Solitary Gastric Metastasis from a Stage IA Serous Ovarian Carcinoma: A Case Report with Literature Review

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Abstract

Gastric metastasis from ovarian cancer is exceptionally rare and generally occurs in advanced stages. A 71-year-old woman presented with a solitary gastric submucosal mass 8 years after the diagnosis of a stage IA ovarian serous adenocarcinoma. Endoscopy showed a tumor covered with normal gastric mucosa. Initially, a gastrointestinal stromal tumor was suspected, but biopsy revealed a histology of invasive micropapillary carcinoma, similar to the histological findings of the previously resected ovarian tumor. Clinicians should consider that in patients with a submucosal tumor and a history of ovarian cancer, gastric lesions may be secondary metastases from ovarian cancer.

Key words: ovarian cancer, serous carcinoma, gastric metastasis, submucosal tumor, micropapillary carcinoma, gastrointestinal stromal tumor

(Intern Med 56: 915-919, 2017) (DOI: 10.2169/internalmedicine.56.7784)

Introduction

Metastatic disease involving the stomach is a rare event. The lifetime prevalence is only 0.7-1.7% in patients with known malignancies (1). Common sources are breast cancer, lung cancer, esophageal cancer, renal cell carcinoma, and malignant melanoma (1, 2). Gastric metastasis from ovarian cancer is exceptionally rare. Only 16 cases have been reported in the English literature. We herein present the 17th case of gastric metastasis from ovarian cancer, in which a serous carcinoma of the ovary, FIGO stage IA, developed a solitary intramural metastasis 8 years later. A literature review indicated that all cases of ovarian cancer that developed a metastasis to the stomach were in stages higher than IIB, except for one case of stage IA endometrioid adenocarcinoma. Gastric metastases from stage IA ovarian serous carcinoma have never been reported.

Case Report

A 71-year-old asymptomatic woman was seen for the evaluation of a gastric submucosal tumor. Eight years earlier, she had undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy with omentectomy for ovarian cancer. Histologically, the tumor was limited to the left ovary without metastasis, and serous adenocarcinoma, grade 3 (G3), FIGO stage IA was diagnosed. Carboplatin and docetaxel were given, but she developed dyspnea, so chemotherapy was discontinued after one cycle. Afterwards, she was followed up every 6 months and remained disease-free for 8 years, when her serum CA125 and CA72-4 levels increased to 122 U/mL (reference range: <35 U/mL) and 25.2 U/mL (reference range: <8.0 U/mL), respectively. Computed tomography (CT) of the chest to the pelvis revealed a 29 × 24 mm submucosal mass in the gastric antrum and swelling of the perigastric and paraaortic lymph nodes. Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography

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Received for publication May 31, 2016; Accepted for publication August 3, 2016
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(PET) combined with CT (18F-FDG PET/CT) showed intense FDG uptake in the gastric mass, perigastric lymph nodes, paraaortic lymph nodes, and left supraclavicular lymph nodes (Fig. 1). Upper gastrointestinal endoscopy revealed a submucosal tumor covered with normal gastric mucosa (Fig. 2). Clinical differential diagnoses included malignant gastrointestinal stromal tumor (GIST) with metastases, malignant lymphoma, and gastric recurrence from ovarian carcinoma. She underwent gastric boring biopsy, the specimen from which revealed a poorly differentiated adenocarcinoma with a micropapillary component (Fig. 3A). Initially, invasive micropapillary carcinoma (IMPC) of the stomach was considered; however, because of her history of ovarian cancer, the specimen was compared to the previous ovarian carcinoma. The tumor was confirmed as a metastatic serous adenocarcinoma from the ovary (Fig. 3B). Immunohistochemically, both the gastric tumor and the ovarian tumor were positive for CA125, cytokeratin 7 (CK7), Wilms’ tumor 1 (WT1), estrogen receptor (ER), PAX8, and p53, whereas they were negative for progesterone receptor (PR) and cytokeratin 20 (CK20). The expression of p53 was detected in >90% of cells in both tumors. The patient received 6 cycles of carboplatin and pegylated liposomal doxorubicin and is currently in complete remission 8 months after gastric biopsy.

Discussion

We herein describe the case of a solitary gastric recurrence 8 years after the initial ovarian carcinoma was diagnosed. Although several lymph nodes appeared to be involved, no obvious metastasis to other organs or the peritoneal surface was identified. There has been no previous report in which a stage IA serous ovarian carcinoma metastasized to the stomach. The reasons for this recurrence may have been insufficient initial chemotherapy due to adverse effects in this patient, and the absence of lymph node sampling at the time of ovarian surgery, because there were no findings suggestive of lymph node metastasis by imaging and intraoperative findings.

Ovarian carcinoma usually metastasizes along the peritoneal surface. About 31-38% of ovarian cancer patients develop distant metastasis during the course of the disease, of which 8-18% are synchronous metastases (3, 4). The most common metastatic sites are the pleura, liver, lung, distant lymph nodes, and, less commonly, the central nervous system, skin, pericardium, bone, spleen, and breast (3, 4). Significant risk factors for distant metastasis development are higher stage, higher histological grade, and lymph node involvement at the time of the initial diagnosis. The median interval to metastasis is 44 months, and the median survival after distant metastasis is 12-144 months (median, 39 months), similar to the interval for overall distant metastases. Asymptomatic patients predominated (10 patients), and the other 7 patients had some symptoms, such as abdominal pain, discomfort, and dyspepsia (Table). Gastric tumors had ulceration in nine cases and no ulceration in seven. In 11 cases, the serum CA125 levels were checked, and all showed elevated levels. Because the information provided in the case reports is limited and varied, survival after documentation of gastric metastasis is not conclusive at this time.

Gastric metastasis without peritoneal seeding suggests metastasis through a hematogenous route or lymphatic spread. Despite the swelling of the paraaortic and perigastric lymph nodes, swelling of the pelvic lymph nodes was not observed in this patient. This finding supports the idea that gastric metastasis occurred through the paraaortic lymph node route (6).

Clinically, gastric metastases from ovarian cancer mimic GISTs (10, 11, 19). A GIST was suspected in the present case based on the imaging and endoscopic findings. Biopsy and pathological investigation are necessary to confirm gastric tumors as metastases. Histologically, the differential diagnosis from gastric adenocarcinoma, especially IMPC, is important. The present case also showed micropapillary architecture on histology. Our literature search did not reveal any IMPC cases covered with normal gastric mucosa without ulceration. Although a few intramural gastric adenocarcinomas have arisen from the diverticulum or ectopic pancreatic tissue (21, 22), the tumor cells are of the gastric or pancreaticobiliary epithelial phenotype. Clinical information and comparison with the previous ovarian cancer histology are important. In difficult cases, immunohistochemistry would further help to differentiate a metastasis from a primary gastric tumor. Specifically, a combination of PAX8, WT1, ER,
Figure 1. Computed tomography (CT) images combined with fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET/CT). (A) CT revealed a 29×24 mm mass in the gastric antrum (arrows) with perigastric and paraaortic lymph node swelling (arrow heads). (B) FDG-PET/CT showed intense FDG uptake in the corresponding mass and swellings.

Figure 2. Upper gastrointestinal endoscopy revealed a submucosal tumor covered with smooth mucosa in the gastric antrum.

Figure 3. Light microscopy of gastric biopsy and ovarian tumor specimens. (A) Gastric biopsy revealed an adenocarcinoma with papillary and micropapillary growth patterns (Hematoxylin and Eosin (H&E) staining, original magnification ×20). With higher magnification, the tumor cells showed high nuclear grades with high nuclear/cytoplasmic ratios (inset, H&E staining, original magnification ×40). (B) Histology of the previous ovarian tumor showed a similar growth pattern to that of the gastric tumor (H&E staining, original magnification ×20, inset ×40).
Table. Summary of Clinicopathological Findings of Gastric Metastases from Ovarian Carcinomas.

| Reference | Age (years) | Histology  | Stage | Therapy for primary tumor | Recurrent organs | Duration to gastric recurrence (months) | Symptoms at gastric recurrence | Ulcer | Serum CA125 at gastric recurrence | Immuno-histochemistry | Follow-up after gastric metastasis |
|-----------|-------------|------------|-------|----------------------------|------------------|----------------------------------------|--------------------------------|-------|-------------------------------|----------------------|--------------------------|
| 1         | 1           | Serous     | ≥ IIIB| Tumor reduction + chemotherapy | Stomach, pelvic mass | 20                       | Asymptomatic - | NA       | NA                             | NA                   | NA                      |
| 2         | 6           | Endometrioid | IA    | TAHBSO + LN + omentectomy + chemotherapy | Stomach, paraaortic LNs | 12                       | Asymptomatic - | high    | NA                             | NA                   | 6 months, DOD          |
| 3         | 7           | Serous, G3 | IIIC  | Surgery + chemotherapy | Stomach, lung, liver | 15                       | Abdominal discomfort + | high    | CA125-, CK-AE1/AE3+, CK7+, CK20+, vimentin-, CD117-, CEA- | NA                   | NA                      |
| 4         | 8           | Poorly differentiated carcinoma | NA    | Surgery + chemotherapy | Stomach | 84                       | Belching, reflux, discomfort + | high    | NA                             | CK-AE1/ AE3+, CK7+, CK20, ER, PR- | 12 months, NED         |
| 5         | 9           | Serous, G3 | IIIC  | TAH-BSO + bowel nodule resection + chemotherapy | Stomach, perigastric LNs | 13                       | Asymptomatic | NA      | high                           | CK-AE1/ AE3+, CK7+, WT1+, CK20, ER, PR- | 12 months, NED         |
| 6         | 10          | Serous     | IV    | TAHBSO + omentectomy + chemotherapy | Stomach, right adrenal gland, superiorvphrenic mass | 0                       | Epigastric pain, fullness | high    | NA                             | NA                   | 18 months, NED          |
| 7         | 11          | Serous     | ≥ IIB | TAH-BSO + LN + resection of colon metastasis + chemotherapy | Stomach | 42                       | Asymptomatic - | high    | NA                             | NA                   | NA                      |
| 8         | 12          | Serous     | IV    | NA | Stomach | 0                       | Dyspepsia + | NA       | NA                             | NA                   | NA                      |
| 9         | 13          | Serous, G3 | NA    | Surgery + chemotherapy | Stomach | 144                      | Asymptomatic + | high    | CA125+, CK+, WT1+, CK20, PR, CDX2- | 5 months, NED         |
| 10        | 14          | Serous     | III   | TAHBSO + omentectomy + chemotherapy | Stomach, spleen, peritoneum | 60                       | Fatigue, melena - | NA      | ER+, PR+, p53+             | NA                   | NA                      |
| 11        | 15          | Serous, G3 | IV    | TAHBSO + LN + omentectomy + chemotherapy | Stomach, hepatoduodenal LN | 0                       | Pain, perforation + | high    | CA125+, WT1+, CK20       | NA                   | NA                      |
| 12        | 16          | Serous     | III   | TAHBSO + LN + omentectomy + chemotherapy | Stomach, peritoneum, omentum, pelvis, iliac perigastric LN | 36                       | Asymptomatic + | NA      | WT1+, GCDFP-15+, CD117 | NA                   | NA                      |
| 13        | 17          | Serous     | NA    | TAHBSO + LN + chemotherapy | Stomach | 72                       | Asymptomatic + | NA      | CA125+, ER+, PR+           | 9 months, DOD        |
| 14        | 18          | Serous     | NA    | Tumor reduction + chemotherapy | Stomach, rectum, lymph nodes (paraaoartic, peripancreatic, perigastric, cecum) | 84                       | Epigastric pain, dyspepsia + | NA       | NA                             | 94 months, DOD        |
| 15        | 19          | Serous     | III   | TAHBSO + LN + omentectomy + chemotherapy | Stomach, perigastric LNs | 20                       | Asymptomatic - | high    | WT1+, ER+, PR+, CK20        | NA                   | NA                      |
| 16        | 20          | Serous     | NA    | Surgery | Stomach, pancreas | 25                       | Asymptomatic - | high    | CA125+, CK7+, ER, PR, CD56+, CK20, CDX2- | NA                   | NA                      |
| 17        | Present case | Serous, G3 | A     | TAHBSO + omentectomy + chemotherapy | Stomach, lymph nodes (paraaoartic, perigastric, left suprACLavicle) | 96                       | Asymptomatic - | high    | CA125+, CK7+, WT1+, ER+, p53+, PR+, CK20       | 8 months, NED        |

BSO: bilateral salpingo-oophorectomy, CK: cytokeratin, DOD: died of disease, ER: estrogen receptor, LN: lymphadenectomy, LNs: lymph nodes, NA: not available, NED: no evidence of disease, PR: progesterone receptor, TAH: total abdominal hysterectomy, WT1: Wilms' tumor 1
CEA, and CDX2 generally resolves this issue, since PAX8, WT1, and ER are highly sensitive to ovarian adenocarcinoma, whereas CEA and CDX2 are sensitive to gastric adenocarcinoma (23-25).

In conclusion, although gastric metastasis from ovarian carcinoma is exceptionally rare, clinicians should nevertheless be aware that, in patients with a submucosal tumor and a history of ovarian cancer, gastric lesions may be secondary metastases from the ovarian cancer. For gastric metastatic lesions, complete cytoreductive surgery is recommended when possible; however, at present, it is not clear which factors most influence survival after gastric metastasis.

The authors state that they have no Conflict of Interest (COI).

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