

## Case report

## BRCA-2 (+) high-grade serous fallopian tube cancer diagnosed as an isolated breast mass by mammography

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## ABSTRACT

Ovarian cancer typically presents at advanced stage with intra-abdominal metastases. Rarely, ovarian cancer presents with distant metastases with little to no intra-abdominal disease burden. The patient was a BRCA-2 germline mutation carrier diagnosed with a Stage IVB high-grade carcinoma of the fallopian tube following discovery of a right axillary breast mass on screening mammography. Pre-operative imaging was without evidence of metastatic disease in the abdomen or pelvis. She underwent surgical staging followed by adjuvant chemotherapy and maintenance poly-ADP ribose polymerase (PARP) inhibition. She is without evidence of disease 24 months following her surgical staging procedure. An isolated oligo metastasis in the axilla is a rare presentation of ovarian carcinoma. Extra-abdominal metastases can present a diagnostic challenge in ovarian cancer necessitating thorough pathologic and radiologic work-up, particularly in the absence of intra-abdominal disease.

## 1. Introduction

The diagnosis of ovarian cancer often occurs at a late stage with a large intra-abdominal disease burden. This occurs, in part, because of the vague nature of symptoms associated with ovarian cancer: abdominal pain, bloating, gastrointestinal symptoms, etc. Nearly 80% of high grade serous carcinomas, the most common ovarian carcinoma, are diagnosed at an advanced stage (Prat and Oncology FCoG, 2014). Distant metastases are less common, occurring in only 8% of patients at the time of diagnosis (Cormio et al., 2003). The breast is a relatively uncommon site of metastatic spread. Only 0.3–6.3% of malignant breast tumors originate from a solid tumor somewhere other than the breast (Antuono et al., 2018). Ovarian cancer metastasizes to the breast very rarely, in only 0.03–0.6% of cases (El Attrache et al., 2017).

We describe a clinical case of a patient with germline BRCA-2 mutation diagnosed with Stage IVB high grade serous carcinoma of the fallopian tube initially presenting as a breast mass on routine screening mammography with no pre-operative identified intra-abdominal disease burden. She underwent surgical staging followed by standard-of-care adjuvant chemotherapy and PARP inhibition due to BRCA 2 mutation status. She is currently without evidence of disease.

## 2. Case report

The patient is a 69-year-old with BRCA-2 germline mutation and past medical history of basal and squamous cell carcinomas of the skin who underwent routine digital screening mammography noting an enlarged, 9 mm (mm) right axillary lymph node. She subsequently underwent diagnostic mammography confirming a morphologically abnormal appearing right axillary lymph node at 10 o'clock, approximately 8.0 cm from the right nipple. Axillary needle core biopsy was performed and with the result of high grade metastatic carcinoma overall consistent with a Mullerian primary (Fig. 1). The presence of a high grade carcinoma within the axillary lymph node without a definitive breast mass on imaging at the time of biopsy, raised the suspicion of a primary other than the breast. Appropriate immunohistochemical work in an attempt to identify the primary site was performed on the biopsy tissue. Based on morphologic and immunohistochemical findings (positive: PAX-8, WT-1, estrogen-receptor; negative: progesterone receptor, GATA-3, SOX-10, mammaglobin, TTF-1, thyroglobulin, p40, chromogranin, SPT-24), a Mullerian primary was favored. Tumor markers were obtained as follows: CA-125 = 37, CA 19-9 = 11, CEA = 0.8. She was subsequently referred to gynecologic oncology for further management.

Computed-tomography (CT) of the chest, abdomen, and pelvis

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identified no evidence of metastatic disease in the chest, abdomen, or pelvis. Transvaginal ultrasound (TVUS) identified a normal uterus with a  $2.2 \times 1.4 \times 1.6$  cm (cm) heterogeneous mass along the anterior aspect of the cervix possibly representing a lower uterine fibroid. The right ovary was normal in size and appearance without abnormal vascular flow on Color Doppler imaging. The left ovary was not well visualized. Fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT demonstrated a focus of intense FDG uptake corresponding to a 1.7 cm nodule in the right axilla/lateral right breast tissue corresponding to known biopsy-proven metastatic carcinoma (Fig. 2). Two foci of intense increased FDG avidity were noted within the left greater than right pelvic sidewall without corresponding abnormalities on the CT. These were favored to represent excreted urine activity within bilateral ureters. The uterus and cervix showed homogenous mild FDG uptake without discrete focal abnormalities to suspect primary malignancy. No other areas of abnormal FDG activity to suspect primary or metastatic disease. As PET/CT is unable to identify microscopic pelvic disease, surgery was indicated to identify the primary site of disease.

Subsequently, she underwent an uncomplicated total laparoscopic hysterectomy, bilateral salpingo-oophorectomy, peritoneal biopsy of the bladder peritoneum, right diaphragm biopsy, omentectomy, and removal of the enlarged right axillary lymph node. Intra-operative findings were notable for nodularity along the bladder peritoneum on the left pelvic sidewall, bilateral fimbriated ends of the fallopian tubes, ovaries, and the right diaphragm. No other evidence of intra-abdominal disease was noted. Final pathology revealed a Stage IVB high grade serous carcinoma of the fallopian tube with disease present in the right axillary node, bladder peritoneum, bilateral ovaries, and omentum. The right diaphragm was negative for metastatic disease. She received standard-of-care adjuvant therapy including six cycles of carboplatin (AUC 6) and paclitaxel ( $175 \text{ mg/m}^2$ ). She underwent genetic testing and was found to have a germline BRCA-2 mutation. Following cytotoxic chemotherapy, she was started on maintenance PARP inhibitor therapy with olaparib 300 mg daily. She is currently without evidence of disease 24 months following her surgical staging procedure. With regard to her

breast cancer risk secondary to BRCA-2 germline mutation, she was referred to our institution's high-risk inherited cancer syndrome center and is being followed closely with annual mammograms and breast MRI without evidence of primary breast malignancy at present.

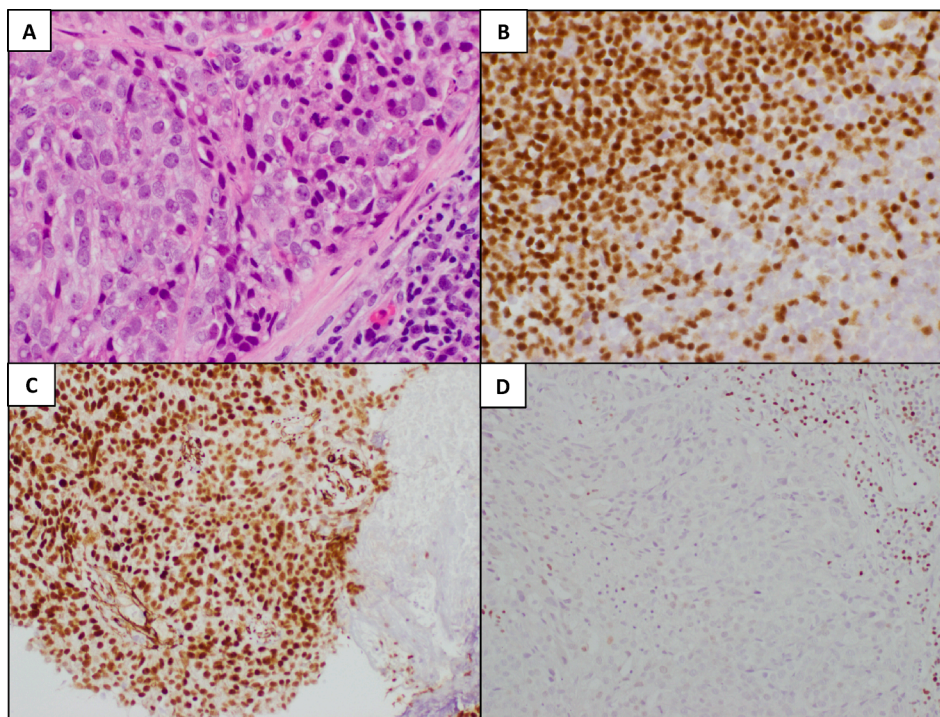
### 3. Discussion

Only approximately 100 cases of metastatic ovarian cancer to the breast have been reported in the literature. In two larger case series of metastatic lesions to the breast and axilla, the ovaries were the primary site of disease in 14–16% of cases (Abbas et al., 2013; DeLair et al., 2013). Ovarian cancer presenting as an oligometastasis to the breast without evidence of intra-abdominal disease is uncommon. Individual case reports of metastatic ovarian cancer to the breast demonstrate this most commonly occurs in the recurrent setting, up to 5 years following treatment (Mori et al., 2017; Patel et al., 2014; Skagias et al., 2008). Cases of metastatic ovarian cancer presenting as inflammatory breast cancer have also been reported (El Attrache et al., 2017; Klein et al., 2010). Even more rarely, enlarged intermammary and axillary lymph nodes identified on routine screening mammography are the initial presentation of metastatic ovarian cancer (Susini et al., 2010).

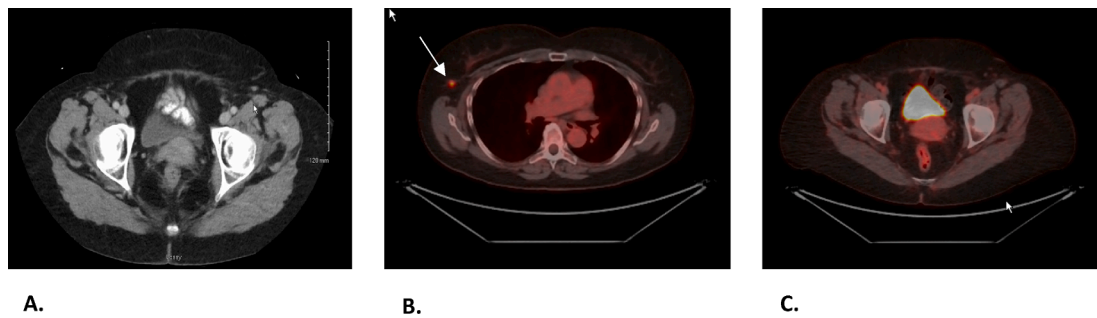
Oligometastases of ovarian carcinoma to the breast are incredibly rare and offer a diagnostic challenge. In our case, comprehensive pathologic and radiologic work-up were crucial to the appropriate diagnosis of an advanced stage high-grade serous carcinoma of the fallopian tube. Once diagnosed, standard of care surgical staging and adjuvant therapy were utilized to successfully treat this patient who remains on maintenance PARP therapy without evidence of disease 24 months following her surgical staging procedure.

### 4. Consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this



**Fig. 1.** Metastatic high-grade carcinoma from a right axillary lymph node consistent with a Mullerian Primary. A - High power view of HE slide showing large tumor cells with prominent nucleoli and frequent mitotic figures; B -Tumor nuclei show positive staining with IHC for PAX-8; C - Tumor nuclei show positive staining with IHC for WT-1; D -Tumor nuclei are negative with IHC for GATA-3 (positive staining in background lymphocytes).



**Fig. 2.** A. Computed tomography (CT) noting a normal appearing uterus and pelvis without evidence of gynecologic malignancy. B. Fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT noting FDG avid right axillary/breast mass. C. FDG PET/CT noting homogenous mild FDG uptake in the uterus without discrete focal abnormalities to suspect primary malignancy.

journal on request.

#### CRediT authorship contribution statement

**Janelle N. Sobacki:** Conceptualization, Data curation, Writing - original draft, Writing - review & editing. **Kathryn A. Dryer:** Conceptualization, Writing - original draft. **Aparna M. Mahajan:** Data curation, Writing - review & editing. **Ryan J. Spencer:** Conceptualization, Writing - review & editing.

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