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Large Omental Metastases of a Gastrointestinal Stromal Tumor

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Summary. *Gastrointestinal stromal tumors are rare tumors, originating from the interstitial cells of Cajal. They are the most common mesenchymal tumors of the gastrointestinal tract. Metastatic tumor is treated with imatinib mesylate. A case of large metastases of a gastrointestinal stromal tumor to the omentum, diagnosis and treatment principles are presented in this case report.*

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common nonepithelial mesenchymal tumors of the gastrointestinal tract. Based on literature data, the estimated annual incidence in Lithuania should reach 10–20 cases per 1 000 000 population (50–60 new cases per year). Gastrointestinal stromal tumors usually affect 50- to 70-year-old persons, with the male-to-female ratio being 1:1 (1).

It is known that GISTs originate from the interstitial cells of Cajal that are believed to serve as pacemaker cells to regulate the motility and autonomic nerve function of the gastrointestinal tract. GIST is thought to be predominantly caused by a mutation of the *c-kit* protooncogene or platelet-derived growth factor receptor α (PDGFR-α), resulting in the uncontrolled proliferation of the Cajal cells and their resistance to apoptosis, and the cells become cancerous (1, 2).

Tumors can vary in size from a few millimeters to 40 cm; they are generally well circumscribed by a thin, fragile pseudocapsule. Most tumors are submucosal and typically grow in an endophytic pattern parallel to the organ lumen, with overlying mucosal ulceration and necrosis. GISTs can also grow exophytically or bilaterally (1, 2).

GISTs are most common in the walls of the following organs: stomach (60%–70%), small intestine (20%–30%), colon and rectum (10%), and esophagus (<5%). Primary GISTs in the omentum, mesentery, and retroperitoneum are reported occasionally and account for 5% of all GISTs (2–4).

Numerous studies have reported that GISTs metastasize in 17% to 24% of cases, and during the first 5 years after resection of the primary tumor without adjuvant therapy, 80% to 90% of patients may develop metastases (3–5). The most common sites of metastases are the liver and peritoneum; metastases to the mesentery and omentum are rarely seen. Extragastrointestinal metastases occur in 15% of cases (3). One of the risk factors reported to be associated with metastases (recurrence) is the primary tumor location: GISTs of the intestine metastasize in 40% of cases versus 9% of cases when the stomach is the primary tumor location (4). The size of primary tumor ($\geqslant$10 cm), high mitotic index, tumor rupture during surgery, and incomplete resection of primary tumor are other important risk factors for higher reoccurrence rate (3, 4). Metastases in the setting of GIST are the main risk factor contributing to mortality. Median survival for patients with metastases ranges from 9 to 12 months (3–5).

The first step toward good outcome is early diagnosis and adequate treatment, started by radical surgery and followed by treatment with imatinib mesylate.

In this article, a case of large metastases of a gastrointestinal stromal tumor to the omentum and the effect, which is assessed radiologically, of surgical treatment and treatment with imatinib mesylate are presented.

Case Report

A 59-year-old woman was operated on for suspected cystic pathology in the true pelvis in the Regional Hospital of Marijampolė in April 2005. During the surgery, a 12×12×12-cm mass, not attached to the internal genitalia and arising from the lumen of the ileum, was found in the lower portion of the abdomen. The patient underwent resection of the involved segment of the small intestine followed by end-to-end anastomosis. The pathohistological report confirmed a diagnosis of a gastrointestinal stromal tumor. The postoperative course was unre-

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markable; the patient did not receive chemotherapy. After 8 months, during the follow-up sonography of the abdomen, no pathological abnormalities in internal organs were found.

Forty months after the first surgery, the patient presented with complaints of fatigue, increased abdominal girth, abdominal distention, shortness of breath provoked by marginal physical load, and weight loss (10 kg within 6 months).

In November 2009, repeat sonography of the abdomen was performed, which demonstrated multiple masses up to 5.5×4.0 cm in size, forming variably sized conglomerates, in the abdominal cavity. Other organs of the abdomen were without pathological lesions. Being suspicious of tumorous process, 1 month after repeated sonography, the patient was referred to the Department of Surgery, tertiary teaching Oncology Hospital, affiliated with the Hospital of Lithuanian University of Health Sciences, for further examination and treatment. At admission, health status of the patient was satisfactory; except increased abdominal girth, no other abnormalities were noted. The findings of laboratory blood test were within normal limits. A computed tomography scan of the abdomen and true pelvis revealed isolated and solid masses in the entire abdomen and true pelvis (Fig. 1).

In December 2009 (56 months after the first surgery), the patient underwent surgery. During the surgical intervention, multiple, variably sized (0.5–3 cm in diameter) masses of different colors (whitish, pinkish, dark red) were observed in the entire abdominal cavity and true pelvis. Isolated masses and their conglomerates along with the segments of the peritoneum and omentum were resected (Fig. 2). The weight of the resected specimen was 4.5 kg. The patient had an uneventful postoperative course; two weeks after surgery, she was discharged from the hospital in good condition. The pathohistological report confirmed a metastasis of high-risk GIST (gastrointestinal stromal sarcoma) to the omentum (Figs. 3 and 4).

During the follow-up visit in 1 month after the

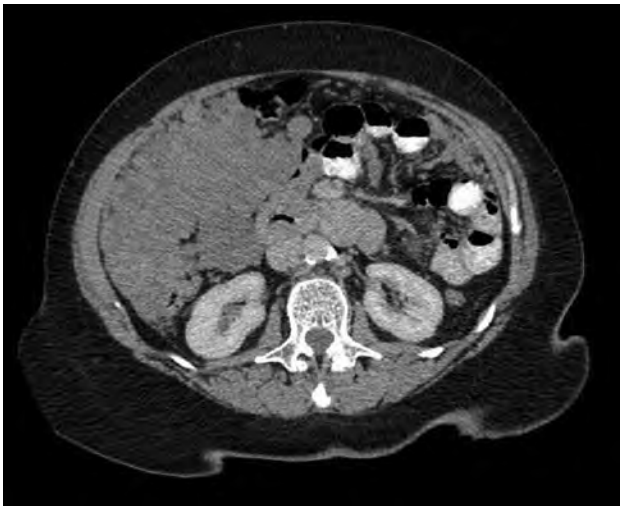

Fig. 1. A computed tomography scan of the abdomen and true pelvis, dated December 2, 2009, demonstrating solid and isolated, variably sized masses in the abdomen and the true pelvis

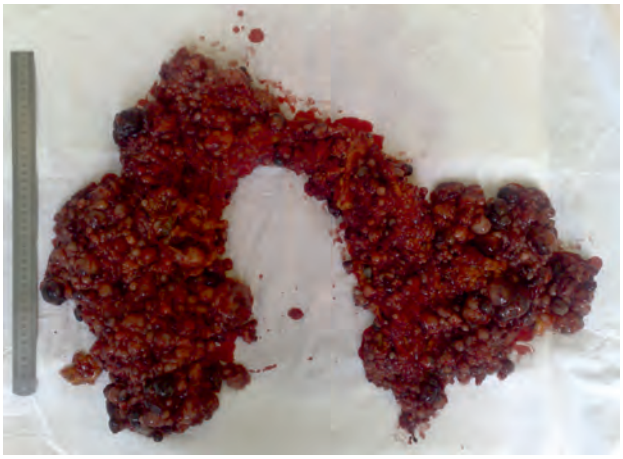

Fig. 2. The specimen resected during surgery (weight, 4.5 kg)

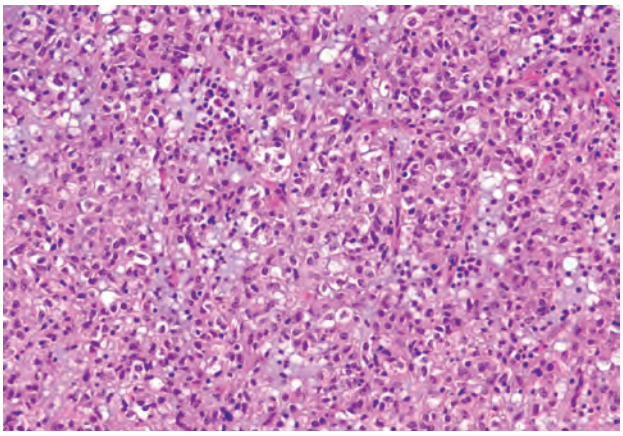

Fig. 3. A histological section showing large cells with round-to-oval nuclei and abundant and moderately abundant cytoplasm (mitotic count, 8 per 50 high-power fields)

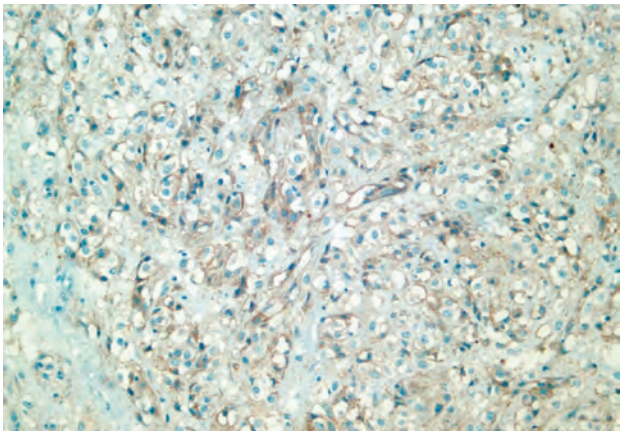

Fig. 4. Immunohistochemistry with CD117 immunomarker (nearly 90% of cell are moderately positive for CD117 immunomarker)

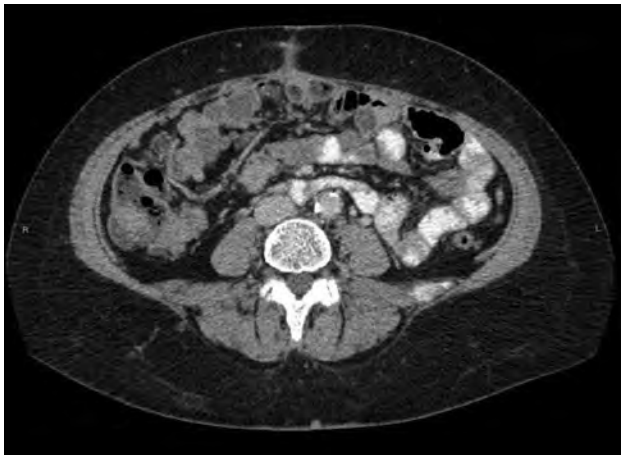

Fig. 5. A follow-up computed tomography scan of the abdomen and true pelvis showing multiple tumorous masses up to 1.0–1.8 cm in diameter in the peritoneal cavity and true pelvis

The uterus and its appendages are seen as single conglomerate measuring 7.4×9.1 cm with a deformed, polycyclic uterine contour.

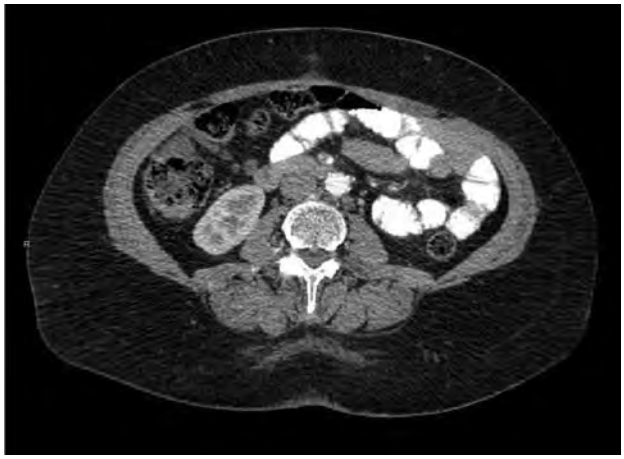

Fig. 6. A follow-up computed tomography scan of the abdomen and true pelvis demonstrating reduced multiple tumorous lesions measuring 1.2–1.4 cm

No abnormalities in the true pelvis are seen. The uterus is 6.2×3.5 cm in size with a smooth and clear contour without evidence of infiltration.

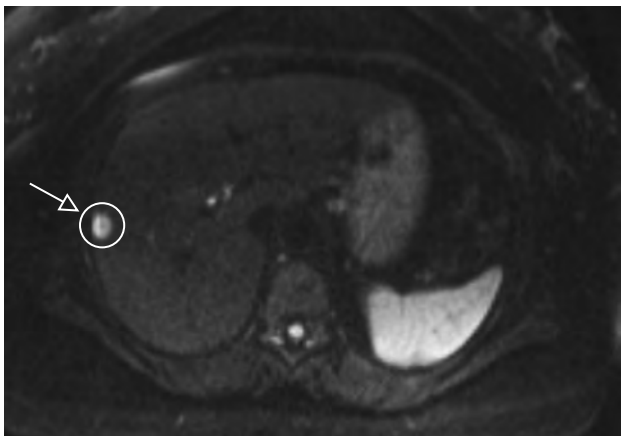

Fig. 7. Follow-up magnetic resonance imaging of the hepatic area

In segment VII of the liver, a 1.6×1.5-cm hyperintense lesion on the fat-suppressed T2-weighted image was noted subcapsularly (hypointense on the T1-weighted image, no contrast uptake).

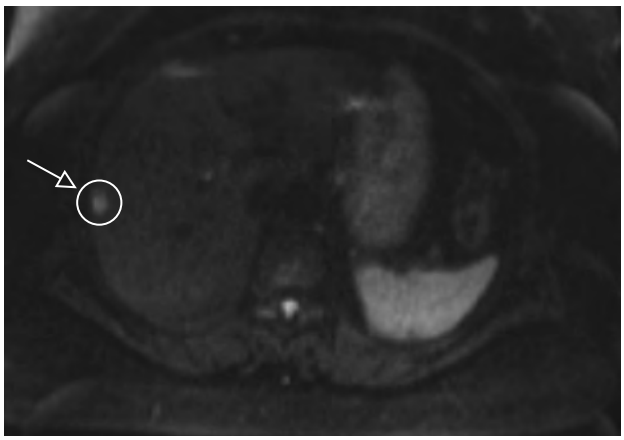

Fig. 8. Follow-up magnetic resonance imaging of the hepatic area

The lesion in segment VII of the liver decreased to 1.3×0.9 cm in size.

second surgery, all these above findings prompted a decision to start the treatment with a biologic agent, imatinib mesylate, at a dosage of 400 per day. During the conservative treatment, follow-up computed tomography and magnetic resonance imaging of the abdomen and true pelvis were performed 1 month (Fig. 5), 3 months (Fig. 6), 5 months (Fig. 7), 9 months, and 12 months (Fig. 8) after the second surgery, aiming to assess the effectiveness of treatment.

Discussion

Early diagnosis of GIST is not very simple. Diagnostic difficulties may arise due to nonspecific clinical symptoms (vague abdominal pain, bleeding from the gastrointestinal tract, presence of a palpable abdominal mass; more rare complaints are nausea, vomiting, weight loss; up to 77% of cases are asymptomatic), which are related to tumor size and location and mitotic activity of malignant cells (4, 5). The main investigative modalities in the diagnosis of GIST are endoscopic ultrasound (diagnosing gastric GIST) and intravenous contrast-enhanced computed tomography (diagnosing GISTs of other location). Esophagogastroduodenoscopy and upper abdominal endoscopic ultrasound are less valuable methods used for diagnosing GISTs. Magnetic resonance imaging and positron emission tomography are expensive and not routinely used imagining modalities (1–2, 6). The diagnosis of GIST is confirmed by histological examination and immunohistochemistry

(CD 117 marker; specificity, 95%) (1–3).

Surgery remains the main treatment modality for primary tumors. Primary or primary metastatic resectable GIST is the indication for surgical treatment. As GISTs rarely metastasize to lymph nodes, lymphadenectomy is not routinely performed (5, 7). According to literature data, after the complete resection of primary tumor, the 5-year survival reaches 46% to 79% (8–9). Despite the effectiveness of surgical treatment, the rate of local and distant recurrence is high. As both conventional chemotherapy and radiation therapy are also of minimal value (the response rate is low), since 2000, a tyrosine kinase receptor antagonist, imatinib mesylate, which inhibits the activity of the GIST-associated *c-kit* and PDGFR-α protooncogenes, has been extensively used for the treatment of metastatic GISTs. Imatinib mesylate is the first-line treatment for patients with metastatic GIST. In up to 80% of cases, at least a partial response is achieved or disease progression is stopped (5, 9–10). Therefore, combined treatment, i.e., surgery with imatinib mesylate (adjuvant treatment), is increasingly being applied worldwide. The value of neoadjuvant therapy with imatinib mesylate remains unclear, but it is thought that a combination of neoadjuvant therapy with imatinib mesylate and surgery has a positive effect. However, with increasing use of therapy with imatinib mesylate, the increasing number of cases resistant to imatinib mesylate is observed, typically after more than 1 year of therapy. Therefore, the efficacy of second-line tyrosine kinase inhibitors and the use of other biologic agents in the treatment of GIST are currently being examined (9, 10).

In rare cases (treating single GIST metastases in the liver), radiofrequency ablation can be applied, but its effectiveness in the treatment of GISTs is low (1, 3, 8, 10).

Concluding Remarks

Gastrointestinal stromal tumors are the most common mesenchymal tumors of the gastrointestinal tract, and surgery is the main treatment modality in the treatment of these tumors.

Despite the benefits from surgical treatment, up to 80%–90% of patients with gastrointestinal tumors develop metastatic disease, and this is a risk factor for poor outcome. Routine postoperative surveillance of patients who underwent primary surgical treatment is reasonable for timely detection of primary tumor metastases. The gold standard for the treatment of metastatic gastrointestinal stromal tumors is imatinib mesylate.

Statement of Conflict of Interest

The authors state no conflict of interest.

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