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CASE REPORT

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Müllerian-type carcinosarcoma arising in gastric endometriosis: Case report and review of the literature

Rayne Peerenboom[1] | **Sabrina Wang**[1] | **Ryan Morgan**[2] | **Seth Sankary**[2] | **Lindsay Yassan**[3] | **Katherine Kurnit**[4] | **Mitchell C. Posner**[5]

[1]University of Chicago, Pritzker School of Medicine, Chicago, Illinois, USA

[2]Department of General Surgery, Univeristy of Chicago, Chicago, Illinois, USA

[3]Department of Pathology, Univeristy of Chicago, Chicago, Illinois, USA

[4]Department of Obstetrics and Gynecology, Section of Gynecologic Oncology, Univeristy of Chicago, Chicago, Illinois, USA

[5]Department of General Surgery, Section of Surgical Oncology, Univeristy of Chicago, Chicago, Illinois, USA

Correspondence
Rayne Peerenboom, University of Chicago, Pritzker School of Medicine, Chicago, IL, USA.
Email: rpeerenboom@uchicago.edu

Key Clinical Message

Although endometriosis is a common condition, both extrapelvic endometriosis and endometriosis associated malignancy (EAM) are rare. We describe the first reported case of a patient with Müllerian-type carcinosarcoma arising in gastric endometriosis.

KEYWORDS

carcinosarcoma, cell transformation, endometriosis, gastrointestinal neoplasms, gynecologic neoplasms, stomach neoplasms

1 | INTRODUCTION

Endometriosis is a common condition, affecting approximately 10% of women of reproductive age. However, both extrapelvic endometriosis and malignant transformation are rare.[1] When intestinal endometriosis does occur, it most commonly involves the sigmoid colon and rectum.[2] To date, there have been eight case reports of gastric endometriosis (Table 1).[3–10] Endometriosis may also involve various other abdominal and extra-abdominal sites, including the urinary tract, abdominal wall, liver, kidney, pancreas, biliary system, thorax, and central nervous system.[11]

Although both pelvic and extrapelvic endometriosis are benign conditions, malignant transformation can occur. The overall risk of malignant transformation has been estimated at 1% for premenopausal females and 1%–2.5% for postmenopausal females.[1] Endometriosis-associated ovarian cancer (EAOC) constitutes the majority (76%) of these cases.[1] However, endometriosis-associated intestinal tumors (EAIT) have also been reported, exclusively in the small and large bowel, as has EAM arising in the liver.[12,13] To date, there have been no reports of EAM occurring in the stomach. We describe a patient with Müllerian-type carcinosarcoma arising in gastric endometriosis.

TABLE 1 Clinical, imaging, pathology, and treatment details of reported cases of gastric endometriosis.

Case	Age	Prior endo[a]	Presentation	Tumor markers	Imaging and GI studies	Biopsy	Treatment	Final pathology	Follow-up
Kashyap et al.[3]	35	No	Epigastric pain, nausea, vomiting, melena	NR	EGD: 3-cm submucosal tumor with 1-cm ulceration. EUS: 6 × 6 cm, inhomogeneous mass with irregular outer borders in the proximal gastric body and extending to the spleen, L hemidiaphragm, and pancreatic tail	FNA: decidua suggestive of endometriosis	En bloc partial gastrectomy and splenectomy	Endometriosis with endometrial glands and decidualized stroma	~20 weeks, symptom-free
Anaf et al.[4]	28	NR	General abdominal pain (catamenial), alternating constipation and diarrhea, pain at defecation, dyspepsia, epigastric postprandial pain, ×4 years	NR	DCBE: deep endometriotic involvement of the transverse colon. Laparoscopy: fixed pelvis with severe rectosigmoid stenosis, deep infiltrating mid transverse colon stenosis of 6 cm, infiltration of the gastrocolic ligament, and induration of the stomach antrum over a length of 6 cm with serosal lesion	Not done	Rectosigmoid resection with end-to-end anastomosis and partial gastrectomy with gastrocolic ligament ablation	Deep infiltrating endometriosis in all resected specimen (CD10 positive), with all layers of the stomach involved by endometriosis except the mucosal layer	1 year, symptom-free
Ha et al.[5]	44	No	Asymptomatic, incidental imaging finding	CEA & CA 19–9 WNL pre-op	EGD: well-defined 20 mm subepithelial tumor with negative cushion sign. CT: 2-cm endophytic, homogeneous, hypodense submucosal mass in the posterior wall of the stomach antrum. EUS: homogenous hypoechoic lesion in the proper muscle layer	Not done (per patient preference)	Laparoscopic-assisted distal gastrectomy	Focus of endometriosis containing endometrial glands and hemosiderin-laden macrophages within the muscular layer of the stomach near an intramural hemorrhagic cyst	3 years, no recurrence on EGD
Mohamed et al.[6]	60	No	Epigastric pain, left loin pain, nausea	NR	Abd US: gastric antral mass lesion. CT: large, irregular, inhomogeneously enhancing soft tissue mass in the inferior wall of the gastric antrum with large exophytic component and few satellite nodules, measuring 4.5 × 6.5 × 4.5 cm	Not done	Open excision of gastric mass with sleeve gastrectomy of the greater curvature, together with partial transverse colectomy with end-to-end colonic anastomosis	Extensive areas of hemorrhage and hemorrhagic necrosis, separated and bordered by proliferation of spindle cells and hemosiderin-laden macrophages, extending to the serosa of the stomach and the colon (CD10 and SMA positive)	NR

TABLE 1 (Continued)

Case	Age	Prior endo[a]	Presentation	Tumor markers	Imaging and GI studies	Biopsy	Treatment	Final pathology	Follow-up
Bal et al.[7]	40	No	Epigastric pain, RUQ abdominal pain, slow digestion, early satiety, diarrhea, ×2 years	CEA & CA 19–9 WNL pre-op	EGD: diffuse superficial gastritis and extra-luminal compressed mass or submucosal tumor in peripyloric major curvature with stenosis. CT abd: 4.3 × 3.5 cm hypodense mass in the anterior wall of peripyloric portion with luminal narrowing	Not done	Surgical resection (details NR)	Endometrioid glands and stromal nests in gastric mucosa and muscularis propria, with invasion of endometrioid glands to muscular layer	NR
Nasirian & Parsa[8]	44	NR	Abdominal and back pain, ×2 years	NR	CT: 3 × 3 cm submucosal gastric mass. EGD: submucosal mass	Biopsy: gastritis	Surgical resection (details NR)	Background of fibrous tissue with fragments of compressed ovarian stroma with endometrial glands	NR
Peerenboom et al. (present case)	49	Yes	Asymptomatic, incidental imaging finding	CA 125 WNL post-op	CT: cystic lesion emanating from the lesser curvature in the proximal stomach. EGD/EUS: submucosal cystic mass measuring 10.3 cm, located 3 cm distal to the GEJ, with internal solid component	Needle core biopsy: invasive poorly differentiated carcinoma with focal squamous differentiation	Open subtotal gastrectomy with end-to-side retrocolic Roux-en-Y gastrojejunostomy	Müllerian-type carcinosarcoma (PAX-8 positive) with squamous and chondro-sarcomatous components	4 months, recurrence (peritoneal carcinoma-tosis, diffuse osseous disease)

Abbreviations: Abd, abdominal; CA 19–9, carbohydrate antigen 19–9; CA 125, cancer antigen 125; CEA, carcinoembryonic antigen; CT, computed tomography. DCBE, double contrast barium enema; EGD, esophagogastroduodenoscopy; EUS, endoscopic ultrasound; FNA, fine needle aspiration; GEJ, gastroesophageal junction; GI, gastrointestinal; NR, not reported; Para, paracentesis; RUQ, right upper quadrant; WNL, within normal limits.

[a]Prior symptoms or diagnosis of endometriosis.

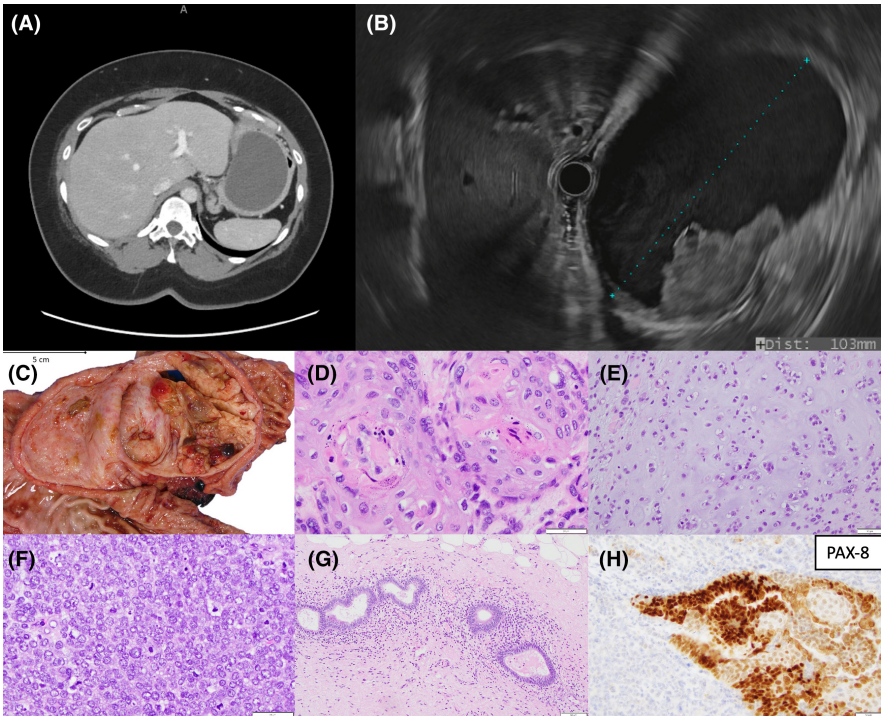

FIGURE 1 Imaging findings, including (A) CT demonstrating cystic lesion emanating from the lesser curvature in the proximal stomach and (B) EUS with submucosal cystic mass measuring 10.3 cm, located 3 cm distal to gastroesophageal junction, with internal solid component; and final pathology, including (C) opened 11.0 × 7.6 × 3.8 cm cystic lesion with nodular excrescences in the gastric body near the lesser curvature, (D) areas of squamous differentiation, (E) chondrosarcomatous component, (F) solid areas composed of poorly differentiated cells, suggestive of a dedifferentiated component with readily identifiable mitotic figures, (G) background of endometriosis, and (H) carcinomatous component with patchy PAX-8 nuclear staining.

2 | CASE PRESENTATION/ EXAMINATION

The patient was a 49-year-old woman with history of pelvic and thoracic endometriosis, which resulted in catamenial pneumothorax. This was initially managed with placement of a right-sided chest tube, followed by right video-assisted thoracoscopic surgery due to hemothorax. Due to the severity of her symptoms, the patient underwent total laparoscopic hysterectomy with bilateral salpingo-oophorectomy (TLH-BSO) at age 34 with subsequent improvement in endometriosis-related symptoms. She did not receive hormonal therapy following surgery.

Fifteen years later, a 5.1 × 5.1 × 5.4 cm cystic lesion in the proximal stomach was discovered incidentally on CT during a hospitalization for diverticulitis (Figure 1A). She reported diffuse lower abdominal pain during the admission that resolved with treatment of the diverticulitis, but she remained asymptomatic with respect to the gastric mass. On outpatient follow-up, abdominal exam was unremarkable. Review of systems was negative for early satiety, dysphagia, nausea, vomiting, and weight loss.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT)

EGD/EUS demonstrated a submucosal cystic lesion measuring 10.3 cm (Figure 1B). Differential diagnosis included congenital cystic lesions such as duplication cyst verses neoplastic lesions such as cystic degeneration of a GIST.[14] Initial biopsies showed invasive poorly differentiated carcinoma with focal squamous differentiation. Full body PET and CT of the chest, abdomen, and pelvis were negative for metastatic disease.

Following this workup, the patient underwent exploratory laparotomy and subtotal gastrectomy with end-to-side retrocolic Roux-en-Y gastrojejunostomy, which was uncomplicated. Final pathology demonstrated a Müllerian carcinosarcoma composed of a range of epithelioid components and a chondrosarcomatous mesenchymal component. The carcinomatous component showed endometrioid differentiation, which was highlighted by PAX-8 and estrogen receptor immunohistochemical stains, consistent with Müllerian origin. Areas of squamous differentiation and poorly differentiated areas, suggestive of a dedifferentiated component,

were also present. The carcinosarcoma was seen in close association with a background of typical and atypical endometriosis (Figure 1C–H). Resection margins were negative, and 13 lymph nodes were negative for malignancy. CA-125 was within normal limits at six-week follow-up, and MRI pelvis was non-concerning for residual disease. Postoperative PET CT was also negative. Adjuvant chemotherapy (carboplatin and paclitaxel) was recommended; however, the patient opted for close clinical surveillance with symptom assessment, clinical and pelvic exams, and monitoring of CA-125 every 3 months.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

Four months postoperatively, the patient presented with abdominal pain. A CT of the abdomen and pelvis demonstrated peritoneal implants and ascites, as well as subtle sclerotic lesions. A paracentesis was performed, and cytology was consistent with metastatic adenocarcinoma. A nuclear medicine bone scan demonstrated diffuse osseous metastatic disease. The patient was recommended for systemic chemotherapy. She initiated treatment and is currently receiving carboplatin and paclitaxel.

5 | DISCUSSION

To our knowledge, this is the first report of EAM in the stomach. To date, there have been six reports of gastric endometriosis in English (Table 1), one in Russian, and one in Spanish.[3–10] EAITs have been reported at other sites in the gastrointestinal tract, most commonly the rectum and sigmoid colon, and other upper abdominal organs including the liver.[15,16] Similar to EAOC, endometrioid and clear cell histologies are the predominant subtypes.[1] However, in extra-ovarian EAM, including EAITs, more reports of endometrial stromal sarcomas, or adenosarcomas are seen in the literature.[1,16,17] Carcinosarcoma is less commonly reported. Despite its mesenchymal component, carcinosarcomas are now understood to arise from an epithelial precursor, such as endometrioid or clear cell tumors, and are considered to be epithelial tumors.

The mechanism of spread of endometriosis beyond the uterus is unknown, although several theories exist to explain the pathogenesis.[18] Initiating events may include metastatic spread via retrograde menstruation, vascular or lymphatic spread, or iatrogenic implantation; metaplasia of specialized cells in the mesothelial lining; persistence and growth of residual Wolffian or Müllerian duct cells; or transformation of resident undifferentiated cells. Several predisposing and propagating factors, including oxidative stress, immune dysfunction, genetic factors, and hormonal changes, may also play a role.[18]

The rarity of extrapelvic EAM/EAIT leads to challenges in diagnosis and management. In the present case, the initial imaging findings of a submucosal, cystic lesion favored a duplication cyst, or gastrointestinal stromal tumor. Notably, the majority of previously reported cases of endometriosis in visceral abdominal organs similarly appeared as cystic lesions on CT,[11] and prior cases of gastric endometriosis most often appeared as submucosal lesions on gastrointestinal studies (Table 1). However, pathognomonic imaging findings have not been described for EAM; thus, microscopic examination combined with immunohistochemistry is required for diagnosis. In the present case, initial biopsy results demonstrated poorly differentiated carcinoma with focal squamous differentiation but did not reveal the chondrosarcomatous or endometrioid components of the tumor. This highlights the importance of comprehensive pathologic examination and sampling of various tumor components for definitive diagnosis of EAM.

Currently, there are no definitive guidelines for the management of EAIT or EAM. Median 5-year survival for EAM arising in all sites has been estimated at 80%.[19] EAOC, which constitutes the majority of EAM, is generally treated similarly to other forms of ovarian cancer, including use of platinum-taxane combinations as adjuvant therapy.[20] One review of EAIT found that adjuvant treatment (chemotherapy and/or radiotherapy) was administered for only 10 of 29 patients.[15] EAM arising in the liver has similarly been managed with either adjuvant chemotherapy or clinical surveillance.[13,21] In the present case, adjuvant chemotherapy was recommended; however, the patient initially opted for clinical surveillance. Unfortunately, disease recurrence (peritoneal carcinomatosis and diffuse osseous metastatic disease) was confirmed 4 months postoperatively, and the patient initiated treatment with carboplatin and paclitaxel.

Our case demonstrates that, although rare, EAM may be considered on the differential for a submucosal gastric lesion. Adequate tissue sampling is required for definitive diagnosis. Close collaboration in an interdisciplinary team including radiology, gastroenterology, pathology, surgical oncology, and gynecologic oncology is necessary for both accurate diagnosis and optimal management.

AUTHOR CONTRIBUTIONS

Rayne Peerenboom: Conceptualization; data curation; visualization; writing – original draft; writing – review and editing. **Sabrina Wang:** Data curation;

investigation; visualization; writing – review and editing. **Ryan Morgan:** Data curation; investigation; supervision; validation; visualization; writing – review and editing. **Seth Sankary:** Data curation; investigation; supervision; visualization; writing – review and editing. **Lindsay Yassan:** Data curation; investigation; supervision; visualization; writing – review and editing. **Katherine Kurnit:** Data curation; investigation; supervision; visualization; writing – review and editing. **Mitchell C. Posner:** Conceptualization; data curation; investigation; supervision; validation; visualization; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interests to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

Written consent was obtained from the patient.

ORCID

Rayne Peerenboom https://orcid.org/0000-0001-6783-0058

REFERENCES

1. Stern RC, Dash R, Bentley RC, Snyder MJ, Haney AF, Robboy SJ. Malignancy in endometriosis: frequency and comparison of ovarian and Extraovarian types. *Int J Gynecol Pathol*. 2001;20(2):133-139.
2. Jubanyik KJ, Comite F. extrapelvic endometriosis. *Obstet Gynecol Clin North Am*. 1997;24(2):411-440. doi:10.1016/S0889-8545(05)70311-9
3. Kashyap P, Medeiros F, Levy M, Larson M. Unusual submucosal tumor in the stomach: Diagnosis endometriosis. *Gastroenterology*. 2011;140(7):e7-e8. doi:10.1053/j.gastro.2010.03.081
4. Anaf V, Buggenhout A, Franchimont D, Nöel JC. Gastric endometriosis associated with transverse colon endometriosis: a case report of a very rare event. *Arch Gynecol Obstet*. 2014;290(6):1275-1277. doi:10.1007/s00404-014-3373-7
5. Ha JK, Choi CW, Kim HW, et al. An extremely rare case of gastric subepithelial tumor: gastric endometriosis. *Clin Endosc*. 2015;48(1):74-77. doi:10.5946/ce.2015.48.1.74
6. Mohamed AAA, Selim YARM, Arif MA, Albroumi SA. Gastric wall endometriosis in a postmenopausal woman. *Egypt J Radiol Nucl Med*. 2016;47(4):1783-1786. doi:10.1016/j.ejrnm.2016.08.005
7. Bal O, Chadraa Y, Tsagaan N, et al. Gastric endometriosis. *Central Asian J Med Sci*. 2017;1:95-99.
8. Nasirian N, Parsa H. A case report of Abdominal Wall endometriosis with manifestation of abdominal and back pain. *JBUMS*. 2022;24(1):83-87. doi:10.22088/jbums.24.1.83
9. Mariscal G, Laynez M. Comments on a case of gastric endometriosis. *Rev Esp Enferm Apar Dig*. 1971;33(5):603-604.
10. Iaroshenko VI, Salokhina MB. Endometriosis of the stomach. *Vestn Khir Im I I Grek*. 1979;123(8):82-83.
11. Andres MP, Arcoverde FVL, Souza CCC, Fernandes LFC, Abrão MS, Kho RM. Extrapelvic endometriosis: a systematic review. *J Minim Invasive Gynecol*. 2020;27(2):373-389. doi:10.1016/j.jmig.2019.10.004
12. Hoang CD, Boettcher AK, Jessurun J, Pambuccian SE, Bullard KM. An unusual Rectosigmoid mass: Endometrioid adenocarcinoma arising in colonic endometriosis: case report and literature review. *Am Surg*. 2005;71(8):694-697. doi:10.1177/000313480507100815
13. Wang D, Yang Q, Wang H, Liu C. Malignant transformation of hepatic endometriosis: a case report and literature review. *BMC Womens Health*. 2021;21:249. doi:10.1186/s12905-021-01366-6
14. Lee J, Park CM, Kim KA, et al. Cystic lesions of the gastrointestinal tract: multimodality imaging with pathologic correlations. *Korean J Radiol*. 2010;11(4):457-468. doi:10.3348/kjr.2010.11.4.457
15. Nasu K, Okamoto M, Kawano Y, et al. Endometrioid adenocarcinoma arising from intestinal endometriosis. *J Endomet Pelvic Pain Disord*. 2014;6(2):112-118. doi:10.5301/je.5000186
16. Khan A, Craig M, Jarmulowicz M, Davidson B. Liver tumours due to endometriosis and endometrial stromal sarcoma. *HPB (Oxford)*. 2002;4(1):43-45. doi:10.1080/136518202753598735
17. Mourra N, Tiret E, Parc Y, de Saint-Maur P, Parc R, Flejou JF. Endometrial stromal sarcoma of the Rectosigmoid colon arising in Extragonadal endometriosis and revealed by portal vein thrombosis. *Arch Pathol Lab Med*. 2001;125(8):1088-1090. doi:10.5858/2001-125-1088-ESSOTR
18. Sourial S, Tempest N, Hapangama DK. Theories on the pathogenesis of endometriosis. *Int J Reprod Med*. 2014;2014:179515. doi:10.1155/2014/179515
19. Heaps JM, Nieberg RK, Berek JS. Malignant neoplasms arising in endometriosis. *Obstet Gynecol*. 1990;75(6):1023-1028.
20. Li N, Zhou W, Zhao L, Zhou J. Endometriosis-associated recto-sigmoid cancer: a case report. *BMC Cancer*. 2018;18:905. doi:10.1186/s12885-018-4797-4
21. N'Senda P, Wendum D, Balladur P, Dahan H, Tubiana JM, Arrivé L. Adenosarcoma arising in hepatic endometriosis. *Eur Radiol*. 2000;10(8):1287-1289. doi:10.1007/s003300000322

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