folia medica

Folia Medica 66(6):923-928
DOI: 10.3897/folmed.66.e125700

Case Report

Synchronous Local Recurrence and Liver Metastasis from Extragastrointestinal Stromal Tumor in the Rectovaginal Septum: a Unique Case Presentation

Eleni Papamattheou[1], Ioannis Katsaros[2], Eirini Chorianopoulou[1], Kyriaki Theodorolea[1], Gabriela Stanc[3], Christos Iavazzo[1], Elissaios Kontis[2]

[1] *Department of Gynecologic Oncology, Metaxa Cancer Hospital, Piraeus, Greece*

[2] *Department of Surgical Oncology, Metaxa Cancer Hospital, Piraeus, Greece*

[3] *Department of Pathology, Metaxa Cancer Hospital, Piraeus, Greece*

Corresponding author: Ioannis Katsaros, Department of Surgical Oncology, Metaxa Cancer Hospital, Piraeus, Greece, Piraeus, Greece; Email: ioankats@med.uoa.gr

Received: 18 April 2024 ♦ **Accepted:** 1 July 2024 ♦ **Published:** 31 December 2024

Citation: Papamattheou E, Katsaros I, Chorianopoulou E, Theodorolea K, Stanc G, Iavazzo C, Kontis E. Synchronous local recurrence and liver metastasis from extragastrointestinal stromal tumor in the rectovaginal septum: a unique case presentation. Folia Med (Plovdiv) 2024;66(6):923-928. doi: 10.3897/folmed.66.e125700.

Abstract

The rectovaginal septum is a rare location for gastrointestinal stromal tumors (GIST) to occur. The aim of this study was to present a case of synchronous local recurrence of solitary liver metastasis originating from an extra gastrointestinal tumor (E-GIST) of the rectovaginal space.

A 55-year-old woman, with a medical history of a resected meningioma, was referred to our department due to a 5 cm solitary liver metastasis located within the left lateral segment. The patient had undergone a transvaginal resection of a low-risk E-GIST 6 months prior without receiving adjuvant chemotherapy. The patient underwent a synchronous laparoscopic left lateral hepatectomy and a transvaginal resection with posterior vaginal wall reconstruction. Her postoperative course was uneventful and was discharged on the fifth postoperative day. The histological examination of the vaginal lesion revealed the development of neoplasm with pathological characteristics consistent with the initial histology expect for a mitotic index exceeding >20%. Liver histology report also included a high-risk GIST with CKIT (+), DOG1 (+), ki67 ≥30%, high mitotic activity and clear resection margins. The patient was referred for adjuvant chemotherapy.

E-GISTs are rare neoplasms with low malignant potential. However, these tumors may exhibit metastatic potential and require aggressive treatment.

Keywords

case report, EGIST, extragastrointestinal stromal tumor, rectovaginal septum

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors, which derive from interstitial cells of Cajal that regulate the motility of the gastrointestinal tract (GI).[1] GISTs are usually found in the stomach (approximately 70% of cases) or the small intestine (20%–30%), while less than 5% arise from sites outside the GI tract, including mesentery,

Copyright by authors. This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

PENSOFT.

omentum, and the rectovaginal septum.[2] The latter are defined as extragastrointestinal stromal tumors (EGISTs) and share similar morphological and phenotypical characteristics with GISTs.[3]

EGISTs have a more aggressive biologic behavior and poorer prognosis compared to GI tract GISTs.[4] The recurrence rate of these neoplasms is up to 23% and they metastasize in up to 30% of patients.[4] Rectovaginal EGISTs recur locally approximately in 40% of the cases, but they rarely present with distant metastases.[2] Nevertheless, surgical excision of the tumor and postoperative adjuvant treatment with imatinib can further reduce the possibility of recurrence, especially in high-risk cases.[2,3] The most common site of metastasis among patients with EGIST is the liver followed by the peritoneum, lungs, bones. In most cases the metastatic liver disease is multifocal, and surgical treatment is not indicated, thus only a few cases undergo surgical resection.[5] Hereafter, we present the management of a patient who presented with local recurrence of a rectovaginal EGIST and solitary liver metastasis.

CASE PRESENTATION

This case presentation was conducted according to the Declaration of Helsinki and CARE Guidelines (Consensus-based Clinical Case Reporting Guideline Development) and an informed patient's consent was obtained prior to submission.[6]

A 54-year-old gravida 2 para 2 female patient was referred to our department for a 5-cm, biopsy proven, solitary liver metastasis from a GIST. Her past medical history included resection of a 3.5 cm grade 2 meningioma one year ago, which was diagnosed following investigations for an epileptic seizure. During the staging computed tomography (CT) at that time, for the meningioma she was found to have a 3.5 cm mass at the rectovaginal space. The Multidisciplinary Tumor board (MDT) at her treating hospital decided for the meningioma to take precedence with surgical excision and adjuvant radiotherapy.

Following the completion of radiotherapy (6 months after the initial diagnosis), the patient was referred to her treating gynecology team for resection of the mass. Unfortunately, only a rectoscopy was performed to exclude rectal involvement during her preoperative investigation. The patient underwent a transvaginal piecemeal resection of the mass in 5 parts, with a total volume of 4.7×3.8×3.5 cm. The pathology report revealed a grade 3 EGIST [DOG-1(+), CD117(+), CD34(+), STAT-6 (–), Desmin (–), SMA (–), S-100 (–), Ki 67 12%]. Upper and lower GI endoscopies were performed to exclude the presence of concurrent GI GIST. Additionally, a Magnetic Resonance Imaging (MRI) scan of the lower abdomen showed no residual disease. Thus, the tumor was classified as stage I (T2N0M0, grade 3, mitotic index 0-5) and low risk by NIH classification.[7] The local MDT did not offer adjuvant treatment and the patient underwent close follow-up for both pathologies, i.e. EGIST and meningioma.

Three months postoperatively, a PET-C/T was conducted as part of her routine follow-up and revealed a hypermetabolic 3.3 cm lesion at segment II of the liver (SUV max: 5.1) ***(Fig. 1)****. An MRI of the upper abdomen confirmed the existence of a solitary mass (3×3 cm) within the left lateral segment of the liver* ***(Fig. 2)****. A fine-needle biopsy (FNB) of the mass was carried out, which showed a GIST. In hindsight, this lesion corresponded to an indeterminate 7-mm lesion, found in her initial staging CT for the meningioma. Given her relevant past medical history, it was considered to be a metastatic deposit from the initial rectovaginal site. In addition, genetic analysis revealed mutations of exons 13 and 11 of the C-KIT gene. The patient was referred to our hospital for further management.*

During preoperative investigation, pelvic examination revealed a local recurrence in the posterior wall of the vagina. The patient reported no vaginal bleeding, abdominal pain, or bowel dysfunction. After discussion at the MDT, the patient was offered simultaneous excision of the local recurrence as well as a concomitant liver resection.

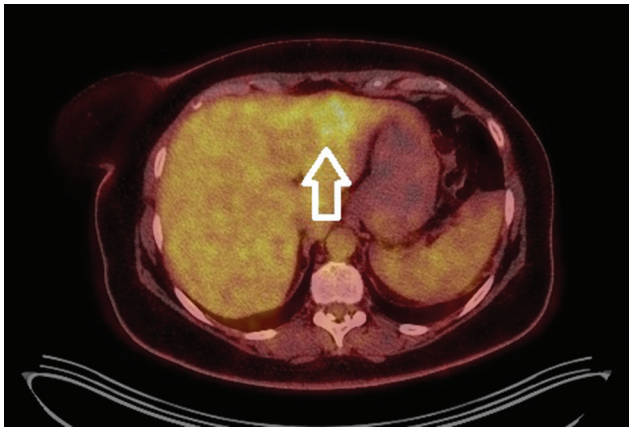

Figure 1. [^{18}F]Fluorodeoxyglucose positron emission tomography scan. A 3.3 cm avid lesion (SUV max: 5.1) is found within the left lateral segment of the liver (white arrow).

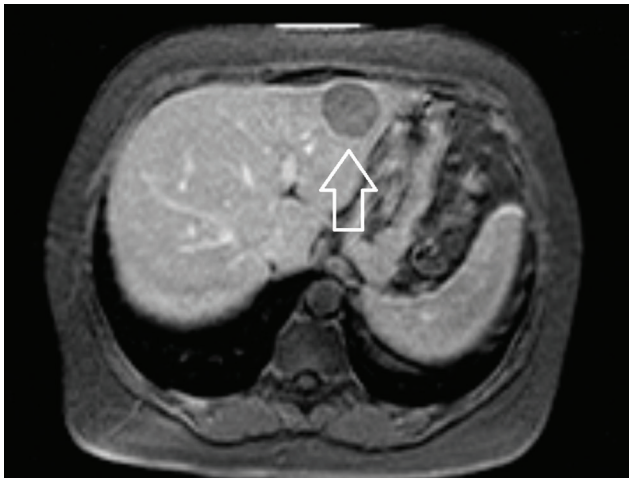

Figure 2. Magnetic resonance imaging (MRI) T2-weighted image. A hypointense 3 cm liver lesion is found in segments II/III (white arrow).

The patient underwent transvaginal excision of the local recurrence with posterior colporrhaphy and laparoscopic left lateral hepatectomy. She had an uneventful postoperative course and was discharged on the 5th postoperative day. Histology reported a vaginal mass 4×3.5×1.2 cm as well as a 5.3×4.5×4.3 cm liver lesion with clear resection margins. Both lesions were grade 3 GIST with the same immunohistochemistry as the previous report; however, the mitotic index was high (>20/HPF) ***(Fig. 3)****. Given the location (non-gastric), size (>5 cm), high mitotic grade, and stage IV of the disease, it was considered as high-risk rectovaginal GIST; the patient was offered with adjuvant therapy with imatinib mesylate. Following the completion of chemotherapy, she is now on surveillance and currently remains disease free at 18 months.*

DISCUSSION

EGISTs are rare mesenchymal neoplasms that develop outside the GI tract and are typically found in the mesentery, omentum, retroperitoneum, and the rectovaginal septum. There are less than 50 published cases concerning rectovaginal EGISTs and only one case report of a metastatic rectovaginal EGIST to the liver.[5-7]

The clinical presentation of rectovaginal EGISTs can vary widely depending on the size and extent of the tumor. Patients present with a wide range of non-specific symptoms, including abdominal pain or distension, a palpable vaginal mass, vaginal bleeding, or symptoms from adjacent organs due to extrinsic pressure.[1] The diagnosis of EGISTs can be challenging due to their rarity and diverse clinical presentation, and it requires a multidisciplinary approach.[4,8] Furthermore, their vague symptomatology could potentially lead to a delayed diagnosis, hence necessitating extensive procedures (i.e. pelvic exenteration).[9] A transvaginal ultrasound should always be performed during gynecologic examination of a patient presenting with the aforementioned symptoms.[10] According to a study of Ambrosio et al, the presence of a tumor in the pelvis or abdomen, which is an incidental finding during a transvaginal or transabdominal ultrasound and does not originate from the bowel or uterus, is likely to be an EGIST.[10] In the context of a rectovaginal mass, endoscopic ultrasound (EUS) can help in determining the origin, size, and characteristics of the mass. It allows for detailed examination of the layers of the rectum and vaginal wall, aiding in the identification of origin of the tumor and accurately provide local staging of the tumor, thus helping to guide treatment decisions.[11]

Immunohistochemical staining for CD117 (c-kit) and DOG1 is usually positive, which is consistent with the diagnosis of an EGIST. Additionally, other immunological markers can be found, namely BCL-2 (80%), CD34 (70%), smooth muscle actin (30%), desmin (5%) and DOG1. The

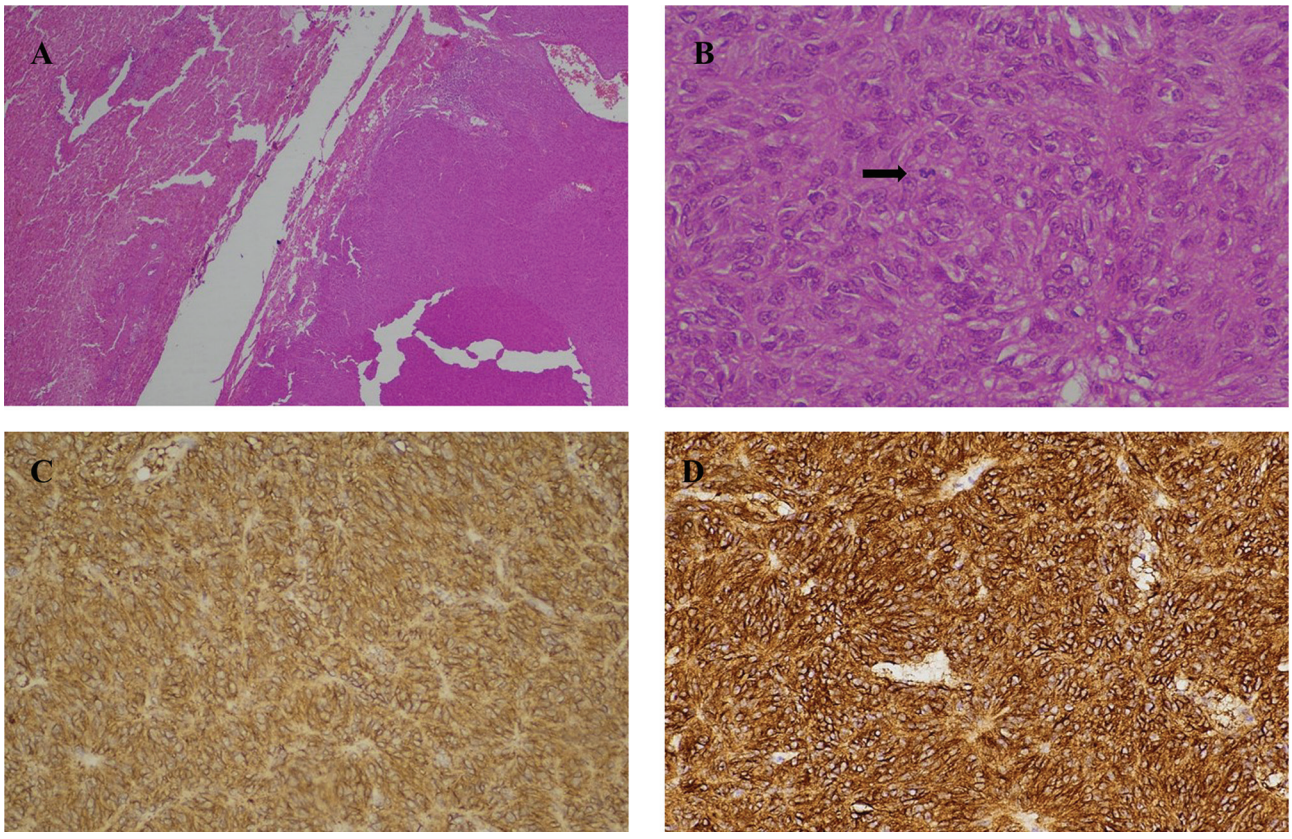

Figure 3. (**A**). H/E ×40 (hematoxylin-eosin) – metastatic E-GIST in the liver; (**B**). HE ×400 (hematoxylin-eosin) The tumor was composed of monotonous spindle cells (black arrow shows a mitotic figure); (**C**) Diffuse and strong DOG1 positive expression in the tumor cells (×200); (**D**) Diffuse and strong CD117/c-kit positive expression in the tumor cells (×200).

Folia Medica

DOG1 marker represents a sensitive and specific marker for the GISTs, including cases of extragastrointestinal and metastatic lesions.[12] Most common mutations among GISTs are within the KIT gene, a transmembrane receptor with tyrosine kinase activity, and the platelet-derived growth factor receptor alpha (PDGFRA) gene. Approximately 80% of GISTs express these mutations. However, it was discovered that only 37.5% of the cases of EGISTs harbor KIT mutation at exon 11, contrary to most patients with GI GISTs.[13] The molecular identity of the tumor is important for tumor prognosis with systematic treatment. In our case imatinib mesylate was chosen as adjuvant treatment, as KIT exon 11 and 13 mutant GISTs are sensitive to imatinib.[14]

Adjuvant therapy with tyrosine kinase inhibitors (TKIs), such as imatinib mesylate, is given postoperatively and continued for up to 3 years to decrease the chance of recurrence. Sunitinib malate and ponatinib are used for treatment when patients exhibit resistance or partial response to imatinib. Tumor features, including stage, size, mitotic count, location and intraoperative tumor rupture are well documented prognostic factors for adjuvant therapy.[14] Neoadjuvant therapy is the primary approach for unresectable tumors or EGISTs with multiple metastases, to downstage the disease. In this patient, despite being initially classified as low risk, she presented with local recurrence in less than 6 months postoperatively; in hindsight, the metastatic liver lesion, was present at diagnosis, although its size was below the diagnostic threshold of any imaging modality. To date, there are no evidence to support neoadjuvant treatment in the setting of resectable metastatic EGIST's, as such the patient was offered with upfront resection.

The surgical resection of the tumor is the standard of care for EGISTs.[13] The goal of surgery is the resection of the tumor with clear surgical margins and no intraoperative tumor rupture. In addition, the systemic regional lymphadenectomy is not recommended because lymph node metastases are rare. Minimally invasive approach can be offered without compromising the oncological outcome and with reduced operative time, length of hospitalization and postoperative morbidity.[15] Given the anatomy of the rectovaginal region, it is quite challenging to achieve R0 resections with no residual tumor and, thus, higher recurrence rates are reported.[2] Tumor rupture is an additional adverse prognostic factor and associated with poorer outcomes. Patients who have microscopically positive margins and pre-operative tumor rupture have 15%–20% risk of having recurrent disease.[8] Piecemeal resection of the primary tumor in the present case could be a possible explanation for the quick disease recurrence.

Treatment of recurrent or metastatic EGISTs includes both surgical resection and adjuvant therapy with TKIs of the recurrence and metastatic site, when feasible. In cases of inoperable tumors or patients who develop recurrence while on TKIs treatment, the patient should be considered for alternate systemic treatment.[1,8,12] Usually, these tumors recur locally and metastasize to the liver, the mesentery and omentum, lung, subcutaneous tissues, lymph nodes, or bone.[1] The patient in this study is the second patient reported to date with a metastatic rectovaginal EGIST. Interestingly, the initial tumor showed a mitotic index increase from 0-5 to >20/HPF over just 3 months and despite not having any adjuvant therapy. According to the NCCN 2023 guidelines for GIST and non-gastric GIST, this patient should receive lifelong TKIs treatment, because of the metastasis and the local recurrence, and should be followed closely. The follow-up includes physical examination and abdominal/pelvic CT or MRI every 3 months for 3 to 5 years and then annually, as it is a high risk EGIST. PET/CT should be considered, in case CT results are ambiguous.

The long-term prognosis for patients with rectovaginal EGISTs that have metastasized to the liver can vary significantly based on several factors, including the tumor's size, mitotic rate, and response to treatment.[8] According to recent studies, the use of tyrosine kinase inhibitors (TKIs) like imatinib has significantly improved the survival rates for patients with metastatic GISTs.[16] The NCCN guidelines recommend lifelong TKI therapy due to the high risk of recurrence and progression.[17] Alternative treatment options, such as sunitinib or regorafenib, are considered for cases resistant to imatinib. These therapies have shown efficacy in extending progression-free survival, although they may come with different side effect profiles. Prognostic data suggest that patients on TKI therapy can have a median overall survival of several years, with quality of life being maintained through careful management of treatment-related adverse effects.[17] Furthermore, advances in understanding the mechanisms of distant metastasis, such as angiogenesis, highlight potential areas for future therapeutic intervention.[18] Emerging diagnostic techniques, including liquid biopsies and next-generation sequencing, offer promising avenues for early detection and personalized treatment strategies, potentially improving outcomes for patients with similar presentations.[19]

In conclusion, this case report highlights the diagnostic challenges and therapeutic strategies involved in managing rectovaginal extragastrointestinal stromal tumors (EGISTs) with liver metastasis. The case underscores the importance of a multidisciplinary approach and the utility of advanced imaging techniques, such as endoscopic ultrasound, in differential diagnosis. Lifelong TKI therapy plays a crucial role in managing metastatic EGISTs, offering improved survival rates and quality of life for patients. The discussion of distant metastasis mechanisms and emerging diagnostic tools emphasizes the need for ongoing research and innovation in this field. By sharing this rare and complex case, we aim to enhance clinical awareness and contribute valuable insights into the management of EGISTs, ultimately improving patient outcomes through informed and comprehensive care.

Funding

The authors have no funding to report.

Competing interests

The authors have declared that no competing interests exist.

REFERENCES

1. Gheorghe G, Bacalbasa N, Ceobanu G, et al. Gastrointestinal stromal tumors – a mini review. J Personal Med 2021; 11(8):694.
2. Addley S, Alazzam M, Johnson C, et al. Rectovaginal extragastrointestinal stromal tumour (EGIST): an additional entity to be considered in the differential diagnosis of tumours of the rectovaginal septum. BMJ Case Reports 2021; 14(3):e237669.
3. Cheng M, Liu CH, Horng HC, et al. Gastrointestinal stromal tumor presenting as a rectovaginal septal mass: A case report and review of literature. Medicine 2019; 98(17):e15398.
4. El-Helou E, Chamma L, Mazraani HB, et al. Extra-gastrointestinal stromal tumor (EGIST) in the pelvis mimicking retroperitoneal sarcoma. The Surgery Journal 2022; 8(3):e266–e9.
5. Frilling A, Malago M, Testa G, et al. Liver transplantation for metastasized extragastrointestinal stromal tumor: a case report and an overview of literature. Transplantation Proceedings 2010; 42(9):3843–8.
6. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. Glob Adv Integr Med Health 2013; 2(5):38–43.
7. Parab TM, DeRogatis MJ, Boaz AM, et al. Gastrointestinal stromal tumors: a comprehensive review. J Gastrointes Oncol 2019; 10(1):144–54.
8. Ahmed M. Recent advances in the management of gastrointestinal stromal tumor. World J Clin Cases 2020; 8(15):3142–55.
9. Ashoor AA, Barefah G. Unusual presentation of a large GIST in an extraintestinal site: a challenging diagnosis dilemma. BMJ Case Reports 2020;13(2):e229839.
10. Ambrosio M, Testa AC, Moro F, et al. Imaging in gynecological disease (19): clinical and ultrasound features of extragastrointestinal stromal tumors (eGIST). Ultrasound Obstet Gynecol 2020; 56(5):749–58.
11. Chen YH, Wang DB, Guo CS. Accuracy of physical examination, transvaginal sonography, magnetic resonance imaging, and rectal endoscopic sonography for preoperative evaluation of rectovaginal endometriosis. Ultrasound Quarterly 2019; 35(1):54–60.
12. Fang JM, Li J, Shi J. An update on the diagnosis of gastroenteropancreatic neuroendocrine neoplasms. World J Gastroenterol 2022; 28(10):1009–23.
13. Almeida CC, Caroço TV, Albano M, et al. Extragastrointestinal stromal tumour (EGIST) presented as a mesenteric and retroperitoneal mass. BMJ Case Reports CP 2019; 12(12):e232481.
14. Blay JY, Kang YK, Nishida T, et al. Gastrointestinal stromal tumours. Nat Rev Dis Primers 2021; 7(1):22.
15. Schwameis K, Fochtmann A, Schwameis M, et al. Surgical treatment of GIST – An institutional experience of a high-volume center. Int J Surg 2013; 11(9):801–6.
16. Tan AD, Willemsma K, MacNeill A, et al. Tyrosine kinase inhibitors significantly improved survival outcomes in patients with metastatic gastrointestinal stromal tumour: a multi-institutional cohort study. Current oncology (Toronto, Ont) 2020; 27(3):e276–e82.
17. Von Mehren M, Randall RL, Benjamin RS, et al. Soft tissue sarcoma, Version 2.2018, NCCN clinical practice guidelines in oncology. J Nation Comprehen Cancer Network 2018; 16(5):536–63.
18. Papadakos SP, Tsagkaris C, Papadakis M, et al. Angiogenesis in gastrointestinal stromal tumors: From bench to bedside. World J Gastrointest Oncol 2022; 14(8):1469–77.
19. Calderillo-Ruíz G, Pérez-Yepez EA, García-Gámez MA, et al. Genomic profiling in GIST: Implications in clinical outcome and future challenges. Neoplasia 2024; 48:100959.

Синхронный местный рецидив и метастазы в печень из экстрагастроинтестинальной стромальной опухоли в ректовагинальной перегородке: презентация уникального случая

Елени Папаматеу[1], Йоанис Кацарос[2], Ейрини Хорианопулу[1], Кирияки Теодорелеа[1], Габриела Станк[3], Христос Явазо[1], Елисайос Контис[2]

[1] *Отделение гинекологической онкологии, Онкологическая больница „Метакса", Пирей, Греция*

[2] *Отделение хирургической онкологии, Онкологическая больница „Метакса", Пирей, Греция*

[3] *Отделение патологоанатомии, Онкологическая больница „Метакса", Пирей, Греция*

Адрес для корреспонденции: Йоанис Кацарос, Отделение хирургической онкологии, Онкологическая больница „Метакса", Пирей, Греция; Email: ioankats@med.uoa.gr

Дата получения: 18 апреля 2024 г. ♦ **Дата приемки:** 1 июля 2024 г. ♦ **Дата публикации:** 31 декабря 2024 г.

Образец цитирования: Papamattheou E, Katsaros I, Chorianopoulou E, Theodorolea K, Stanc G, Iavazzo C, Kontis E. Synchronous local recurrence and liver metastasis from extragastrointestinal stromal tumor in the rectovaginal septum: a unique case presentation. Folia Med (Plovdiv) 2024;66(6):923-928. doi: 10.3897/folmed.66.e125700.

Резюме

Ректовагинальная перегородка является редким местом возникновения гастроинтестинальных стромальных опухолей (GIST). Целью данного исследования было представить случай локального рецидива и синхронного одиночного метастаза в печень, возникшего из внегастроинтестинальной опухоли (E-GIST) ректовагинального пространства. 55-летняя женщина с историей резецированной менингиомы была направлена в наше отделение из-за одиночного метастаза в печень размером 5 см, расположенного в левом латеральном сегменте. Пациентка перенесла трансвагинальную резекцию E-GIST низкого риска 6 месяцев назад без применения адъювантной химиотерапии. Пациентке была проведена синхронная лапароскопическая левосторонняя гепатэктомия и трансвагинальная резекция с реконструкцией задней стенки влагалища. Послеоперационный период протекал без осложнений, и пациентка была выписана на пятый послеоперационный день. Гистологическое исследование вагинального поражения выявило развитие новообразования с патологическими характеристиками, соответствующими первоначальной гистологии, за исключением митотического индекса, превышающего >20 %. Отчёт по гистологии печени также включал GIST высокого риска с CKIT (+), DOG1 (+), ki67 ≥30%, высокой митотической активностью и чёткими краями резекции. Пациентка была направлена на адъювантную химиотерапию.

E-GIST являются редкими новообразованиями с низким злокачественным потенциалом. Однако эти опухоли могут проявлять метастатический потенциал и требуют агрессивного лечения.

Ключевые слова

отчёт о клиническом случае, EGIST, внежелудочно-кишечная стромальная опухоль, ректовагинальная перегородка