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CASE REPORT

Splenic metastasis from endometrial carcinoma: report of a case and review of literature

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Abstract
Introduction Splenic metastasis from endometrial carcinoma is a rare clinical event, with only 11 cases documented previously in the literature.
Case report A 58-year-old woman had surgery and radiotherapy for stage IIB endometrial carcinoma. Eighteen months later, PET scan discovered a hypermetabolic splenic mass and two hypermetabolic lung nodules. Spleen biopsy showed metastasis from endometrial carcinoma. Chemotherapy with six cycles of cyclophosphamide, adriamycin and cisplatin effected a partial response of the splenic and lung metastasis. After few months, however, splenectomy was performed because of substantial growth of the spelnic metastasis and it confirmed that the splenic metastasis was of endometrial origin and solitary in the peritoneal cavity. After splenectomy, the patient received chemotherapy with six cycles of paclitaxel. To date, 6 months after splenectomy, she is alive with no intraperitoneal disease and with few stable lung metastases.
Conclusion This is the 12th reported case of splenic metastasis from endometrial carcinoma. Splenic metastasis from endometrial carcinoma is usually solitary splenic metastasis limited to the splenic parenchyma. Splenectomy is an appropriate treatment to avoid splenic rupture, splenic vein thrombosis and painful splenomegaly, to circumvent the splenic metastasis being a source of secondary metastatic disease, and to provide the potential for cure or extended survival. Since patients with splenic metastasis may be asymptomatic and the interval between the diagnoses of endometrial carcinoma and splenic metastasis may be prolonged, careful and extended follow-up after primary treatment of endometrial carcinoma is warranted.

Keywords Endometrial carcinoma · Imaging studies · Metastasis · Spleen · Splenecomy

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Introduction

The spleen is an uncommon site of metastasis, with a frequency of 2.3–7.1% in large autopsy series of cancer patients, and with <100 cases in living cancer patients reported in the literature [1–3]. Several hypotheses have been suggested to explain the rarity of splenic metastasis [3–7]:

1. The constant blood flow through the spleen impedes implantation of cancer cells in the spleen.
2. The sharp angle of the splenic artery branching from the celiac artery and the tortuosity of splenic artery make it difficult for tumor emboli to enter the spleen.
3. The rhythmic contractions of the spleen squeeze tumor emboli from the spleen and prevent their implanting in the spleen.
4. The scarcity of afferent lymphatic vessels in the spleen limits the transport of metastatic tumor cells into the spleen.

5. The role of the splenic capsule as physical barrier.
6. The presence of anti-tumor humoral factors and high concentration of phagocytes in the spleen.

Yet, the frequency of splenic metastasis in living cancer patients may have been underestimated since splenic metastasis is often asymptomatic and may not be associated with spelenomegaly [2]. In recent years, however, reports of splenic metastasis in living cancer patients have been increasing due to the advanced use of imaging studies, such as CT, MRI and PET, in the diagnostic work-up and follow-up of cancer patients [4, 5]. The most common sources of splenic metastasis from solid tumors are breast cancer, lung cancer and melanoma, but a rising incidence of splenic metastasis from female genital tract cancers, especially ovarian carcinoma, has been suggested [5, 6, 8].

In the vast majority of cases of splenic metastasis from various cancers, splenic metastasis is part of a disseminated disease rather than solitary splenic metastasis. The involvement of the spleen may occur by one or more of the following pathways: direct extension, transperitoneal spread, hematogenous route and lymphatogenous route [6, 9]. Consequently, in cases of splenic metastasis as part of a disseminated disease, the metastasis may be located either on the splenic capsule (capsular metastasis) or in the spelenic parenchyma (parenchymal metastasis) or both [6, 9]. In solitary splenic metastasis, however, the metastatic spread to the spleen occurs mainly by the hematogenous route and the metastasis is located as a rule within the splenic parenchyma [3, 6]. Splenic metastasis may also be distinguished as either "synchronous" (detected at the time of diagnosis of the primary tumor) or "metachronous" (detected after an interval from the diagnosis of the primary tumor).

Endometrial carcinoma ranges from the third to the fifth most common malignancy and from the first to the second most common genital tract cancer among women in developed countries [10–12]. Although the majority of endometrial carcinoma patients are diagnosed at an early stage with an excellent long-term prognosis, 10–30% of patients develop a recurrent disease [10–12]. Nevertheless, splenic metastasis from endometrial carcinoma is rare with only 11 cases previously documented in the literature [13–23]. We describe the 12th case of splenic metastasis from endometrial carcinoma and review pertinent literature.

Case report

A 58-year-old married, gravida 5, para 4, Caucasian woman underwent in November 2005 total abdominal hysterectomy, bilateral salpingo-oophorectomy and bilateral pelvic lymphadenectomy for stage IIB endometrial adenocarcinoma (Fig. 1). Postoperatively, the patient received external pelvic radiotherapy followed by three applications of high-dose rate brachytherapy. She tolerated radiotherapy well and remained asymptomatic and disease-free for the next 18 months.

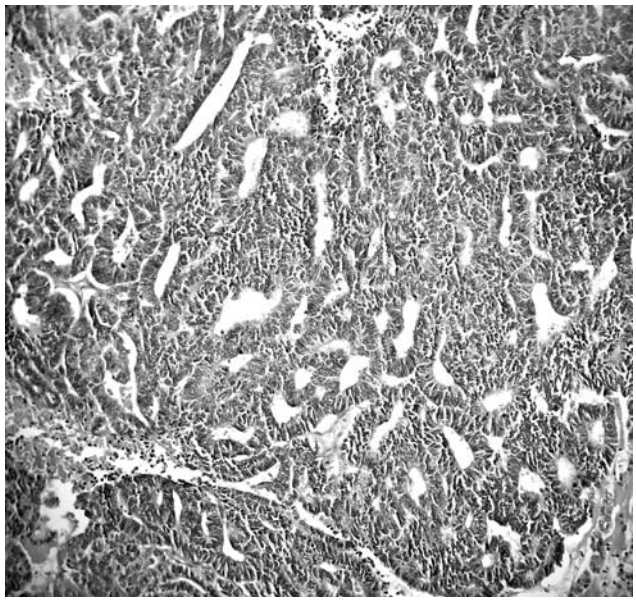

Fig. 1 Microscopic image of the primary endometrial adenocarcinoma shows FIGO grade 2 endometrioid carcinoma with glandular formation (H&E, ×400)

In May 2007, PET scan detected a 6.4 × 4.1-cm hypermetabolic mass in the splenic parenchyma, 1.4-cm hypermetabolic nodule in the lower lobe of the right lung and 0.9-cm hypermetabolic nodule in the lower lobe of the left lung. CT-guided Tru-Cut biopsy of the splenic mass revealed metastatic adenocarcinoma with histologic features similar to those of the primary endometrial tumor. From August 2007 to January 2008, the patient received intravenous combination chemotherapy with six cycles of CAP (cyclophosphamide 500 mg/m^2, doxorubicin 50 mg/m^2 and cisplatin 50 mg/m^2 in day 1, every 21 days). The patient tolerated chemotherapy well and had only sporadic episodes of hematological toxicity that were noncumulative and easily manageable. In February 2008, PET scan demonstrated that the splenic mass remained hypermetabolic but decreased to 2.5 × 2 cm, the nodule in the right lung ceased to be hypermetabolic and decreased to 0.8 cm, and the nodule in the left lung disappeared. Since the patient remained asymptomatic and physical examination was unremarkable, a policy of "wait and see" was adopted. In May 2008, CT demonstrated a 4.6 × 3.6 × 3-cm splenic parenchymal mass, 0.7-cm right lung nodule and 0.8-cm left lung nodule. In August 2008, CT showed substantial increase in the size of the splenic mass to 9.1 × 7.3 cm (Fig. 2), increase in size of the right lung nodule to 2 × 1.1 cm and increase in size of the left lung nodule to

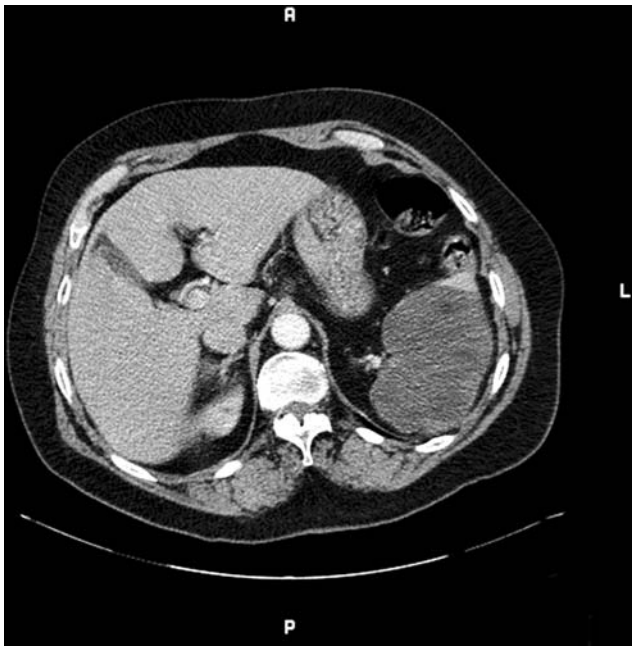

Fig. 2 CT image of the liver and spleen shows metastases occupying almost completely the splenic parenchyma

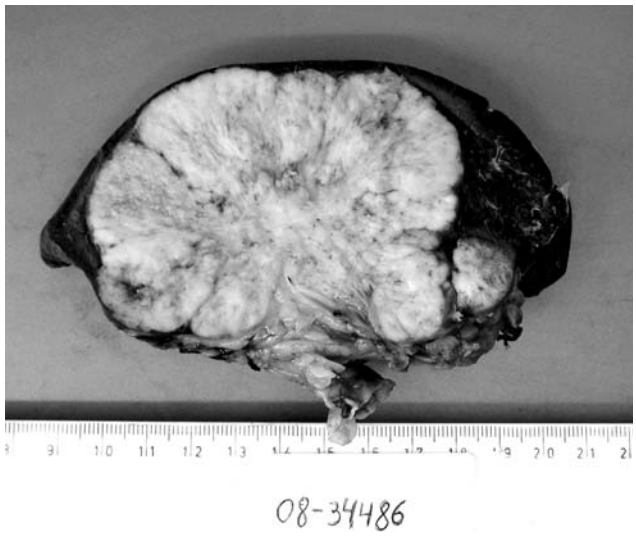

Fig. 3 Sectioned spleen shows a tumor mass measuring 10 × 8 × 6 cm with irregular borders, occupying almost the entire splenic parenchyma and spreading to the splenic hilum

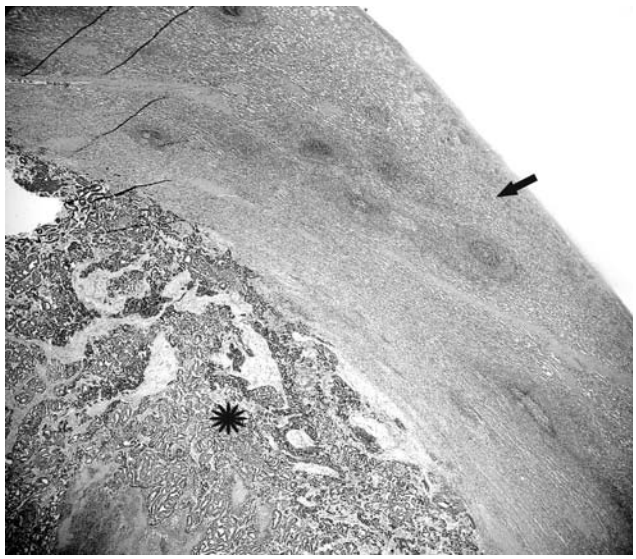

Fig. 4 Histologic section from the interface between normal splenic tissue (*arrow*) and metastatic adenocarcinoma with histologic features similar to those of the primary endometrial carcinoma (*asterisk*) (H&E, ×200)

0.9 cm. At this stage, a decision was made to perform a splenectomy.

At laparotomy, performed in September 2008 with use of a transverse incision in the left upper abdominal wall below the left costal margin, a 15-cm enlarged spleen with intact capsule was identified; there was no other evidence of intra-abdominal disease. Total splenectomy was performed. On gross examination, the spleen measured 13 × 12 × 7 cm and weighted 408 g. Slicing of the spleen showed a whitish necrotic tumor measuring 10 × 8 × 6 cm with irregular borders, almost completely occupying the splenic parenchyma and spreading to the splenic hilum (Fig. 3). Microscopic examination of the splenic tumor confirmed metastatic adenocarcinoma compatible with endometrial origin (Fig. 4). The patient had an unremarkable postoperative recovery and started intravenous single-agent chemotherapy with paclitaxel 175 mg/m^2 in day 1, every 21 days. To date, 6 months after splenectomy and six cycles of paclitaxel, the patient is alive and well and without evidence of intra-abdominal disease or increase in the size of the lung nodules.

Discussion

Splenic metastasis from endometrial carcinoma is rare. Sohaib et al. [12] found that only 4/86 (4.6%) patients with recurrent endometrial carcinoma had splenic metastasis and in all four patients, splenic metastasis was part of a disseminated disease. Univariate and multivariate analyses demonstrated that splenic metastasis is a significant predictor of poor survival in patients with recurrent endometrial carcinoma [12]. Bristow et al. [10] demonstrated that splenectomy for splenic metastasis was performed in only 1/35 (2.8%) patients having cytoreductive surgery for recurrent endometrial carcinoma and concluded that splencetomy might have a role in the management of recurrent endometrial carcinoma involving the spleen. Sauer et al. [4] found that 75/789 (9.5%) endometrial carcinoma patients developed

metastatic disease and only two (2.7%) of the 75 patients with metastatic endometrial carcinoma had splenic metastasis. Lee et al. [3] found splenic metastasis from endometrial carcinoma in only 1/28 (3.6%) women undergoing splenectomy for splenic metastasis form various cancers. Awtrey et al. [11] could not find any case of splenic metastasis in 27 patients undergoing surgery for recurrent endometrial carcinoma. Of 34 Chinese women with splenic metastasis reviewed by Lam and Tang [2], none had splenic metastasis from endometrial carcinoma.

Details of the 12 documented cases (including this case) of splenic metastasis from endometrial carcinoma are displayed in Table 1. Ten cases were reported in English ([14–16, 18–23], this case), one in French [17], and one in Polish [13]. Since we were unable to obtain either full text or abstract of the Polish paper [13], this review is based on 11 cases ([14–23], this case). All endometrial carcinomas were of endometrioid type. Mean age at diagnosis of was 57.5 (range 43–72, median 59) years. Primary surgery in all cases was at least total abdominal hysterectomy and bilateral salpingo-oophorectomy. Original stage of the endometrial carcinoma was I: 6 patients (54.5%), II: 3 (27.3%), III: 1 (9.1%) and unknown: 1 (9.1%). Post-hysterectomy adjuvant therapy was given to seven patients and included external pelvic radiotherapy—3 patients, external pelvic radiotherapy and brachytherapy—2, chemotherapy and external pelvic radiotherapy—1, and hormone therapy—1. In all cases, the diagnosis of splenic metastasis was metachronous in relation to the diagnosis of endometrial carcinoma. Mean interval between the diagnoses of endometrial carcinoma and splenic metastasis was 40.7 (range 11–120, median 28) months. Five patients (45.4%) presented with left hypochondrial pain and had clinically palpable splenomegaly [15–17, 20, 21], two (18.2%) were asymptomatic but had clinically palpable splenomegaly [14, 22], and one (9.1%) presented with vaginal bleeding due to recurrence at the vaginal wall but had no left hypochondrial pain and no clinically palpable splenomegaly [19]. In these eight patients (72.7%), who were symptomatic and/or had clinically palpable splenomegaly, imaging studies confirmed a splenic mass. In the remaining three patients (27.3%) who were asymptomatic and had no clinically palpable splenomegaly, splenic mass was detected incidentally by routine follow-up imaging studies ([18, 23], this case). Two patients (18.2%) had biopsy of the splenic mass confirming splenic metastasis from endometrial carcinoma ([16], this case). Splenic metastasis was solitary in nine patients (81.8%) [14–18, 20–23], associated with pelvic recurrence in one patient [19], and solitary in the peritoneal cavity but associated with few lung metastases in one patient (this case). In all patients, splenectomy was performed and the splenic metastasis was limited to the splenic parenchyma without involvement of the splenic capsule. Treatment after splenectomy was recorded in seven patients and included chemotherapy in three patients ([19, 21], this case), oral progestin—2 [15, 22], irradiation to splenic bed—1 [14] and irradiation to splenic bed and oral progestin—1 [17]. Follow-up after splenectomy ranged from 6 to 46 months and at the end follow-up, six patients (54.5%) were alive without disease, one (9.1%) was alive with disease, three (27.3%) died of disease and in one (9.1%) the outcome was not recorded.

Splenic metastasis from endometrial carcinoma is usually solitary and limited to the splenic parenchyma. This affirms the notion of endometrial carcinoma metastasizing to the spleen predominantly by the hematogenous route [6, 9]. This is in contrast to ovarian carcinoma that metastasizes to the spleen mostly by transperitoneal spread and, thus, splenic metastasis from ovarian carcinoma is more often part of a disseminated disease rather than solitary splenic metastasis [6, 9]. While stage III is the most common original stage of disease in patients with splenic metastasis from ovarian carcinoma, the predominant original stage of disease in patients with splenic metastasis from endometrial carcinoma is stage I (54.5%) followed by stage II (27.3%).

In one-third of the patients, splenic metastasis from endometrial carcinoma did not elicit left hypochondrial pain and/or clinically palpable splenomegaly and was detected incidentally by routine follow-up imaging studies. In all patients, splenic metastasis was metachronous in relation to the diagnosis of endometrial carcinoma and the interval between the diagnoses of endometrial carcinoma and splenic metastasis was quite prolonged. This suggests that follow-up with periodic clinical examinations and imaging studies is required for more than 5 years after initial treatment of endometrial carcinoma.

In terms of management, splenectomy was performed in all patients. In the current case, we were reluctant initially to offer splenectomy in the presence of lung metastasis. However, splenectomy was performed eventually because of substantial growth of the splenic metastasis. Splenectomy for splenic metastasis appears to be justified (1) to avoid potential complications of splenic metastasis such as splenic rupture, splenic vein thrombosis, and painful splenomegaly, (2) to circumvent splenic metastasis being a source of secondary metastatic disease and (3) to provide the potential for cure or extended survival [2–4].

In conclusion, splenic metastasis from endometrial carcinoma is rare. It is usually solitary splenic metastasis limited to the splenic parenchyma. Splenectomy seems to be appropriate treatment. Since patients with splenic metastasis may be asymptomatic and the interval between

Table 1 Details of published cases of splenic metastasis from endometrial carcinoma

Author	Age[a]	Endometrial carcinoma: stage and treatment	Splenic metastasis: interval from hysterectomy, symptoms, treatment and findings	Follow-up and outcome after splenectomy
Kopacz et al. [13][b]				
Klein et al. [14]	66	IAG2, TAH + BSO, pelvic RT and BT	20 months, asymptomatic, splenomegaly, US showed 8-cm splenic mass, splenectomy, RT to splenic bed	31 months, abdominal carcinomatosis, intestinal obstruction, DOD
Jorgensen and Chrintz [15]	59	IAG3, TAH + BSO	11 months, left hypochondrial pain, splenomegaly, splenectomy (spleen measured 20 × 14 × 8 cm and weighted 2,050 g), oral progestin (MPA)	10 months, involvement of colon, DOD
Gilks et al. [16]	72	IBG2, TAH + BSO	33 months, left hypochondrial pain, splenomegaly, CT showed 10-cm splenic mass, FNAB revealed G3 carcinoma, splenectomy (spleen weighed 867 g and contained a 10-cm tumor)	6 months, abdominal carcinomatosis, abdominal RT, DOD
Arend et al. [17]	62	IB, TAH + BSO, pelvic RT	12 months, left hypochondrial pain, splenomegaly, splenectomy (spleen measured 17 × 16 × 7 cm, weighted 750 g and contained a 10 × 10 × 7-cm necrotic tumor), oral progestin (MPA) and RT to splenic bed	6 months, intra-abdominal metastasis, chemotherapy (CCb), AWD
Hamy et al. [18]	47	III, TAH + BSO, chemotherapy (CAP), pelvic RT (3,000 cGy)	73 months, asymptomatic, routine US and CT detected a splenic mass, splenectomy	28 months, NED
Giuliani et al. [19]	55	IG2, TAH + BSO + BPLND	28 months, recurrence at vaginal vault, CT showed 5-cm pelvic mass and 3-cm splenic mass, pelvic RT and BT. 3 months later, CT showed disappearance of pelvic mass but progression of splenic mass. 2 months later, splenectomy (spleen measured 18 × 10 × 6 cm and contained a 6-cm tumor), chemotherapy (ND)	12 months, NED
Agha-Mohammadi and Calne [20]	62	IIG1, RH + BSO + BPLND	72 months, left upper abdominal pain, splenomegaly, CT confirmed splenomegaly (sized 21 cm), splenecomy	Not recorded
Gogas et al. [21]	49	IBG2, TAH + BSO, pelvic RT	43 months, left hypochondrial pain, splenomegaly, CT showed splenic mass, splenectomy (spleen measured 21 × 12 × 8.5 cm and contained a 7.5 × 7 × 6.5-cm tumor), chemotherapy (AP × 6)	46 months, NED
Hadjileontis et al. [22]	43	TAH + BSO, hormone therapy (ND)	120 months, splenomegaly, CT showed a 5-cm splenic mass, splenectomy, hormone therapy (ND)	NED, follow-up time not recorded
Takahashi et al. [23]	60	II, TAH + BSO, pelvic RT	18 months, asymptomatic, US, CT and MRI showed splenic tumor, hand-assisted laparoscopic splenectomy + resection of part of stomach wall, (spleen contained 6-cm tumor)	18 months, NED
Piura et al. (this case)	58	IIBG2, TAH + BSO + BPLND, pelvic RT and BT	18 months, asymptomatic, PET revealed splenic tumor, CT-guided biopsy confirmed splenic metastases, chemotherapy (CAP × 6). 16 months later, CT showed progression of splenic mass (9.1 × 7.3 cm), splenectomy (spleen measured 13 × 12 × 7 cm, weighted 408 g and contained a 10 × 8 × 6-cm tumor), chemotherapy (Tax)	6 months, NED

TAH total abdominal hysterectomy, *RH* radical hysterectomy, *BSO* bilateral salpingo-oophorectomy, *BPLND* bilateral pelvic lymph node dissection, *RT* radiotherapy, *BT* brachytherapy, *US* ultrasound, *MPA* medroxyprogesterone acetate, *DOD* died of disease, *ND* not detailed, *C* cyclophosphamide, *A* adriamycin (doxorubicin), *P* cisplatin, *Cb* carboplain, *Tax* paclitaxel, *CT* computerized tomography, *MRI* magnetic resonance imaging, *PET* positron emission tomography, *NED* no evidence of disease, *FNAB* fine needle aspiration biopsy

[a] Age in years at the time of diagnosis of endometrial carcinoma

[b] Details were not available

the diagnoses of endometrial carcinoma and splenic metastasis may be prolonged, careful and extended follow-up after primary treatment of endometrial carcinoma is warranted.

Conflict of interest statement We declare that we have no conflict of interest.

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