CLINICAL CASE

1. Department of Pathological Anatomy. San Carlos Clinical Hospital, Madrid, Spain.
2. Department of Legal Medicine, Psychiatry, and Pathology. Faculty of Medicine, Complutense University of Madrid. Madrid, Spain.

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Corresponding author:
Dra. Cristina Díaz del Arco
Departamento de Anatomía Patológica. Hospital Clínico San Carlos. c/Profesor Martín Lagos s/n 28040 Madrid (España)
+34 91 330 30 00
crisdelarco@gmail.com

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A tumor within a tumor: gastric carcinoma metastasizing to a uterine leiomyoma

Un tumor dentro de otro: carcinoma gástrico con metástasis en un leiomioma uterino

Cristina Díaz del Arco MD PhD[1,2], Ignacio Lample Brusel MD[1], Miguel de Hita Castillo MD[1], María Jesús Fernández Aceñero MD PhD[1,2]

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ABSTRACT
Metastasis from one tumor to another is a rare clinical finding, as is the spread of extragenital tumors to the female genital tract, with involvement of the uterine wall being particularly rare. This study presents a case of gastric carcinoma metastasis in a uterine leiomyoma, diagnosed after resection of the lesion due to hypermenorrhea. In addition, 39 previously described cases of extragenital metastases in leiomyomas are reviewed, in which the breast is the predominant origin (74.4%), followed by lung, skin, gastric, renal, and thyroid tumors. Despite the rarity of these cases, recognizing the possibility of extragenital metastases in uterine lesions is essential for guiding appropriate treatment and improving the patient's quality of life.
Keywords: Gastric neoplasms; leiomyoma; neoplastic metastasis; adenocarcinoma; uterine neoplasms.

RESUMEN
La metástasis de un tumor en otro constituye un hallazgo clínico poco frecuente, al igual que la diseminación de tumores extragenitales al tracto genital femenino, siendo especialmente rara la afectación de la pared uterina. Este estudio presenta un caso de metástasis de carcinoma gástrico en un leiomioma uterino, diagnosticado tras la resección de la lesión por hipermenorrea. Además se revisan 39 casos previamente descritos de metástasis extragenitales en leiomiomas, en los que predomina el origen mamario (74,4%), seguido de tumores pulmonares, cutáneos, gástricos, renales y tiroideos. A pesar de la rareza de estos casos, reconocer la posibilidad de metástasis extragenitales en lesiones uterinas resulta fundamental para orientar adecuadamente el tratamiento y mejorar la calidad de vida del paciente.
Palabras clave: Neoplasias gástricas; leiomioma; metástasis de la neoplasia; adenocarcinoma; neoplasias uterinas

Introduction

The appearance of a tumor within another tumor (tumor-to-tumor metastasis) is rare in clinical practice. Distant metastatic involvement of the female genital tract is also uncommon[1]. These metastases are mainly located in the ovarian parenchyma, followed by the vagina, with uterine involvement being extremely rare (less than 10% of cases)[2].

The most frequent primary sources of extragenital metastases to the female genital tract are colorectal carcinoma (37.6%), followed by breast carcinoma (34.9%), gastric carcinoma (5.4%), and appendiceal carcinoma (2.7%)[2]. Uterine involvement most commonly arises from breast or colorectal malignancies, and the majority of reported cases are described as isolated case reports[3]. Furthermore, rare instances of metastatic involvement within uterine tumors, including endometrial polyps and leiomyomas, have been documented[4].

The present study reports a case of gastric carcinoma metastasizing to a uterine leiomyoma that was surgically resected for the management of hypermenorrhea. In addition, a review of previously published cases of extragenital tumor metastases to uterine leiomyomas is presented. This study was approved by the Healthcare Ethics Committee of Hospital Clínico San Carlos (minutes 06/2025, code 25-034).

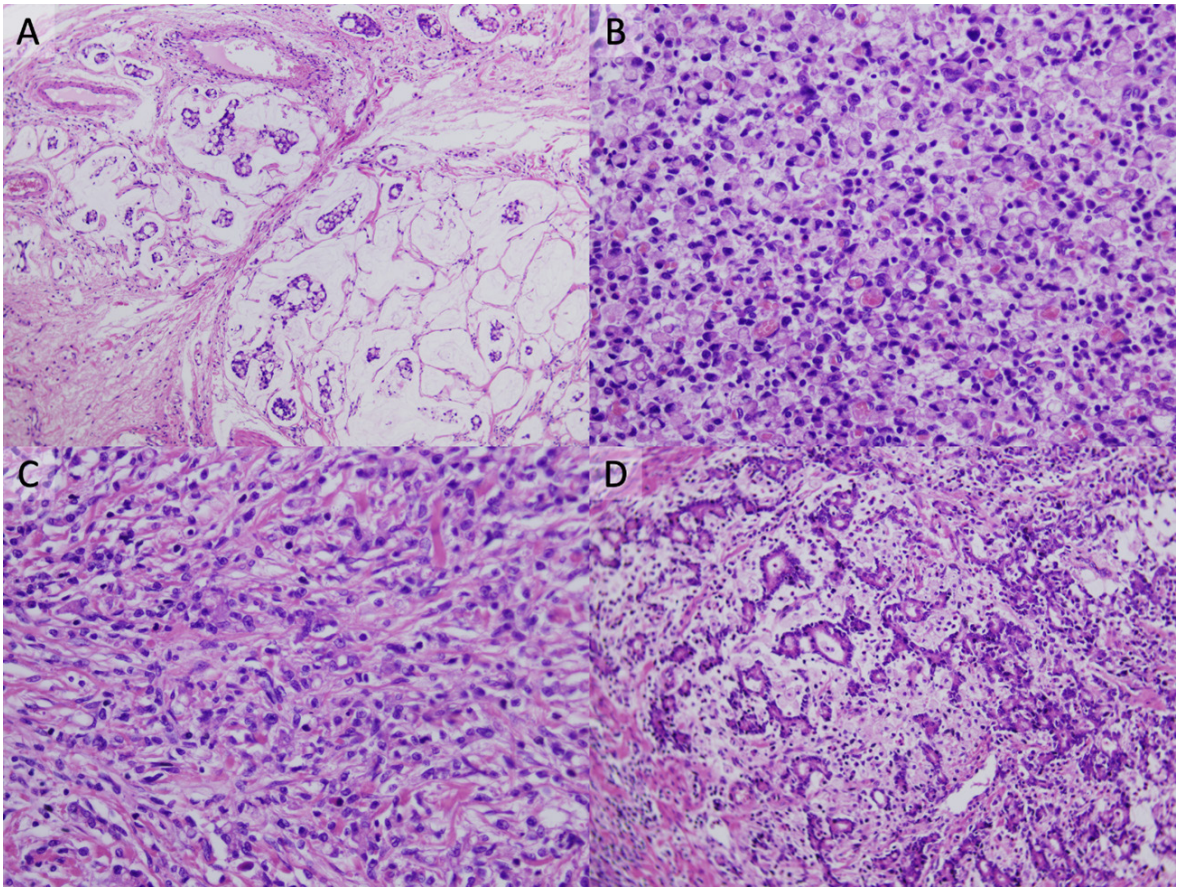
Case report

A 55-year-old woman with a medical history significant for treated Helicobacter pylori infection and uterine leiomyomatosis was evaluated following the detection of occult blood in the stool. Upper gastrointestinal endoscopy revealed a 5 cm ulcerated lesion located in the antral region. Histopathological examination of biopsy specimens demonstrated a poorly differentiated tubular adenocarcinoma with signet ring cell features. Immunohistochemical analysis for HER2 was negative (HERCEPTEST score 0), performed using the HercepTest™ on the Dako Autostainer in accordance with the American Society of Clinical Pathologists guidelines for HER2 assessment in gastric carcinoma. Preserved expression of the mismatch repair proteins MSH2, MSH6, PMS2, and MLH1 was observed, and programmed death-ligand 1 (PD-L1) expression showed a combined positive score of 5 (PD-L1 antibody clone 22C3; Dako, Denmark).

Staging computed tomography (CT) revealed multiple perigastric and peripancreatic lymphadenopathies. The patient subsequently received neoadjuvant chemotherapy with the FLOT regimen (5-fluorouracil, leucovorin, oxaliplatin, and docetaxel), followed by subtotal gastrectomy. Pathological examination of the surgical specimen identified a mixed-type adenocarcinoma measuring 9 × 8.5 cm, composed of discoid, tubular, and signet ring cell components, and staged as ypT4a and ypN3b (Figure 1). The histopathological response to neoadjuvant therapy was minimal (Ryan grade 3). Adjuvant chemotherapy with the same regimen was subsequently initiated.

During follow-up, the patient presented with hypermenorrhea attributed to a 45 x 40 mm leiomyoma on the posterior wall of the uterus, which was resected transcervically. Microscopic examination showed proliferation of smooth muscle bundles without atypia, necrosis, or

Figure 1. Representative areas of gastric carcinoma (surgical specimen). A) Glandular structures in abundant extracellular mucin. Hematoxylin-eosin, x100. B) Signet ring cells. Hematoxylin-eosin, x400. C) Diffuse growth pattern. Hematoxylin-eosin, x400. D) Tubular pattern on the surface. Hematoxylin-eosin, x200.



significant mitosis. This proliferation was extensively infiltrated by a malignant epithelial neoplasm, with formation of nests and glandular structures, extracellular mucin, and occasional signet ring cells (Figure 2). Immunohistochemical techniques showed that the epithelial proliferation was positive for CK7 and negative for PAX8, GATA3, TTF1, estrogen and progesterone receptors, CK20, and CDX2. These findings, together with the patient's oncological history, were consistent with intralyomyo metastasis of gastric carcinoma.

The follow-up thoracoabdominal CT scan showed hypoattenuating adnexal masses measuring 7.5 x 7 cm (left) and 6 x 5 cm (right), not detected in previous studies, suggestive of bilateral ovarian metastases. Given the progression of the disease, treatment was initiated with FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) combined with nivolumab.

Discussion

Tumor-to-tumor metastasis is an uncommon pathological phenomenon in which one primary neoplasm metastasizes to another distinct tumor. This entity is distinct from collision tumors or lymphovascular invasion, as it is characterized by true metastatic deposits within the neoplastic tissue of the recipient tumor[5]. Within this context, breast carcinoma represents the most frequently reported donor tumor, whereas meningioma is the most common recipient tumor[6].

The preference of cancer cells for certain metastatic sites depends on the interaction between these cells and the microenvironment of the recipient organ. In the female genital tract, metastases are most frequently located in the ovaries, probably due to their rich vascularization, well-developed lymphatic network, favorable pH, and adequate oxygen pressure, which facilita-

Figure 2. Leiomyoma with extensive carcinoma infiltration. A) Areas with glandular formations and extracellular mucin. Hematoxylin-eosin, x100. B and C) Infiltration in the form of irregular glands and cords. Hematoxylin-eosin, x200. D) Negativity for estrogen receptors, which are positive in the underlying leiomyoma. Estrogen receptors, x400.

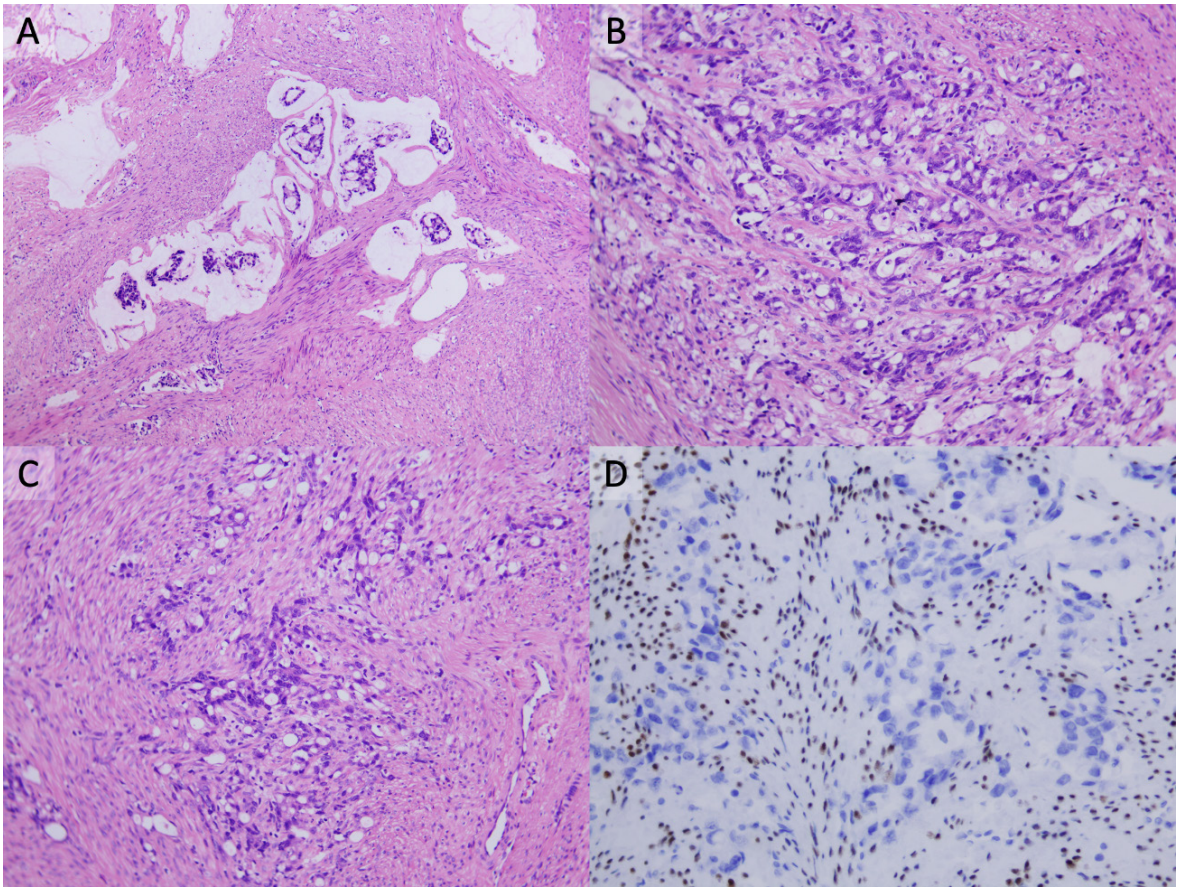


Table 1. Reported cases of metastasis of extragenital tumors in uterine leiomyomas.

Case	Primary	Type	Age	Author	Year	Reference*
1	Breast	NOS[a]	39	Weingold	1961	7
2	Breast	Scirrhous	48	Birdsall	1964	11
3	Breast	NOS	44	Banooni	1971	15
4	Breast	Scirrhous	47	Manabe	1979	11
5	Breast	NOS	44	Manabe	1979	11
6	Breast	NOS	46	Spiro	1979	15
7	Breast	Lobular	NS[b]	Spiro	1979	15
8	Breast	Lobular	NS	Di Bonito	1985	7
9	Breast	NOS	40	O'Brien	1992	15
10	Breast	NOS	63	Beattie	1993	15
11	Breast	NS	NS	Afriat	1993	1
12	Breast	Lobular	51	Sugiyama	1995	4
13	Breast	Lobular	54	Liebmann	1998	15
14	Breast	NOS	37	Minelli	1998	4
15	Breast	NOS	65	Uner	2002	1
16	Breast	NOS	51	Charvolin	2002	7
17	Breast	NOS	61	Blecharz	2004	11
18	Breast	Lobular	46	Blecharz	2004	11
19	Breast	Lobular	40	Jashnani	2007	11
20	Breast	NOS	55	Kondo	2009	12
21	Breast	Lobular	48	Işçi	2011	2
22	Breast	Lobular	53	Abaid	2011	4
23	Breast	NOS	70	Van Meurs	2012	11
24	Breast	NOS	47	Dirican	2012	8
25	Breast	Lobular	52	Kirubamani	2013	11
26	Breast	Lobular	62	Toyoshima	2015	11
27	Breast	NOS	58	Razia	2017	7
28	Breast	NOS	67	Ludovisi	2018	10
29	Breast	NOS	42	Eroglu	2024	2
30	Stomach	NS	62	Kiyokoba	2015	6
31	Lung	Adeno[c]	45	Srhoff	1989	11
32	Lung	Adeno	58	Rauff	2014	11
33	Lung	Adeno	47	Rush	2017	9
34	Thyroid	Papillary	53	Bertrand	2019	3
35	Synovial sarcoma	Biphasic	38	Sakai	2020	11
36	Kidney	Clear C[d]	50	Karamooz	2024	5
37	Skin	Melanoma	49	Bakelaar	2008	13
38	Skin	Melanoma	44	Chanthasenanont	2015	9
39	Unknown	Signet ring cell	55	Lanjewar	1997	14

**Due to limitations in the number of possible references, the original reference or the article that includes the original reference is included.*
a NOS: not otherwise specified (formerly ductal).
b NS: not specified.
c Adeno: adenocarcinoma.
d Clear cell: clear cells.

tes the implantation of malignant cells[7]. Other structures of the female genital tract appear to be more resistant to metastatic spread. Thus, a previous study showed that metastases are mainly found in the ovaries (75.8%), vagina (13.4%), and uterus (8.1%, including the cervix)[7]. Within the uterus, the myometrium is the most frequent location (63.5%)[2].

Regarding the routes of dissemination to the uterine wall, it has been postulated that the involvement may occur through retrograde lym-

phatic dissemination from ovarian metastases, or via hematogenous spread in cases of isolated uterine involvement[1]. In our case, the first option seems the most likely, given the finding of adnexal masses suggestive of bilateral ovarian metastases.

The primary tumors that most frequently metastasize to the uterus are breast carcinomas (especially lobular), followed by gastrointestinal, lung, renal, and melanoma[7]. The distinction between a primary tumor of the genital tract and a metastatic tumor in these cases is crucial, because it implies radically different therapeutic approaches. Therefore, pathological examination is essential. Despite the rarity of these cases, it is essential that pathologists be alert to the possibility of metastasis of extragenital cancers to the uterus or uterine lesions.

In the literature review, 39 cases of extragenital metastases in uterine leiomyomas were identified (Table 1)[1-15], 74.4% of which were of mammary origin. The mean age in cases of breast cancer was 51 years (range: 37–70), with metastases originating from both NOS-type carcinomas (16/29, 55.2%) and lobular carcinomas (10/29, 34.5%). The high incidence of uterine metastases from breast cancer could be explained by the hormonal dependence of these cells[4]. Clinically, patients with metastatic involvement of the uterine wall presented with abnormal genital bleeding and/or growth of new or previously known uterine masses[8,9].

In addition to breast cancer, metastases of lung adenocarcinoma (3 cases), melanoma (2 cases), gastric cancer (2 cases, including ours), clear cell renal carcinoma (1 case), papillary thyroid carcinoma (1 case), and biphasic synovial sarcoma (1 case) were documented. The previous case of gastric metastasis described was a 62-year-old woman with poorly differentiated stage IV gastric cancer, with peritoneal dissemination and a 9 cm pelvic mass identified by imaging techniques[6]. Chemotherapy was initiated, and a partial response was observed in the primary tumor and peritoneal implants. Resection of the pelvic mass was performed, and the pathological study showed a uterine lipoleiomyoma infiltrated by gastric carcinoma.

Regarding follow-up, while some authors consider that strict gynecological monitoring does not improve the prognosis in cases of metastasis to the genital tract[1], routine evaluation is still recommended in patients receiving tamoxifen, due to the increased risk of endometrial lesions, including neoplasms[8]. This may have facilitated the detection of uterine metastases in cases of breast cancer.

With respect to management, pelvic surgery does not appear to have a significant impact on overall prognosis in most patients. Consequently, the surgical interventions reported in the literature have primarily been undertaken for symptomatic control of metastatic involvement, particularly in cases of abnormal uterine bleeding[1,9]. In the present case, despite the poor prognosis associated with advanced, aggressive gastric carcinoma and the limited response to chemotherapy, surgical resection of the leiomyoma effectively controlled hypermenorrhea, a clinically significant symptom for the patient, who declined blood transfusion for religious reasons. Nevertheless, some studies suggest that, in carefully selected patients with breast carcinoma, resection of isolated metastases, with or without adjuvant radiotherapy, may confer a survival benefit. In instances of uterine metastasis of breast origin, hysterectomy without oophorectomy has been proposed as a strategy that could positively influence survival outcomes[2,8]. However, further studies involving larger case series are required to establish definitive treatment recommendations.

Extragenital metastases have also been described in endometrial polyps and uterine leiomyosarcomas, predominantly originating from breast carcinoma[4,7]. A review published in 2017 analyzed 17 cases of breast cancer metastasis to endometrial polyps, of which 47% (8/17) were of lobular histology[7].

In conclusion, this report highlights the rare occurrence of gastric carcinoma metastasizing to a uterine leiomyoma, an unusual event that emphasizes the importance of precise pathological evaluation. Although uterine metastases from extragenital malignancies are uncommon, their early recognition is essential to ensure appropriate clinical management. While surgical intervention does not generally alter prognosis, it may play a valuable role in symptom control and in improving patients' quality of life.

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