



Rare Metastasis of Esophageal Adenocarcinoma to the Female Reproductive Tract

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ABSTRACT

Esophageal cancer is common and typically metastasizes to the liver, lung, and lymph nodes. Reproductive tract metastases are extremely rare. In fact, to the best of our knowledge, only 2 cases of esophageal carcinoma metastasizing to the ovaries have been reported. Thus, increased recognition of unusual metastatic sites is necessary to decrease the morbidity and mortality from distant esophageal metastases. We present a case of ovarian and fallopian tube metastases from esophageal adenocarcinoma in a 59-year-old woman.

KEYWORDS: esophageal cancer; ovarian; metastasis

INTRODUCTION

Esophageal cancer has 2 main subtypes, squamous cell carcinoma and adenocarcinoma. Prognosis is poor and is the sixth highest cause of deaths related to cancer.¹ The most common metastatic sites include the liver, lungs, and lymph nodes.² Distant metastasis occurs at a rate of 25%.³ Reports indicating uncommon metastatic sites include maxillary bone,⁴ skeletal muscle,⁵ subcutaneous tissue,⁶ and the oral cavity.⁷ However, scant literature has been published regarding metastasis to the female reproductive tract, with only 2 published cases demonstrating esophageal metastasis to the ovaries.^{8,9} Early detection may prevent unproductive treatment and improve prognosis.² We report a case of esophageal adenocarcinoma metastasizing to the bilateral ovaries and 1 fallopian tube.

CASE REPORT

A 59-year-old White woman presented after dysphagia and choking with a globus sensation, prompting gastroenterology evaluation. Upper endoscopy (EGD) revealed a malignant appearing mass in the midesophageal to distal esophageal, and pathology demonstrated esophageal adenocarcinoma. Staging endoscopic ultrasound revealed cT2N1 disease. Subsequent cross-sectional imaging did not reveal any metastatic disease. She received trimodality therapy with chemotherapy, radiation, and subsequent Ivor Lewis esophagectomy, for cancer resection. Lymphadenectomy evaluated for malignancy. Pyloroplasty and jejunostomy were performed for nutrition. Splenectomy was performed because of intraoperative bleeding. Pathology revealed moderately differentiated invasive adenocarcinoma extending into the adventitia, 17 lymph nodes negative for carcinoma and 1 lymph node with therapy effect. Three months after the esophagectomy, her EGD revealed normal, healthy-appearing anastomosis.

One year after surgery, she presented to the hospital with a few months of subacute right flank and pelvic pain. She endorsed nausea, vomiting, and constipation. Computed tomography showed esophageal thickening, left hydronephrosis, and adnexal soft-tissue densities. Laboratory tests revealed leukocytosis and lactic acidosis. Blood and urine cultures were obtained, and antibiotic treatment was started for sepsis. An EGD demonstrated an esophageal ulcer at the level of esophagogastric anastomosis, and biopsies were consistent with epithelial atypia in the presence of inflammation without evidence of intestinal metaplasia.

A follow-up transvaginal ultrasound was notable for a suspicious-appearing right adnexal complex cystic mass. On further workup, CA-125 returned elevated at 132, whereas CA19-9 and CEA were 28 and 2.7, respectively. Paracentesis and pleurocentesis were both negative for malignant cells. Repeat transvaginal ultrasound was performed and revealed an irregular multilobulated mass in the left adnexa, pelvic ascites, and a thickened endometrium. A laparotomy was performed for improved visualization of ovaries and fallopian tubes, showing enlargement and dense deposits. The peritoneum and pelvis were thickened, concerning for malignancy. The intraoperative decision was made to perform a bilateral salpingo-oophorectomy, cholecystectomy, and lysis of adhesions. Intraoperative pathology revealed adenocarcinoma of unknown origin in the left fallopian tube and ovary. Metastatic cancer was suspected from mesenteric and peritoneal appearance. Final pathology revealed metastatic adenocarcinoma consistent with esophageal primary involving the mesentery, left and right ovaries, and right fallopian tube. Pathology was supported by immunohistochemical staining, which revealed reactivity for CDX2, AE1/AE3, CK7, and villin. After her diagnosis, she pursued hospice care.

DISCUSSION

It is well known that esophageal cancer frequently metastasizes to distant sites.³ Recent literature has shown metastases to unusual sites.⁴⁻⁷ Shaheen et al¹⁰ found the most common unexpected metastatic site group was the head and neck, and of specific organs, skin was most common. Within abdominopelvic, the kidneys, pancreas, and spleen were most common. Two penile and 2 spermatic cord metastatic cases were noted, but not 1 metastasis in any female reproductive organ was noted, magnifying this case's uniqueness. Versteegen et al² found that of evaluated cases, 56% had liver and 50% had lung metastases, but only 1.1% had female reproductive organ metastases. Surveillance, Epidemiology, and End Results study assessing distant metastatic esophageal sites in 9,934 individuals emphasizes the exceedingly rare nature of reproductive organ metastasis. It showed 15.6% metastases to the liver, without any in the female reproductive organs.¹¹

One case study reported metastasis of esophageal adenocarcinoma to the ovaries as a Krukenberg tumor in a 41-year-old woman, with immunohistochemistry positive staining for CDX2 and CK20.⁸ A second case study was a 28-year-old woman with adenocarcinoma of the gastroesophageal junction who presented with abdominal swelling that appeared to be an inguinal hernia. However, she was instead found to have advanced esophageal disease and a Krukenberg tumor.⁹

The pathogenesis of metastasis to the ovary is unknown. Shaheen et al¹⁰ hypothesize that uncommon metastases occur through an arterial route, supported by the presence of the aortoesophageal ligament and the esophagus' multiple arterial

sources. This route may explain metastases that are isolated and metachronous without primary tumor recurrence. This is supported by Gray's¹² summary of studies showing higher levels of circulating tumor cells in arterial vs venous blood. In our case, the patient had distant metastasis in her female reproductive organs metachronous with her initial adenocarcinoma and without recurrence of primary tumor.¹⁰ The implications of arterial metastasis include increased organ susceptibility, which may modify screenings and treatment. This is relevant in this case because it emphasizes the importance of thorough evaluation even without recurrence of primary cancer.

In the United States in 2020, there were more than 50,000 individuals with esophageal cancer. Annually, 4.2 per 100,000 men and women are newly diagnosed with esophageal cancer.¹³ For local esophageal cancer, the 5-year survival rate is 39%. However, it decreases significantly to 4% with distant metastasis.¹⁴ For patients with advanced metastatic disease, treatment depends on performance status. For patients with a Karnofsky rating of >60%, human epidermal growth factor 2 neu molecular testing should be performed, and if positive, certain chemotherapeutic agents may be considered. If Karnofsky rating is <60%, palliative care is recommended.¹⁵

With the incidence of esophageal cancer rising,¹⁶ this case emphasizes the importance of recognizing unusual metastatic sites. It is vital for patient prognosis and to prevent fruitless localized treatment. Furthermore, this case highlights the importance of continued monitoring with different modalities and surveillance with serial imaging to catch recurrence early. Numerous disciplines contributed to diagnosing this patient, underscoring the necessity of collaboration. Documentation of this case, and all rare cases, is integral for advancement in finding distant metastases earlier, so treatment and outcomes are maximized.

DISCLOSURES

Author contribution: The authors contributed to the conception or design of the work and assisted in drafting, reviewing, and editing it. All authors approve of the final product and agree to be accountable for all aspects of the work. Each author had additional roles, too. A. Garcia communicated between all authors. N. Morris performed the literature review and background for the report. P. Francis provided expert oversight and opinion as a Gastroenterology fellow. D. Baik also provided expert oversight and opinion as a Gastroenterology attending and is the article guarantor.

Financial disclosure: None to report.

Informed consent could not be obtained for this case report. All identifying information has been removed.

Received July 9, 2023; Accepted November 14, 2023

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