index, defined as the percentage of MIB-1 positive tumor cells seen in 500 tumor cells, was less than 10%. Immunohistochemically, the tumor cells showed diffuse and strong positivity for c-kit (CD117), smooth muscle actin (SMA) and human hematopoietic progenitor cell antigen (CD34), with negative internal control marker, as well as weak and focal positivity for caldesmon. Immunostains for desmin and S-100 protein were negative (Figure 5).

Based on Fletcher's classification, the tumor was classified as a low-risk GIST originating in the lesser omentum.⁴

Discussion

Gastrointestinal stromal tumors are currently believed to originate from the interstitial cells of Cajal, a pace-maker cell that controls GI track peristalsis and the only GI track cell that exhibits the CD117⁺/CD34⁺ immunophenotype, which is the diagnostic hallmark of GIST.¹³ The tumors can occur anywhere that these cells exist in the gastrointestinal tract, including the stomach (40-60%), small intestine (30-40%), ano-rectum (7%), colon, and esophagus.^{1,2}

Sakurai *et al.* reported in the normal omentum CD117⁺/CD34⁺ mesenchymal cells, like Cajal cells, from which the EGIST may theoretically arise.

The median age at diagnosis of GISTs is about 60 years and is slightly more prevalent in males than in females.^{1,2,5} In a Medline search, we found 54 omental EGISTs reported in the form of small series or isolated cases.^{5,9,14-40}

According to these cases, the median age at diagnosis is 65 years, with a male female ratio 1:1. Also, we ascertained that there is no difference in incidence between lesser and greater omentum.

Miettinen *et al.* reported that only 3% of Gists are diagnosed before the age of 21 years and GISTs arise only rarely in children.¹²

Omental EGISTs can remain clinically silent despite the large tumor size. The most frequent presenting complaint is an abdominal mass, but patients are often diagnosed incidentally during investigations for other medical conditions.

The omental GIST in our patient showed no myogenic or neural differentiation of myogenic features and neural attributes. Only 16 omental GISTs without myogenic or neurogenic features, including the present case, have ever been reported (Table 1).

The tumor arose in 7 men and 8 women ranging in age from 31 to 89 years. Tumor diameter ranged from 2.5 to 36 cm (median 15.7 cm). Macroscopically, most were large, solid masses exhibiting cystic changes.

The radiological features of omental GISTs

without myogenic or neurogenic features have not been established. Generally, they may be similar to those of omental leiomyomas and leiomyosarcomas. Most GISTs with myogenic features are demonstrated as hypervascular tumors with clear margins on CT and angiography.⁴¹⁻⁴³

It is difficult to differentiate a GIST in the lesser omentum from a GIST in the lesser curvature of the stomach, despite the use of advanced radiological imaging techniques. About half of all omental GISTs are misdiagnosed as extra mucosal tumors of the stomach.^{41,42,44} Additionally, omental EGISTs seem to be morphologically and immunohistochemically identical to their gastric and intestinal counterparts. They are cellular tumors consisting of elongated spindle and epithelioid cells that are typically positive for c-kit (CD117) and, less consistently, for CD34. They may show smooth muscle actin positivity but are negative for desmin and S-100 protein.

C-kit (CD117) may be negative in GISTs (2-5%), either due to limited sampling in the tumor with focal variation or, more rarely, due to a unique subset of CD117-negative GIST with epithelioid morphology. CD34 strongly and diffusely stains approximately 70% of GISTs. The other 30% of GISTs have patchy weak to moderate intensity staining. In GISTs with neural differentiation, fewer cells stain positive for CD34 and the intensity is less compared to GISTs with smooth

muscle differentiation. Most GISTs are desmin negative. Strong desmin staining occurs in approximately 2% of GISTs, although approximately 33% stain focally and weakly. S-100 protein stain the cytoplasm and/or nuclei focally in approximately 50% of neoplasms.⁴⁵⁻⁴⁷ Due to the rarity of omental EGISTs, there are no specific treatment data from clinical trials and surgical resection is the only effective modality, and their

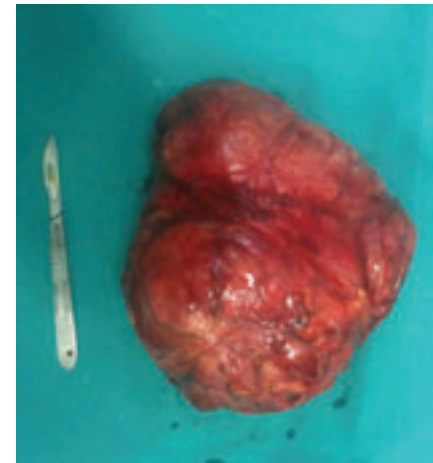


Figure 3. Surgical specimen of the extra-gastrointestinal tumors: macroscopic examination shows that the tumor is clearly defined and has a white curt surface without hemorrhage or necrosis.



Figure 1. Axial computed tomography non enhanced.



Figure 2. Axial computed tomography contrast enhanced.

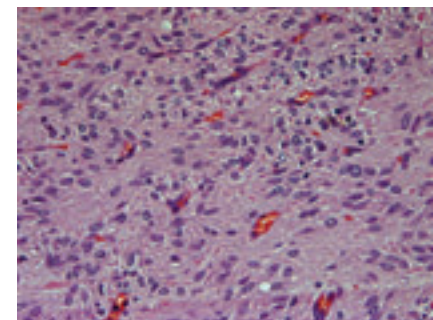


Figure 4. Microscopic imaging of the specimen with mitosis <5/50 high power fields (low grade). Hematoxylin and Eosin 400x.

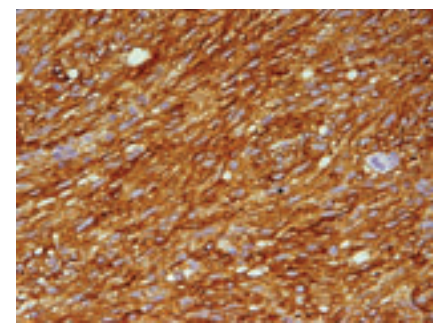


Figure 5. Microscopic imaging. Diffuse positive immunostain for c-kit 400x.

Table 1. Reported cases of lesser omentum gastrointestinal stromal tumor.

First Author	Year	Sex	Age (years)	Size (cm)	Necrosis
Takahashi	1998	F	71	17	Present
Fukuda	2001	M	45	4,5	Absent
Sakurai	2001	F	52	11,5	Absent
Sakurai	2001	F	74	8	Absent
Nakaya	2004	M	69	14	Present
Uchiyama Y,	2009	M	24	18	Absent
Kontopoulos	2009	M	68	15	Absent
Present case	2011	M	63	16	Present

management follows the guidelines applicable to classical GISTs.³

It should be noted here that, according to the National Institutes of Health algorithm for assessing malignancy of classical GISTs,⁴ most omental EGISTs would be classified as *high-risk* due to their large size alone, as in at least 55% of published cases it exceeds 10 cm. However, the tumor size is not a reliable prognostic parameter in the case of omental EGISTs.

Conclusions

Gists without myogenic or neurogenic features that arise in the omentum are very rare and surgical resection is the only effective treatment approach.

Nevertheless, adjuvant therapy following resection of localized disease with imatinib has become standard of care in cases of high risk.⁴⁸⁻⁵⁰

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