CASE REPORT

Metachronous Synchronous Sternal and Colonic Metastasis with Asymptomatic Colo-colic Fistula from Carcinoma Ovary Rare Presentation of Ovarian Cancer

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Received: 6 November 2015 / Accepted: 9 November 2016 / Published online: 3 December 2016
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Abstract Ovarian cancer is one of the most common gynecological cancers worldwide. It is the third leading cause of cancer among women in India. Metastatic disease to the visceral organs from ovarian cancer occurs as a terminal event in the natural history of the disease. In particular, spread to the bone and large bowel is infrequently described. The risk of distant metastasis increases in a recurrent setting. We describe a case of a 77-year-old lady, who was diagnosed for ovarian carcinoma in 2007 and underwent primary cytoreductive surgery, stage IIIC. She presented to us with asymptomatic rising cancer antigen (CA) 125 levels during follow-up. On evaluation she was found to have sternal and colonic deposits. She underwent left hemicolectomy and biopsy of sternal deposit. Histopathology revealed metastasis from the carcinoma ovary to the colon and sternum. This case report highlights the rare synchronous metastatic disease in a metachronous setting from ovarian carcinoma.

Keywords Fistula · Metastasis · Ovarian carcinoma · Sternum · Synchronous

Introduction

Ovarian cancer is the third leading cause of cancer among women in India. The age-adjusted incidence rate is between 5.4 and 8.0 per 100,000 population with incidence varying in different parts of the country [1]. In a retrospective study by

Hussain et al., ovarian cancer constituted 16.11% of all cancers among females [2]. In the setting of recurrent cancers, risk of distant metastasis increases. Cormio et al. observed that 50 out of 162 ovarian carcinoma patients had distant metastases [3]. Thirteen of them (8%) had distant metastases at the time of diagnosis while 37 (22%) at the time of recurrent or progressive disease. We describe a case of carcinoma ovary with synchronous metastasis to large bowel and metachronous osseous metastasis. A brief review of literature follows.

Case Details

A 77-year-old female with positive family history of ovarian carcinoma was diagnosed with ovarian cancer in 2007. She underwent primary cytoreductive surgery. Intra-operative findings included bilateral ovarian tumors, ascites, and peritoneal deposits. Histopathology report revealed ovarian adenocarcinoma stage IIIC. She received adjuvant chemotherapy with 6 cycles of paclitaxel and cisplatin. Patient was on a regular follow-up and was asymptomatic till December 2013 when cancer antigen (CA) 125 showed increasing titres. She was investigated and found to have sternal metastasis (Fig. 1a) which was diagnosed on CT chest (Fig. 1b).

A PET-CT scan done showed an osteolytic lesion in the sternum and medial end of the right clavicle with large pre-sternal and anterior mediastinal soft tissue components measuring 15.5 × 10.3 × 6.6 cm in antero-posterior dimension with a pathologic fracture of the body of the sternum (SUV, 6.8) (Fig. 1c) and a 6.5 × 1.5 cm metabolically active (SUV, 7.5) circumferential wall thickening of the splenic flexure of the colon causing moderate luminal narrowing with pericolic metastatic lymphadenopathy (Fig. 1d). Colonoscopy revealed a proliferative growth in the splenic flexure (Fig. 1e), biopsy of

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Fig. 1 **a** Clinical photograph of sternal deposit measuring 3 × 3 cm including manubrium sterni and upper part of the body of sternum. **b** Coronal section of CT scan of chest shows sternal deposit with bone destruction. **c** Coronal section of PET-CT demonstrating isolated increased uptake in the sternum (SUV, 6.8). **d** Axial PET-CT image demonstrating metabolically increased uptake in the splenic flexure of colon (SUV, 7.5). **e** Colonoscopic view demonstrating intra-luminal mass occupying upper third of the colonic lumen. **f** Immunohistochemistry showing CK positivity (40×). **g** Operative specimen of segment of colon demonstrating colo-colic fistula (hemostat within fistula)

which demonstrated adenocarcinoma. Biopsy of the sternal deposit revealed metastatic adenocarcinomatous deposits. Immunohistochemistry was positive for CA 125, cytokeratin (CK), and CK7 focally (Fig. 1f) and negative for synaptophysin, TTF-1, CD 56, and neuron specific enolase (NSE).

Since patient had an isolated metastasis only to sternum with an asymptomatic partially obstructive growth in the left colon, decision to operate on the left colon was taken. She underwent segmental resection of the colon. Intra-operative findings included growth in the splenic flexure with colo-colic fistula but no peritoneal deposits, ascites, or serosal nodularity. The rest of the abdomen was normal. The cut section of specimen revealed an ulcerated tumor with a fistulous communication with adjacent bowel segment (Fig. 1g). Another solid nodule was seen close to ulcer. Histopathological examination showed metastatic poorly differentiated ovarian adenocarcinoma involving full thickness of the colon (with perforation) with lymphovascular and perineural invasion, free margins, and nodal spread. Immunohistochemistry revealed that the cells were positive for CA 125 (diffuse staining) and negative for CDX2, synaptophysin, and chromogranin.

She is presently undergoing a palliative radiation to the sternum followed by platinum based chemotherapy.

Discussion

Ovarian cancers in their natural history uncommonly present with distant hematogenous or lymphogenous metastases. Organs such as the liver, pleura, lungs, skin, brain, and spleen can be the site of such distant metastases. In an autopsy study of 100 cases with ovarian carcinoma, bowel and bone metastases were present in 52–55 and 11%, respectively [5].

In particular, bone metastasis is exceedingly rare [4]. In a study by Karim et al. [6], based on autopsy data, the authors demonstrate that osseous metastases from ovarian cancers are significantly higher than clinically appreciated and often correlate with advanced stage and grade of tumor. In another study [7], metastasis to bones from ovarian cancer was seen in approximately 0.1–0.12% patients. Osseous spread can occur by direct extension, trans-peritoneal seeding of cells, hematogenous, or by lymphatic dissemination. The vertebral venous system forms an important route through which cancer cells spread to the bone. Furthermore, lung or lymphatic metastases often predict bone metastasis [4].

Bone metastases can result in severe pain, pathological fracture, or paraplegia [4]. These lesions are often focal and osteolytic; however, they can rarely be osteoblastic. Vertebral bodies are the most common site of spread, followed by the ribs, clavicle, skull, and femur [8]. Involvement of the sternum from the carcinoma ovary is uncommon and can occur as a result of direct invasion by the metastatic (enlarged) internal mammary nodes or by hematogenous route. Another unique feature is that these sternal metastatic deposits can be solitary in most cases thus making them surgically resectable [9].

Epithelial ovarian carcinomas namely serous cystadenocarcinomas (15%) are the most common histological type associated with bone metastases followed by

Table 1 Review of studies with bony metastasis from ovarian carcinoma

Study, year	Bone metastases	Incidence	Histology	Site
Zhang et al. [4], 2013	26/2189	0.82%	19 epithelial (13 serous papillary; 6 clear cells), 7 germ cells (3 dysgerminoma; 4 yolk sac tumor).	Cervical vertebra (12), lumbar vertebra (10), pelvis (8), thoracic vertebra (7), limbs (5), ribs (1), <i>sternum</i> (2)
Abdul-Karim et al. [6], 1990	7/49 out of 113	6.19%	High-grade cancers	Thoracic vertebra, clavicle, axial skeleton
Tiwari A et al. [7], 2007	1	NA	Mucinous papillary	L2 vertebra
Kumar L et al. [11], 1992	4/103	3.88%	2 serous, 1 mucinous, 1 mixed germ cell	Vertebra, pelvic bones, skull
Chen et al. [9], 2009	1/90	1.1	Adenosarcoma with endometrioid adenocarcinoma	Vertebrae (T7 and L3)

NA not applicable

mucinous cystadenocarcinomas (12%) and endometrioid adenocarcinomas (10%) [8].

Treatment of bone metastasis from ovarian cancers includes chemotherapy, radiotherapy, and radionuclide therapy including bone strengthening agents [4]. For solitary sternal metastatic deposits, total sternectomy with reconstruction using mesh and regional flaps has been described [9].

The median survival after bone metastasis is generally poor; on an average, it is 7.5 months (range, 6–39 months) [10]. The time interval from diagnosis to appearance of bone metastases serves as a prognostic factor in ovarian cancer. Early onset osseous spread is a poor prognostic sign; however, late onset osseous spread does not influence the survival [11]. This has been highlighted in the present case where the patient presented 7 years after the primary tumor was diagnosed and treated.

Gastrointestinal involvement from ovarian cancers can occur either by invasion from the serosal aspect or involvement of the submucosal capillary network. Distinguishing between a colonic primary and metastasis from the ovary has both diagnostic and therapeutic implications since the type of adjuvant chemotherapy differs for each. Immunohistochemistry (IHC) is useful in this diagnosis. The combined expression of cytokeratin 7 and cytokeratin 20 (CK7/CK20) are the most widely used markers. Colorectal carcinomas are usually CK7 negative and CK20 positive, whereas ovarian carcinomas are usually CK7 positive and CK 20 negative. Unfortunately, these markers lack specificity for ovarian and intestinal epithelium, and overlapping results have been reported. CDX2 is a nuclear homeobox transcription factor that

belongs to the caudal-related family of CDX homeobox genes [12]. CDX2 is expressed in normal small and large intestinal epithelial cells, including absorptive, endocrine, and Paneth cells. Immunohistochemical studies have reported that CDX2 is a specific and sensitive marker for adenocarcinoma of the gastrointestinal tract, particularly colorectal adenocarcinoma where it is positive in 90% of the cases [13]. A fraction of metastatic ovarian adenocarcinomas can also have CDX2 positivity and a panel of IHC markers is most sensitive in diagnosis of ambiguous cases.

The most common operative finding in a case of ovarian metastasis to the colon is seromuscular involvement of the bowel wall and its mesentery. Pathologically, this is often superficial associated with mesenteric shortening and luminal narrowing. However, transmural invasion is rare. In our case, although the gross appearance of the bowel did not have this classical picture, since it lacked any serosal nodularity, the immunohistochemistry staining was positive for CA 125 and negative for CDX2 which is in favor of an ovarian metastasis. The peritoneal dissemination during the primary surgery most likely was the source of her colonic recurrence, which spread transmurally leading to a colo-colic fistula. The fistulous connection ensured that she remained asymptomatic in spite of an obstructive colonic lesion.

Surgery along with chemotherapy forms the mainstay of treatment. In a study by Wu et al. [14], resection of metastatic tumors of the bowel was done in 40 cases, out of which a repair of the perforated intestinal wall was done in 19 patients. Bowel resection was done in 22 cases and a colostomy was fashioned in 6 patients.

Table 2 Reported series of large bowel metastases/involvement from primary ovarian carcinoma

Author, year	Site	Histology	Treatment
Wu PC [14] (62 cases), 1989	Rectosigmoid		Sx+ CT ^a
Zigheboim I [13], 2004	Sigmoid colon	High-grade ovarian papillary serous carcinoma with areas of endometrioid adenocarcinoma	Sx ^b

^a Chemotherapy

^b Surgery

Table 1 shows studies of ovarian cancers with osseous metastasis and Table 2 shows studies of ovarian cancers with colonic metastasis.

Acknowledgments We would like to thank Dr. Kallur KG and Dr. Prashanth, Department of Nuclear Medicine, for the PET-CT photographs.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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